The US Physical Activity Guidelines Advisory Committee Report—Introduction

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The history of the human race is reflected in and shaped by the overall levels of physical activity in which we engage. The benefits of an active lifestyle for human survival throughout most of human history are self-evident. However, as advances in food supply and distribution, transportation, labor, and other important areas of human endeavor grew, the drive for efficiency and convenience supplanted the need to move. The resulting population-level decreases in work-, household-, and transport-related physical activity and increases in sedentary behavior during work and leisure time have contributed significantly to the major noncommunicable diseases representing today's major killers in the United States and globally (1).

A decade ago, the US government published the nation's first formal guidelines related to physical activity and health (2). This groundbreaking policy document was based on an in-depth systematic review and summarization of the available literature conducted independently by the 2008 Physical Activity Guidelines Advisory Committee, which was assembled by the US Department of Health and Human Services (USDHHS) for this purpose (3). The Advisory Committee report confirmed a range of health outcomes for which regular moderate-to-vigorous intensity physical activity plays an important mitigating or beneficial role.

Ten years later, the substantial growth in the scope, depth, and breadth of the physical activity and health literature warranted a second formal US government-sponsored systematic review of this literature. In June of 2016, the 2018 Physical Activity Guidelines Advisory Committee was convened by the Office of Disease Prevention and Health Promotion of the USDHHS and charged with independently reviewing the scientific literature on physical activity and health. The Committee sought to build on and expand the findings described in the 2008 report (3). In addition, the Committee included two topics not addressed in the 2008 Report—sedentary behavior and interventions to promote regular physical activity. The current literature also allowed the Committee to examine several areas for which there was limited or no information in 2008. These areas included health effects in children younger than 6 yr; cognitive function across the lifespan; prevention of excessive weight gain; and the preventive health effects of physical activity among individuals with one or more existing chronic conditions.

The structured review process for the Physical Activity Guidelines for Americans 2018 Scientific Report was extensive. It involved 17 Committee members and additional scientific experts working on nine subcommittees and several working groups across a 2-yr period. All of these individuals volunteered their time throughout the scientific review and report development process. The analytic plan, inclusion and exclusion criteria, and specific search terms were developed jointly by the Committee and the staff of a company named ICF, a research firm under contract with the USDHHS. ICF performed all literature searches, following which the Committee reviewed the searches and selected the articles to be included in the Committee's deliberations. The Committee's final report was presented to the US Secretary of the Department of Health and Human Services in February of 2018. The report was used in the development of the 2018 Guidelines by USDHHS personnel independent of the Committee (4).

The articles in this special issue of MSSE are based on the research performed for the Committee's scientific report. The full methods for the rigorous evidence search and

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systematic review process are described in the 2018 Scientific Report document (5). For most topic areas, the evidence search process captured the relevant literature through 2016. Because of the size of the literature in many areas, most searches were limited to peer-reviewed, high-quality meta-analyses, systematic reviews, pooled analyses, and reports published in English. The articles contained in this issue represent the majority of topics described in the 2018 Scientific Report. In addition, for those topic areas for which the additional literature that became available between 2017 and March of 2018 was manageable in size, the original evidence searches and systematic review processes were applied so as to allow additional new literature to be included in the current articles in this issue.

The articles in this issue are organized into four sections. The first section focuses on new issues in evaluating dimensions of physical activity behavior affecting health (6–9). The *2018 Physical Activity Guidelines Advisory Committee Scientific Report* addressed the following timely questions related to our understanding of the types and amounts of physical activity that influence health outcomes: are there simpler metrics than self-reported estimates of time spent in aerobic moderate-to-vigorous physical activity—such as step counts—for estimating the volume of health-promoting behavior? What, if any, is the value of light-intensity physical activity as represented by step counts? Do short episodes of activity—bouts less than 10-min duration—contribute to accumulated beneficial physical activity? How does high-intensity interval training fit into health recommendations? What are the relationships among sedentary behavior, physical activity and health? For instance, does the effect of moderate-to-vigorous physical activity on all-cause mortality vary by amount of sedentary behavior?

The second section focuses on physical activity and selected health outcomes, which were chosen based on their significance for the US population and the increasing size and robustness of the evidence base in these areas (10–13). Among the systematic reviews included in this section are the effects of physical activity on the brain and cognition; the state of the evidence on physical activity in cancer prevention and survivorship; the role of physical activity for prevention of weight gain in adults; and the current evidence on the effects of moderate-to-vigorous physical activity on all-cause mortality, cardiovascular mortality and cardiovascular disease. While some of the reviews in this section represent an update and extension of the systematic evidence reviews informing the 2008 Physical Activity Guidelines (e.g., cancer, all-cause and cardiovascular mortality), others represent emerging areas not systematically reviewed in the *2008 Physical Activity Guidelines Scientific Report* (e.g., brain and cognition, prevention of weight gain).

The third section focuses on physical activity considerations and health outcomes for selected populations and health conditions (14–18). Included in this section are children under 6 yr of age—a population for which there was too little scientific information for it to be included in the *2008 Physical Activity Guidelines Advisory Committee Report* (3); women during pregnancy and the postpartum period; older adults, with a particular focus on physical function; the role of physical activity in the prevention, treatment, and control of hypertension; and physical activity-related effects on pain, function, quality of life, and disease progression in persons with osteoarthritis.

The final section presents highlights of the systematic review of the extensive evidence base in the physical activity promotion field—an area that was not included in the *2008 Physical Activity Guidelines Advisory Committee Report* (19). Using a social ecological perspective, the range of efficacious and promising interventions for physical activity promotion and sedentary behavior reduction are described.

Taken together, the extensive amount of evidence reviewed across the articles in this issue demonstrates the impact of a regularly active lifestyle in the prevention and/or control of a vast array of areas affecting overall health, function, and well-being. This knowledge, now including the evidence-supported methods for promoting regular physical activity, represents a "clarion call" to health professionals, policy makers, community organizations, and scientists alike to work together in applying this information in promoting a more active—and in turn healthier and more vital—population.

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Daily Step Counts for Measuring Physical Activity Exposure and Its Relation to Health

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ABSTRACT

KRAUS, W. E., K. F. JANZ, K. E. POWELL, W. W. CAMPBELL, J. M. JAKICIC, R. P. TROIANO, K. SPROW, A. TORRES, and K. L. PIERCY, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Daily Step Counts for Measuring Physical Activity Exposure and Its Relation to Health. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1206–1212, 2019. **Purpose:** A systematic primary literature review was conducted to evaluate the relationship of physical activity—as measured by daily step counts—with all-cause mortality, cardiovascular disease mortality, incident cardiovascular disease, and type 2 diabetes mellitus; to evaluate the shape of dose–response relationships; and to interpret findings in the context of development of the *Physical Activity Guidelines for Americans, Second Edition*. **Methods:** A primary literature search encompassing 2011 to March 2018 for existing literature reporting on these relationships was conducted. **Results:** Eleven pertinent articles were identified. Seven longitudinal studies examined the relationship between daily step counts and mortality, disease incidence, or risk. Two studies examined objectively measured steps per day and all-cause mortality; one was restricted to a relatively small elderly population. One study examined cardiovascular events, defined as cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke. The other four longitudinal studies addressed incident type 2 diabetes. All longitudinal studies reported an inverse relationship between steps per day and outcome risk. In one study, 531 cardiovascular events occurred during more than 45,000 person-years of follow-up. Before intervention, each increment of 2000 steps per day up to 10,000 steps was associated with a 10% lower cardiovascular event rate. Also, for every increase of 2000 steps per day over baseline, there was an 8% yearly reduction in cardiovascular event rate in individuals with impaired glucose tolerance. **Conclusions:** Daily step count is a readily accessible means by which to monitor and set physical activity goals. Recent evidence supports previously limited evidence of an inverse dose–response relationship of daily steps with important health outcomes, including all-cause mortality, cardiovascular events, and type 2 diabetes. However, more independent studies will be required before these observations can be translated into public health guidelines. **Key Words:** ALL-CAUSE MORTALITY, CARDIOVASCULAR DISEASE PREVENTION, DIABETES PREVENTION, PHYSICAL ACTIVITY GUIDELINES

Since the release of the *2008 Physical Activity Guidelines Advisory Committee Report* (1), several new methods have emerged by which physical activity and exercise can be measured, quantified, and prescribed to individuals seeking exercise-associated health benefits. The proliferation and popularity of newly developed wearable devices, particularly those worn on the wrist or finger containing accelerometers, have facilitated the monitoring and goal setting for steps per day (see article on *Promotion of Physical Activity* in this issue— (2,3)). There are also some new methods (e.g., machine learning algorithms); however, these do not apply to how steps are estimated from a device. It is now possible to assess the contribution of light activity to step counts per day and therefore to estimate total daily physical activity energy expenditure. Because step counts incorporate both light and moderate-to-vigorous

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physical activity and counting steps has been become a common method of assessing daily physical activity, the Physical Activity Guidelines Advisory Committee (PAGAC;the Committee) considered it important to better understand how the measurement of steps per day might fit into the assessment of daily or weekly physical activity exposures and its relationship to important health outcomes in the context of development of the *Physical Activity Guidelines for Americans, Second Edition*.

For the *2018 Physical Activity Guidelines Advisory Committee Scientific Report* (4), the Committee chose to address one overall question and two subquestions regarding daily step counts, summarized as follows: 1) what is the relationship between step counts per day and all-cause and cardiovascular disease (CVD) mortality, CVD events, and type 2 diabetes? 2) is there a dose–response relationship, and if there is, what is the shape of the relationship? and 3) does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?

METHODS

The overarching methods used to conduct systematic reviews informing the *2018 Physical Activity Guidelines Advisory Committee Scientific Report* are described in detail elsewhere (4,5). The searches were conducted using electronic databases (PubMed®, CINAHL, and Cochrane). An initial search conducted to identify systematic reviews, meta-analyses, and pooled analyses examining the relationship between step counts and various health outcomes did not identify sufficient literature to answer the research questions as determined by the Committee. Therefore, a complete *de novo* search of original research was conducted. The searches were conducted from inception until June 2017 for the 2018 PAGAC report; the search was expanded until March 2018 for this article. The searches were supplemented by asking Committee experts in the area to provide additional articles identified through their familiarity with the literature. Eligibility criteria were original research studies published in English; examining step counts as the physical activity exposure among adults; and health outcomes including all-cause or CVD mortality, incidence of CVD events, type 2 diabetes biomarkers, and incidence. Studies on individuals with existing CVD or high-performance athletes were excluded. The full-search strategy is available at https://health.gov/paguidelines/second-edition/report/supplementary_material/pdf/Exposure_Q4_Steps_Evidence_Portfolio.pdf.

Search terms included steps-specific terms combined with outcome-specific terms. Search term selection was difficult for this specific topic. The use of the terms "step," "stepping," and similar terms containing "step" is prevalent in the medical literature and would have resulted in an overwhelming number of irrelevant articles for review; therefore, based on some preliminary test searches, we restricted our search to articles containing the terms "step count," "steps per day," "daily steps," or "walking."

The titles and abstracts of the identified articles were independently screened by two reviewers. The full texts of relevant articles were reviewed to identify those meeting the inclusion criteria. Two professional librarians independently abstracted data and conducted a quality or risk of bias assessment using the USDA NEL Bias Assessment Tool (6). Discrepancies in article selection or data abstractions were resolved by discussion or by a third reviewer, if needed. The protocol for this review was registered with the PROSPERO database registration ID CRD42018092747.

RESULTS

Search Results and Study Characteristics

A literature tree summarizing the selection of literature for this review is contained in Supplemental Digital Content (see Figure, Supplemental Digital Content 1, Study Selection Literature Tree, http://links.lww.com/MSS/B539). The search strategy only yielded appropriate articles dating back to 2011. The committee reviewed evidence from 11 articles reporting on 7 original research studies (see Figure, Supplemental Digital Content 1, Study Selection Literature Tree, http://links.lww.com/MSS/B539). Of the 11 articles, 4 used a cross-sectional design (7–10), 6 used a prospective design (11–16), and 1 used a randomized controlled design where control and intervention groups were compared, as well as pooled, to examine steps per day with respect to insulin resistance (17). The NAVIGATOR study, a multicenter trial of 9306 individuals with impaired glucose recruited from 40 countries, provided four articles (three longitudinal and one cross-sectional). Since the four-cell two-by-two randomized design examining the effects of two pharmacologic agents on cardiovascular events and progression to type 2 diabetes was null for significant clinical drug effects (18,19), all four NAVIGATOR articles examined the relationship of daily steps to health outcomes after pooling drug intervention and control groups. Therefore, the NAVIGATOR study contributed one cross-sectional (10) and three longitudinal studies (12,15,16), depending on the analytic approach. Participants in all 11 reviewed studies were middle-age or older. Supporting the generalizability of conclusions, men and women, multiple races and ethnicities, a continuum of body sizes, and diverse geographical areas were represented.

Cross-sectional studies cannot control for bidirectional relationships—the outcome causing the exposure as well as the exposure causing the outcome. Because it is likely that individuals with undiagnosed disease may take fewer steps per day than healthy individuals, the reviewed cross-sectional studies were used only to understand usual step counts per day across sample populations and not for primary evidence for relationships.

The longitudinal studies reported health outcomes including all-cause mortality (11,14), a composite of CVD incidence, which included cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke (16), metabolic syndrome (12), and blood glucose concentrations—the latter two as biomarkers of progression toward diabetes mellitus (13,15,17).

The baseline number of steps per day varied across studies, but the median was approximately 5000 steps per day. In one report (17), 80% of the steps taken in a day were of light-intensity physical activity. Cohorts of older adults accumulated fewer daily steps than did middle-age adults. An Australian cohort of Tasmanian adults (mean age at baseline, 50 yr) (13) accumulated nearly twice as many daily steps at baseline as other samples—approximately 10,000, whereas most study baseline steps per day were approximately 5000.

Evidence on the Overall Relationship

Daily step counts and all-cause mortality. Dwyer et al. (11), observing 219 deaths in 2576 residents of Tasmania over 10 yr of follow-up, studied the relation of daily step counts and mortality. The mean age of the population was 58.8 yr. Mean daily step counts were 8781 ± 4538 for men and 8925 ± 8925 for women. Greater daily step counts were inversely and linearly associated with all-cause mortality: adjusted hazard ratio 0.94 (confidence interval, 0.90, 0.98) per 1000 daily steps. In a mean of 3.7 yr of follow-up in repeated assessment, changing from sedentary to 10,000 daily steps was associated with 46% less mortality risk over the ensuing decade when adjusted for baseline daily step counts and other mortality risk factors.

Yamamoto et al. (14) studied 419 physically independent, community-dwelling 71-yr-old elders in Japan. Over a mean follow-up period of 9.8 yr, they observed 18% mortality (76 individuals). Groups were characterized by quartiles of steps per day (<4503, 4503–6110, 6111–7971, >7971 daily steps). Probably because of to the low study numbers, hazard ratios for mortality over the period were only statistically significant when comparing the greatest quartile of daily steps group with the least quartile of daily steps (hazard ratio, 0.46; confidence interval, 0.22–0.96).

Daily step counts and cardiovascular events. Several longitudinal studies examined the relationship between daily step counts and disease incidence or risk. One study examined the relationship of daily step counts to cardiovascular events, defined as cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke in a population at risk for type 2 diabetes (16). This study included more than 45,000 person-years of follow-up in which 531 cardiovascular events occurred. Both baseline daily steps and change in daily steps were inversely associated with risk for cardiovascular events. Compared with the baseline step count, each 2000-daily-step increment up to 10,000 steps was associated with a 10% lower cardiovascular event rate. Also, for every 2000-daily-step increase, there was an 8% yearly reduction in cardiovascular event rate (Fig. 1). This report provides evidence of the benefit of increasing steps per day to reduce cardiovascular event incidence. The relationship can be modeled as a linear relationship (Fig. 2).

Dose–Response

Each of these dose–response relations seemed to be linear across the ranges of daily steps and change in daily steps. The linear relationships and effect sizes approximate those observed by Dwyer et al. (11) in a nondiseased population.

Daily step counts, metabolic syndrome, and type 2 diabetes incidence. Using NAVIGATOR data, Huffman et al. (12) observed a relationship of daily steps with metabolic syndrome score: for every incremental of 2000 greater baseline daily steps, there was a 29% reduction in the 6-yr metabolic syndrome score. Ponsonby et al. (13) estimated that for any average daily step count, additional 2000 steps were associated with a 25% reduction in incidence of dysglycemia over the succeeding 5 yr. Similar to the NAVIGATOR studies (12,16), the relationship between daily step count and health outcome seemed linear in Ponsonby et al. (13).

In a study published just after the search date for this article, Kraus et al. (21) reported on the relationship of baseline daily step counts and incident type 2 diabetes in the NAVIGATOR

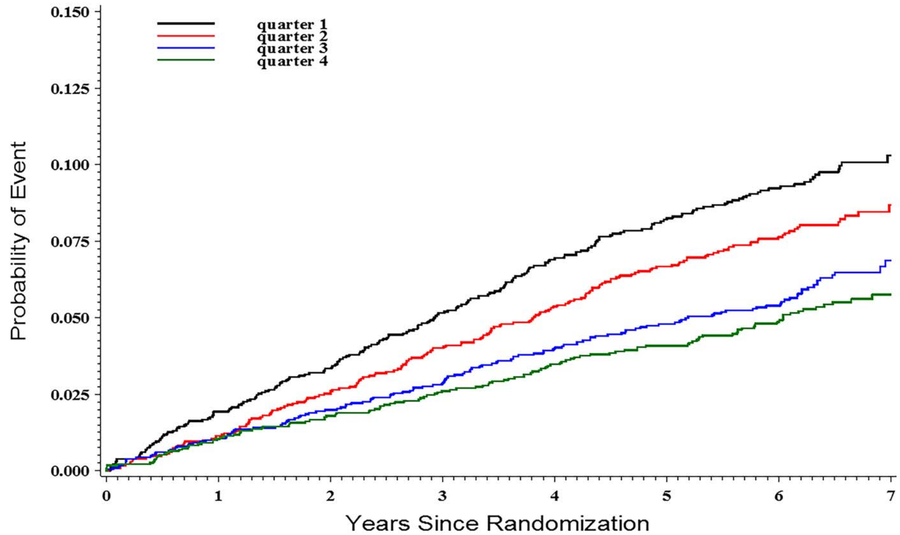

FIGURE 1—Kaplan–Meier survival curves for the death, myocardial infarction, and stroke composite outcome by quartiles of steps per day (16). Survival distributions were compared using log-rank test (P < 0.0001). Individuals at risk at each year of follow-up were as follows: 9306 (Y0), 8930 (Y1), 8659 (Y2), 8355 (Y3), 8008 (Y4), 7660 (Y5), 6244 (Y6), and 1505 (Y7). Quartiles of daily steps were as follows (means (range)): 2006 (859–2859), 4659 (4085–5216), 7093 (6382–7754), and 10569 (9447–12299). Figure developed from data in Refs. (16, 20).

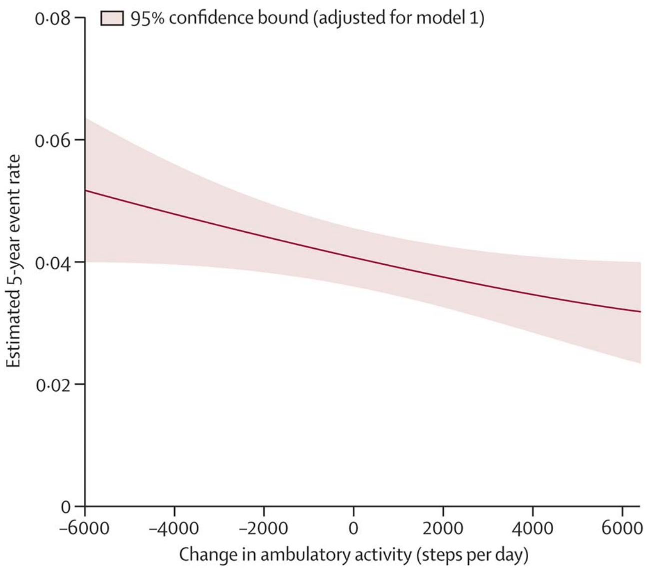

FIGURE 2—Association between change in steps per day and cardiovascular events in individuals with impaired glucose tolerance (16). The association between change in daily ambulatory activity and cardiovascular events in those with impaired glucose tolerance: cohort analysis of the NAVIGATOR trial. Reproduced with permission from Yates T, Haffner SM, Schulte PJ, et al. Association between change in daily ambulatory activity and cardiovascular events in people with impaired glucose tolerance (NAVIGATOR trial): a cohort analysis. *Lancet*. 2014;383(9922):1059–66. Copyright © 2014 Elsevier Ltd. All permission requests for this image should be made to the copyright holder.

study. Pedometer data were obtained on 7118 participants, and 35% developed diabetes. In an unadjusted analysis, each 2000-step increment in the average number of daily steps up to 10,000 was associated with 5.5% lower risk of progression toward diabetes (hazard ratio, 0.95; 95% confidence interval, 0.92–0.97), with a >6% relative risk reduction after adjustment. This relationship also seems linear.

Demographic factors and weight status. The risk reduction for incident cardiovascular events reported in NAVIGATOR was not affected by weight status, sex, age, geographical region, or level of baseline steps per day (16). Negative associations between daily steps and metabolic syndrome score reported in NAVIGATOR were independent of weight status (12). Ponsonby et al. (13) reported associations that were also independent of weight status when examining daily steps and dysglycemia. Thus, for studies evaluating effect modification by demographic or weight status, none were found. Despite these findings, the evidence on these factors was not sufficient for the Committee to draw a conclusion about any relationship.

DISCUSSION

The 2018 PAGAC report (4), strengthened by recently published research (11,14,21), supports using daily step count as a viable metric for assessing the association of physical activity with CVD events, type 2 diabetes mellitus onset, and all-cause mortality.

There is a striking contrast between the linear relationship of steps with mortality, CVD, and type 2 diabetes when compared with the rapidly negative curvilinear relationship of moderate-to-vigorous physical activity for these same health outcomes (see an article in this by Kraus et al. (20)). This contrast raises the question as to whether the apparent linear relationship of daily steps with the measured health outcomes is due to the contribution of light-to-moderate habitual daily activities. There are other possible explanations for this contrast between the shapes of the curves for step counts and moderate-to-vigorous physical activity on mortality. For example, measurement error, wear time, and other factors can affect the data gathered by physical activity trackers (3). That said, very low exposures—those with relatively few daily steps—contribute to reduced disease risk, albeit to a lower extent or with less impact than even a small amount of moderate-to-vigorous physical activity. Certainly, light activity contributes to reduction in disease risk (22). These issues will need to be sorted out with more research.

Finally, it remains unclear how many steps provide the optimal health benefit for the general population and for specific health benefits for those with existing disease. The traditional 10,000 step target already is being adopted by some countries (23) as a national public health goal. Is this the right number? Populations around the world are experiencing both increases in sedentary time (24) and decreases in habitual daily physical activity (25). Estimates that current moderate-to-vigorous physical activity guideline targets constitute 3000 to 6000 daily steps (26,27), when added to spontaneous "background activity" of 2500 to 5000 steps, might suggest that one should aim for more than 10,000 steps per day as a public health target to counteract the effects of increasing sedentary time (24,28).

A specific example might be helpful. A sedentary individual finds that she uses 5000 steps per day in normal daily activity. She measures the number of steps in a 10-min brisk (moderate-intensity) walk to be 1000 steps. Therefore, she finds she can meet the US physical activity guidelines for brisk walking of 150 $\mathrm{min \cdot wk^{-1}}$ by adding approximately 2000 brisk walking steps per day to her baseline activities of daily living—or aim for 7000 steps per day, of which 20 $\mathrm{min \cdot d^{-1}}$ is in the form of her daily walk. Pertinently, a 2011 position stand from the American College of Sports Medicine recommends that adults obtain at least 7000 steps per day (29).

However, there is at least one cautionary note. For some populations, 10,000 daily steps might have harmful effects. Limited data suggest a possible progression of osteoarthritis at step count per day greater than 10,000 (see also an article in this issue by Kraus (30)). However, as argued earlier, these step counts per day do not exceed those equivalent to the current physical activity guidelines.

Daily step counts are a readily accessible means by which to monitor and set physical activity goals (see an article on physical activity promotion in this issue (2)). In this review, we point to emerging evidence of a linear inverse dose–response relationship of daily steps with important health outcomes, including all-cause mortality, cardiovascular events, and type 2 diabetes. However, more evidence will be required before these observations can be translated into public health guidelines.

Public health impact. Steps are a basic unit of locomotion and as such provide an easy-to-understand metric of ambulation—an important component of physical activity. Measuring daily step counts can motivate diverse samples of individuals to increase physical activity levels (see the physical activity promotion article in this issue (2)). Increasingly, the self-assessment of steps can be accomplished through objective, readily obtainable technology with physical activity trackers, particularly those worn on the wrist or finger. Unlike the measure of moderate-to-vigorous physical activity in minutes per week or weekly energy expenditure (e.g., MET-minutes), the metric of *step counts per day* provides a comparable denominator to how dietary energy intake in most dietary guidelines is standardized—*per day*. As a result, daily steps counts might provide a useful tool for researchers and the public to address a variety of health and physical activity issues. In addition, steps can be at light-, moderate-, and vigorous-intensity levels, providing a range of exertion choice to promote walking at all ages and for all levels of fitness in the context of physical activity monitoring and prescription. For these reasons, measuring of daily step counts has the potential to significantly improve the translation of research findings into public health recommendations, policies, and programs.

Evidence statements. Because four of the originally reviewed studies were derived from one study—the NAVIGATOR trial, containing generally older individuals where the generalizability of the findings is suspicious—the Committee originally determined that there was insufficient evidence available to determine whether a relationship exists between steps per day and all-cause and CVD mortality. The grading of the accumulated evidence is available in Supplemental Digital Content 2 (see Table, Supplemental Digital Content 2, evidence statements for conclusions, http://links.lww.com/MSS/B540). However, in the interim, two new articles have come to our attention supporting the relationship between step counts per day and mortality (11,14). The Committee determined that there was limited evidence suggesting that daily step counts are associated with reduced incidence of CVD events and risk of type 2 diabetes. In the interim, one new article has been published supporting the relationship of step counts per day and type 2 diabetes incidence (21); however, this finding was from only one study—the NAVIGATOR trial—and more evidence may be required to change this strength of evidence determination. The Committee determined that there was limited evidence suggesting a dose–response relationship between the measure of steps per day and CVD events and type 2 diabetes risk. However, there are new dose–response data in this report demonstrating a linear relation of step counts per day with all-cause mortality, CVD events, and type 2 diabetes. Finally, the Committee determined that there was insufficient evidence available to determine whether the relationship between the measure of daily step counts and CVD events and type 2 diabetes risk is influenced by age, sex, race/ethnicity, socioeconomic status, or weight status. Thus, although the evidence base supporting the use of daily step counts as a metric for physical activity with respect to its effect on health outcomes is growing, and new evidence supports the previously determined limited evidence, still there is much work to be done before it can be fully adopted.

Needs for future research. Despite a developing literature on the relation of daily step counts and important health outcomes, there remains an insufficient literature to support using this metric as a public health metric for monitoring physical activity exposure. Given this, more research is needed in the following areas.

Advance the understanding of daily step counts and health in research addressing the equivalency of steps per day measured using various devices. Rationale: Peripheral activity monitoring devices include spring-suspended lever arm pedometers, accelerometers converting movement count or gravitational constant data to steps per day, three-dimensional accelerometer-based activity trackers, and smartphone–based mobile applications using internal accelerometers. However, with ever increased interest in personalized health monitoring and more options becoming increasingly available over time, without equivalency research, dose–response understandings will be specific to each device. In addition, newer devices, which more finely parse data, are likely to provide more sensitive metrics for capturing health-related walking behavior—for instance, intensity of steps per day, average stepping rate per day, and stepping cadence. Conversely, advances in daily step count research will inform decisions by product engineers and consumers as to what features are most useful in personalized health monitoring.

Develop more information on the metrics of daily step counts useful for understanding the relationship of steps per day with health outcomes, develop more understanding of the relation of pedometer-measured and accelerometer-measured steps per day, and explore the relationship between stepping cadence and health. This foundational information is critical to understanding how we might use legacy data—such as from National Health and Nutrition Examination Survey, where steps per day data were collected using accelerometers—to develop more detailed information on the relations of daily step counts to health outcomes. Such information will also permit subject-level pooling studies to increase sample sizes by harmonizing pedometer-collected data and accelerometer-collected data. Also requiring more work is the relationship of steps counts measured by pedometer to that of light activity/steps counts measured with accelerometers—not used in this report—and the association of step cadence (measured so far using only accelerometers) with health outcomes (31). Recently, the Consumer Trade Act provided guidelines for all new consumer monitors to meet for quantifying steps per day. This will be useful for getting better consistency between devices and future studies.

Conduct additional longitudinal research in the form of either prospective studies or randomized controlled trials to examine the dose–response relationship between daily step counts and health outcomes. This information is critical for setting target volumes of physical activity using steps per day as a metric for predicting the incidence of future disease outcomes. In this review, only one randomized controlled trial was identified, and it did not include multiple arms to examine the effects of various doses of steps per day on outcomes.

Include measurement methods in prospective and randomized controlled studies examining whether the rate of stepping and bout lengths of continuous stepping influence the relationship between steps per day and disease outcomes. The studies reviewed used simple physical activity trackers providing accumulated steps and could address neither patterns nor intensity of steps. Additional physical activity assessment methods allowing for these data should provide a better target for recommending physical activity volume and effective means for meeting steps per day targets.

Develop more understanding of the relation of individual characteristics—age, sex, infirmity, and disease status—serve as effect modifiers of the relationship of daily step counts and health status. The economy of movement varies by age; walking cadence varies by age; and disease states can influence cadence, energy efficiency, and the safe parameters associated with walking. Therefore, much more information ultimately will be needed before public health and clinical recommendations can be made about the relationships of daily step counts and human health.

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The results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate manipulation. The Committee's work was supported by the US Department of HHS. Committee members were reimbursed for travel and per diem expenses for the five public meetings. Committee members volunteered their time. The authors report no other potential conflicts of interest.

HHS staff provided general administrative support to the Committee and assured that the Committee adhered to the requirements for Federal Advisory Committees. HHS also contracted with ICF, a global consulting services company, to provide technical support for the literature searches conducted by the Committee. HHS and ICF staff collaborated with the Committee in the design and conduct of the searches by assisting with the development of the analytical frameworks, inclusion/exclusion criteria, and search terms for each primary question; using those parameters, ICF performed the literature searches.

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Association between Bout Duration of Physical Activity and Health: Systematic Review

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ABSTRACT

JAKICIC, J. M., W. E. KRAUS, K. E. POWELL, W. W. CAMPBELL, K. F. JANZ, R. P. TROIANO, K SPROW, A TORRES, and K. L. PIERCY, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Association between Bout Duration of Physical Activity and Health: Systematic Review. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1213–1219, 2019. **Purpose:** This study aimed to conduct a systematic literature review to determine whether physical activity episodes of <10 min in duration have health-related benefits or, alternatively, if the benefits are only realized when the duration of physical activity episodes is ≥10 min. **Methods:** The primary literature search was conducted for the *2018 Physical Activity Guidelines Advisory Committee Report* and encompassed literature through June 2017, with an additional literature search conducted to include literature published through March 2018 for inclusion in this systematic review. **Results:** The literature review identified 29 articles that were pertinent to the research question that used either cross-sectional, prospective cohort, or randomized designs. One prospective cohort study ($N = 4840$) reported similar associations between moderate to vigorous physical activity (MVPA) and all-cause mortality when examined as total MVPA, MVPA in bouts ≥5 min in duration, or MVPA in bouts ≥10 min in duration. Additional evidence was identified from cross-sectional and prospective studies to support that bouts of physical activity <10 min in duration are associated with a variety of health outcomes. Randomized studies only examined bouts of physical activity ≥10 min in duration. **Conclusions:** The current evidence, from cross-sectional and prospective cohort studies, supports that physical activity of any bout duration is associated with improved health outcomes, which includes all-cause mortality. This may suggest the need for a contemporary paradigm shift in public health recommendations for physical activity, which supports total MVPA as an important lifestyle behavior regardless of the bout duration. **Key Words:** PHYSICAL ACTIVITY, EXERCISE, BOUTS

Physical activity recommendations have traditionally focused on moderate to vigorous physical activity (MVPA), and this was interpreted as activity performed in a continuous manner. The historical perspective of these recommendations was summarized in the U.S. Surgeon General's Report on Physical Activity and Health (1). In the mid-1980s, Haskell suggested that some forms of physical activity may not result in an improvement in physical fitness, but the acute effects of repetition of physical activity may still result in improvements in health (2).

Emerging evidence began to support the concept that physical activity could have beneficial effects when accumulated in multiple shorter bouts performed across the day rather than solely relying on one longer continuous bout of physical activity. For example, one of the first empirical studies was conducted by Ebisu et al. (3), and results demonstrated that multiple bouts of

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running equivalent to 30 min·d^{-1} (e.g., 3 session of 10 min) over a period of 8 wk improved cardiorespiratory fitness and improved HDL in young men. Pate et al. (4) published the first contemporary recommendation, on behalf of the U.S. Centers for Disease Control and Prevention and the American College of Sports Medicine (ACSM), for MVPA to be "accumulated" to achieve a specific threshold of daily physical activity that, in turn, could result in health and fitness benefits. This recommendation stated that "intermittent bouts of physical activity, as short as 8 to 10 min, totaling 30 min or more on most days provided beneficial health and fitness effects." This resulted in a new paradigm, suggesting the accumulation of physical activity across bouts of short duration would provide health benefits. This paradigm was reinforced in the report by Haskell et al. (5) in the physical activity recommendations for adults from the ACSM and the American Heart Association. The 2008 Physical Activity Guidelines for Americans continued to support this recommendation for adults, stating that "aerobic activity should be performed in episodes of ≥10 min" (6).

The 2018 Physical Activity Guidelines Advisory Committee (PAGAC) recognized, however, that not all free-living physical activity is performed in a continuous manner, and most activity is likely performed in episodes typically <10 min in duration. An example of this may be the short and sporadic bouts of physical activity that can be performed in selective agricultural, goods producing, and manufacturing occupations. Church et al. (7) have demonstrated that these types of occupations have been decreasing in prevalence, which has contributed to a decrease in total energy expenditure, mostly due to a decrease in MVPA, which may also be associated with negative health consequences. Thus, the 2018 PAGAC examined the available scientific literature to determine whether physical activity episodes of <10 min in duration have health-related benefits or, alternatively, if the benefits are only realized when the duration of physical activity episodes is ≥10 min.

METHODS

The overarching methods used to conduct systematic reviews informing the 2018 PAGAC Scientific Report are described in detail elsewhere (8,9). The searches were conducted using electronic databases (PubMed®, CINAHL, and Cochrane). An initial search was conducted to identify systematic reviews, meta-analyses, and pooled analyses examining the relationship between bout duration and various health outcomes, and this search did not identify sufficient literature to answer the proposed research question. Therefore, a *de novo* search of original research was conducted until June 2017 for the 2018 PAGAC report. This *de novo* search of original research was expanded to include literature published through March 2018 for inclusion in this manuscript. Eligibility criteria were original research studies published in English, examining bouts as the physical activity exposure among adults, and health outcomes including weight status, body composition, blood lipids, blood pressure, metabolic syndrome, risk of type 2 diabetes, and risk of cardiovascular disease. The full search strategy is available at https://health.gov/paguidelines/second-edition/report/supplementary_material/pdf/Exposure_Q5_Bouts_Evidence_Portfolio.pdf. For the search conducted to include literature through March 2018, additional outcomes such as frailty and all-cause mortality were permissible as outcomes. Search terms included bout-specific terms combined with outcome-specific terms. However, the PAGAC Scientific Report (10) included a specific section related to high-intensity interval training that was separate from this review, and therefore the literature specific to high-intensity interval training is not included in this review.

The titles and abstracts of the identified articles were independently screened by two reviewers. The full-text of relevant articles were reviewed to identify those meeting the inclusion criteria. Two professional abstractors independently abstracted data and conducted a quality or risk of bias assessment using the USDA NEL Bias Assessment Tool (11). Discrepancies in article selection or data abstractions were resolved by discussion or by a third reviewer, if needed. The protocol for this review was registered with the PROSPERO database registration (CRD42018092854). The summary of the review process for the articles included in this systematic review is shown in Figure 1.

RESULTS

Search Results

For the 2018 PAGAC Report, 25 original manuscripts published from 1995 to 2017, based on 23 original studies, that examined the relationship between bouts of physical activity and different health outcomes were included as sources of evidence (10,12–35). Two pairs of these studies reported on different outcomes from the same studies (13–16). Of the 23 studies examined, 11 used a cross-sectional design (15–18,22–24,27,28,31,32,34), 2 used a prospective design (19,33), and 10 used a randomized design (10,12–14,20,21,25,26,29,30,35). The additional search conducted through March 2018 resulted in four additional original research studies, including one randomized control trial (36), one prospective cohort (37), and two cross-sectional studies (38,39). The analytical sample size across these various studies ranged from 22 to 6321. A summary of the articles, by study design and health outcomes examined, is shown in Table 1.

Measures of Physical Activity Bouts

Within the context of this review, the methods used to assess physical activity were quantified. The majority of studies (n = 18) used objective measure to assess physical activity that included accelerometers (15–19,22–27,31–34,37–39), with other studies using a heart rate monitor and pedometer (10), a combination of self-report and heart rate monitor (13,30,35), and direct supervision of physical activity sessions (20,36). The remaining four studies used self-report (exercise logs and diaries) to quantify physical activity (12,14,21,29).

Duration of Bouts

The duration of bouts varied across the studies that were examined. Cross-sectional (15–18,22–24,27,28,31,32,34,38,39)

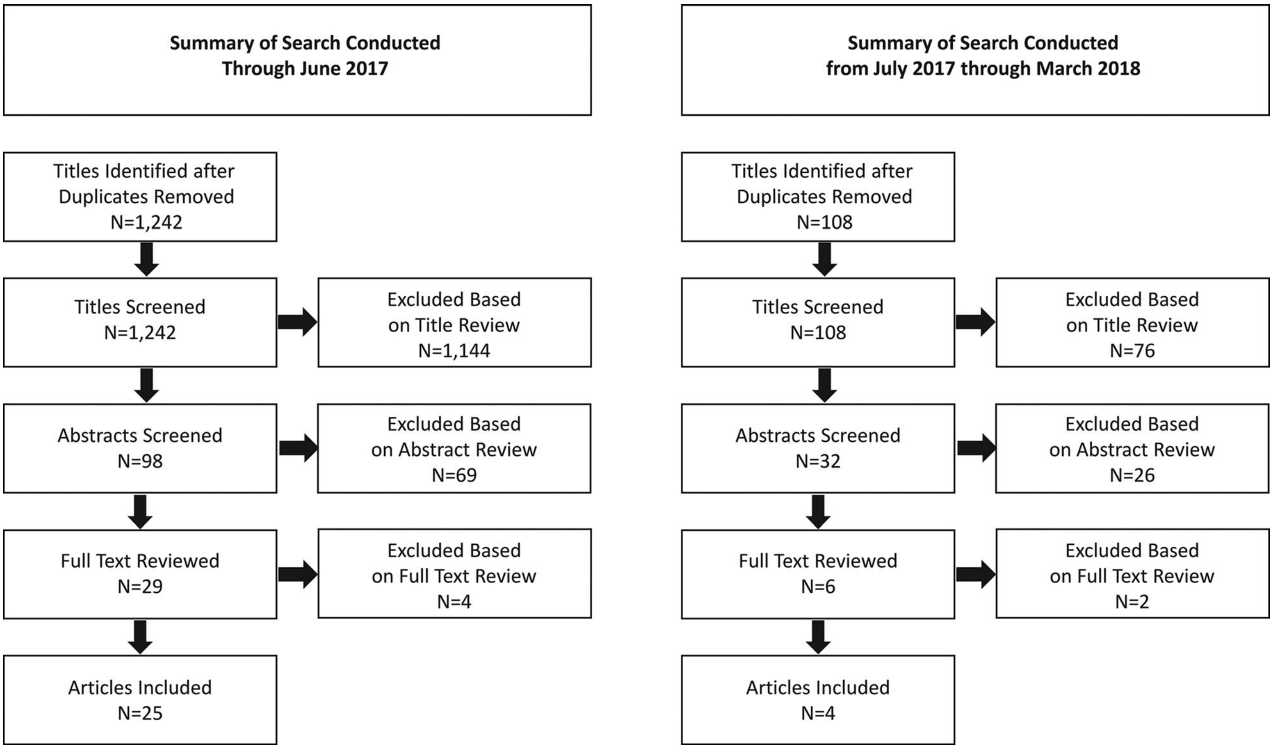

FIGURE 1—Summary of literature search.

and prospective studies (19,33,37) reported on bouts of physical activity that were <10 min, whereas randomized studies (10,12–14,20,21,25,26,29,30,35,36) reported only on bouts that were ≥10 min in duration.

Physical Activity Bout Duration and Health Outcomes: Randomized Studies

Twelve manuscripts reported on randomized designs, and these studies only included bouts of physical activity that were ≥10 min in duration (10,12–14,20,21,25,26,29,30,35,36). In these studies, intermittent bouts resulted in similar or enhanced effects when compared with continuous bouts of physical activity of longer duration for outcomes of weight and body composition (10,12–14,20,21,25,26,29,30,35,36), blood pressure (13,20,21,25,29,36), blood lipids (13,20,29,30,35), or glucose or insulin (13,20,36). These studies, however, do not provide information to evaluate bouts of physical activity of <10 min in duration.

Physical Activity Bout Duration and Health Outcomes: Cross-Sectional and Prospective Studies

The cross-sectional and prospective studies reported on a variety of health outcomes that included body weight or body composition (16,17,22,24,27,28,31,33,34), blood pressure (28,33,34), blood lipids (15,19,24,28,34), glucose or insulin (23,27,34), metabolic syndrome (18,27), inflammatory biomarkers (28,34), a composite of cardiovascular disease risk (32), frailty (38), or multimorbidity (39). In addition, a more recent study reported on all-cause mortality (37). A summary of these findings by health outcome are presented below and also presented in Table 2.

Body mass index, adiposity, and obesity. Some studies have examined whether physical activity accumulated in bouts <10 min in duration are associated with body mass index (BMI) or body fatness (16,17,22,24,27,28,31,33,34). In a cohort study by White et al. (33), physical activity accumulated in bouts of ≥10 min in duration was associated with lower incidence of obesity, whereas physical activity accumulated in <10 min was not associated with lower incidence of obesity.

TABLE 1. Summary of study designs that examined physical activity bout duration by health outcome.

Health Outcomes	Cross-Sectional Studies	Prospective Studies	Randomized Studies
Weight or body composition			
Incidence of obesity		1	
BMI	6		6
Body fatness	7		8
Blood pressure	2	1	6
Lipids			
Total cholesterol			2
LDL cholesterol	1		4
HDL cholesterol	4	1	5
Triglycerides	3		4
Glycemic control			
Fasting blood glucose	3		3
Fasting insulin	2		2
Oral glucose tolerance test			1
HbA1c	1		
Metabolic syndrome	2		
C-reactive protein	2		
Framingham cardiovascular disease risk score	1		
Frailty	1		
Multimorbidity	1		
All-cause mortality		1	

TABLE 2. Summary of the number of studies where health benefits are observed when physical activity in bouts ≥10 min is compare to bouts <10 min.

Health Outcomes	Number of Studies		
	Effect in Bouts <10 min and ≥10 min	Effect in Bouts <10 min but Not in Bouts ≥10 min	Effect in Bouts ≥10 min but Not in Bouts <10 min
Weight or body composition			
Incidence of obesity	0	0	1
BMI	3	1	2
Body fatness	5	1	1
Blood pressure	1	2	0
Lipids			
Total cholesterol	1	0	0
LDL cholesterol	1	0	0
HDL cholesterol	2	1	1
Triglycerides	2	1	0
Glycemic control			
Fasting blood glucose	1	1	0
Fasting insulin	1	1	0
Oral glucose tolerance test	0	0	0
HbA1c	0	1	0
Metabolic syndrome	1	1	0
C-reactive protein	1	1	0
Framingham cardiovascular disease risk score	1	0	0
Frailty	1	0	0
Multimorbidity	1	0	0
All-cause mortality	1	0	0

In cross-sectional studies examining BMI, two favored physical activity accumulated in bouts of ≥10 min compared with physical activity accumulated in bouts <10 min (28,34), one favored physical activity accumulated in <10 min bouts (17), and three did not report a difference between physical activity accumulated in bouts <10 min versus bouts of ≥10 min (22,24,27). Of the seven cross-sectional studies examining measures of body fatness, one favored physical activity accumulated in bouts of ≥10 min (31), one reported that the association between total volume of physical activity was more strongly associated with cardiometabolic health than physical activity accumulated in bouts of ≥10 min (34), and five studies showed no difference between physical activity accumulated in bouts of ≥10 min versus physical activity not accumulated in bouts of ≥10 min (16,17,24,27,28).

Resting blood pressure. Evidence for resting blood pressure is available from one cohort study and two cross-sectional studies. In the cohort study, White et al. (33) demonstrated that physical activity in bouts of either ≥10 min or <10 min in duration was associated with lower incidence of hypertension. Both cross-sectional studies showed that physical activity accumulated in bouts <10 min was associated with lower resting blood pressure (28,34).

Blood lipids. One cross-sectional study showed that physical activity accumulated in bouts of ≥10 min or <10 min in duration was associated with lower total cholesterol (28). In the one cross-sectional study examining LDL cholesterol, both physical activities accumulated in bouts of ≥10 min in duration and in <10 min in duration were inversely associated with LDL cholesterol (28).

For HDL cholesterol, the one prospective study, which was only 14 wk in duration, reported that physical activity accumulated in bouts of ≥10 min in duration predicted change in HDL, whereas when the threshold was reduced to include bouts of at least 5 min, this pattern of physical activity was not predictive of change in HDL (19). Of the four cross-sectional studies reviewed, two showed similar associations between HDL and physical activity accumulated in bouts of ≥10 min and <10 min (24,28), one showed that physical activity accumulated in bouts as short as at least 32 s was associated with higher HDL (15), and one showed that physical activity accumulated in bouts <10 min was more strongly associated with HDL than physical activity accumulated in ≥10 min (34).

Three cross-sectional studies examined the association between physical activity and triglycerides. In two of these studies, there were similar associations of triglycerides with physical activity accumulated in bouts of ≥10 min in duration or in bouts <10 min (24,28). One of these studies showed that physical activity accumulated in bouts of <10 min was more strongly associated with lower triglycerides than physical activity accumulated in bouts of ≥10 min (34).

Fasting glucose, fasting insulin, and HbA1c. Three cross-sectional studies examined the association between physical activity and fasting glucose (15,28,34), two with fasting insulin (27,34) and one with HbA1c (23). For fasting glucose, in one study, bouts of physical activity at least 3 min in duration were associated with lower fasting glucose (15); in one study, there was no difference in the association between fasting glucose and MVPA accumulated in bouts of <10 min versus bouts of ≥10 min (28); and in one study, physical activity accumulated in bouts of <10 min was more strongly associated with lower fasting glucose when compared with physical activity accumulated in bouts of ≥10 min (34). For fasting insulin, one study showed no difference in the association when comparing MVPA accumulated in <10 min and ≥10 min (27), and one study showed that physical activity accumulated in bouts of <10 min was more strongly associated fasting insulin when compared with physical activity accumulated in bouts of ≥10 min in duration (34). In the one study examining HbA1c, physical activity accumulated in bouts <10 min predicted lower HbA1c, whereas physical activity accumulated in bouts of ≥10 min in duration was not predictive of lower HbA1c (23).

Metabolic syndrome. Two cross-sectional studies were reviewed that reported on the association between physical activity and metabolic syndrome (18,27). In one study, MVPA accumulated in bouts of 1 to 9 min, 4 to 9 min, or 7 to 9 min in duration predicted lower odds of having metabolic syndrome (40) independent of MVPA accumulated in bouts of ≥10 min (18). In an additional study, odds of having metabolic syndrome (41) did not differ when comparing physical activity accumulated in bouts of <10 min versus ≥10 min (27).

C-reactive protein. Two cross-sectional studies examined the association between physical activity and C-reactive protein (28,34). One study showed no difference in the association between C-reactive protein and physical activity accumulated in bouts of <10 min in duration and bouts of ≥10 min (28). One study showed that physical activity accumulated in bouts of <10 min was more strongly associated with lower C-reactive protein when compared with physical activity accumulated in bouts of ≥10 min (34).

Cardiovascular risk score. One cross-sectional study examined the association between physical activity and the Framingham Cardiovascular Disease Risk Score (32). In this study, physical activity accumulated in bouts of 1 to 5 min, 6 to 10 min, 11 to 15 min, or 20 to 120 min in duration and during total waking time was negatively associated with Framingham Cardiovascular Disease Risk Score.

Frailty. Aging is typically associated with an increase in frailty. Kehler et al. (38) examined data from the National Health and Nutrition Examination Survey to determine whether MVPA performed in bouts of ≥10 min had a differential influence on the frailty index compared with MVPA performed in bouts of <10 min in adults 50 yr of age or older. In this study, meeting 50%–99% of 150 min·wk^{-1} of MVPA was associated with a reduced frailty index, with similar findings observed regardless of whether MVPA was performed in bouts of ≥10 min or in bouts of <10 min.

Multimorbidity. Multimorbidity is the presence of two or more chronic conditions such as coronary artery disease, stroke, congestive heart failure, hypertension, diabetes, obesity, and others. Loprinzi examined data from the National Health and Nutrition Examination Survey to determine whether physical activity bouts that were ≥10 min in duration or were <10 min in duration were associated with multimorbidity (39). In this analysis, both bouts of MVPA ≥10 min in duration and those <10 min in duration were independently associated with the presence of multimorbidity. These findings provide support for promoting MVPA regardless of bout duration.

All-cause mortality. A recent finding is based on the data that are now available regarding physical activity bout duration and all-cause mortality. In a prospective examination of data from the National Health and Nutrition Examination Survey, Saint-Maurice et al. (37) examined the influence of MVPA of different bout durations (total MVPA regardless of bout duration, MVPA in bouts of at least 5 min, MVPA in bouts of ≥10 min) on all-cause mortality over an average follow-up period of 6.6 yr. In this analysis, the hazard ratios were similar across quartiles of MVPA regardless of bout duration, suggesting that the reduction in mortality risk is independent of how MVPA is accumulated.

DISCUSSION

Summary and public health effect. The 2008 Physical Activity Guidelines for Americans recommended that physical activity be accumulated in bouts of ≥10 min in duration to influence a variety of health-related outcomes (6). This was consistent with an initial paradigm shift that occurred approximately 20 yr early when it was suggested by the Centers for Disease Control and Prevention and the ACSM that physical activity accumulated in bouts of ≥10 min in duration can improve a variety of health-related outcomes (4). This current review of the evidence continues to support that physical activity accumulated in bouts of ≥10 min in duration can improve a variety of health-related outcomes. However, additional evidence, from cross-sectional and prospective cohort studies, suggests that physical activity accumulated in bouts that are <10 min is also associated with favorable health-related outcomes, including all-cause mortality. This is of public health importance because it suggests that engaging in physical activity, regardless of length of the bout, may have health-enhancing effects. This is of particular importance for individuals who are unwilling or unable to engage in physical activity bouts that are ≥10 min in duration. It also adds support to public health initiatives advocating physical activity behaviors that are unlikely to require 10 min, such as climbing a flight of stairs or parking the car in a more distant part of the parking lot. This may suggest the need for a contemporary paradigm shift in public health recommendations for physical activity, which encourages engagement in MVPA as an important lifestyle behavior to enhance health, with potential benefits realized regardless of the bout duration.

Needs for future research. The evidence from this review supports that physical activity accumulated in bouts <10 min in duration are associated with enhanced health across a variety of outcomes. There is, however, a need for additional research related to the accumulation of physical activity and its association with health. These additional research needs are described below.

Conduct longitudinal research, in the form of either prospective studies or randomized controlled trials, to examine whether physical activity accumulated in bouts of <10 min in duration enhances health outcomes. The majority of studies reviewed that support the health benefits of physical activity accumulated in bouts of <10 min in duration used a cross-sectional design, with none of the randomized studies reporting on the effects of physical activity accumulated in bouts of <10 min. Having this knowledge will inform potential cause and effect rather than simply associations.

Conduct research to compare bouts of physical activity of <10 min to ≥10 min, which also equates for volume and total energy expenditure between these physical activity patterns, to examine the effects on health outcomes. The randomized studies that were specifically designed to equate for volume of physical activity or energy expenditure only examined the effects of physical activity performed in bouts ≥10 min. Thus, appropriately designed studies are needed to confirm the findings of the cross-sectional and prospective observational studies regarding the health benefits of physical activity accumulated in bouts ≤10 min in duration.

Conduct large research trials with ample sample sizes to allow for stratum-specific analyses to determine whether the influence of physical activity accumulated in bouts of varying length on health outcomes varies by age, sex, race/ethnicity, socioeconomic status, initial weight status, or other demographic characteristics. On the basis of the studies reviewed, there is limited evidence available on whether the influence of physical activity varies when the exposure to physical activity is consistent across individuals with different demographic characteristics. Having this information will inform public health recommendations about whether physical activity exposure of varying bout length to enhance health needs to vary by age, sex, race/ethnicity, socioeconomic status, weight status, and other demographic characteristics and may allow for more precise individual-level physical activity recommendations.

Include measurement methods in prospective and randomized studies that will allow for the evaluation of whether physical activity performed in a variety of bout lengths has differential effects on health outcomes. On the basis of this review, randomized studies were not identified that reported on physical activity accumulated in bouts that were <10 min in duration, and only three prospective studies were identified that reported on physical activity accumulated in bouts that were <10 min. This may be a result of the methods used to assess physical activity in randomized and prospective studies, suggesting the need to include physical activity assessment methods that allow for these data to be available for analysis. For example, the use of objective monitoring that allows for physical activity data to be collected in 1-min epochs may be preferable to self-reported methods when examining the duration of activity bouts that are associated with improved health.

Conduct meta-analyses and systematic reviews of longitudinal prospective studies to evaluate the effect of physical activity accumulated in varying bout durations on health outcomes. High-quality systematic reviews and meta-analyses were not identified in the literature that has summarized the evidence related to physical activity accumulated in varying bout durations and health outcomes. With specific regard to a summary of the evidence related to physical activity bout durations of <10 min, this may have been influenced by the current lack of sufficient prospective and randomized studies. This resulted in the need to examine the limited number of individual studies that addressed this topic. As additional prospective and randomized studies are conducted on this topic, meta-analyses and systematic reviews should be conducted that will provide information on the consistency and magnitude of the overall effect size of the relationships observed across the original studies.

Conduct appropriately designed studies to examine the mechanistic pathways by which physical activity bouts of varying durations, particularly bouts of physical activity <10 min in duration, may influence various health-related outcomes. This review of the literature was not designed to identify and summarize the scientific literature related to the potential mechanistic pathways of how physical activity bouts of varying durations, particularly <10 min in duration, may influence health-related measures. This may be important for understanding the biology of physical activity, provide a foundation for future research, and may influence for whom physical activity bouts <10 min in duration may be most effective.

Conduct studies to examine the effects of light-intensity physical activity accumulated in bouts of <10 min and ≥10 min on health outcomes. The studies reviewed primarily focused on MVPA within the context of physical activity bout duration. Thus, these studies do not contribute to an understanding of how light-intensity physical activity may influence health outcomes, and whether bout duration of light-intensity physical activity may influence this potential relationship. This is a potentially important public health question given the potential for lifestyle, household, and occupational activity to be performed in bouts <10 min and at a light intensity.

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The results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate manipulation. The committee's work was supported by the HHS. Committee members were reimbursed for travel and per diem expenses for the five public meetings; committee members volunteered their time.

HHS staff provided general administrative support to the committee and assured that the committee adhered to the requirements for Federal Advisory Committees. HHS also contracted with ICF, a global consulting services company, to provide technical support for the literature searches conducted by the committee. HHS and ICF staff collaborated with the committee in the design and conduct of the searches by assisting with the development of the analytical frameworks, inclusion/exclusion criteria, and search terms for each primary question; using those parameters, ICF performed the literature searches.

This article is being published as an official pronouncement of the ACSM. This pronouncement was reviewed for the ACSM by members-at-large and the Pronouncements Committee. Care has been taken to confirm the accuracy of the information present and to describe generally accepted practices. However, the authors, editors, and publisher are not responsible for errors or omissions or for any consequences from application of the information in this publication and make no warranty, expressed or implied, with respect to the currency, completeness, or accuracy of the contents of the publication. The application of this information in a particular situation remains the professional responsibility of the practitioner; the clinical treatments described and recommended may not be considered absolute and universal recommendations.

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AMERICAN COLLEGE of SPORTS MEDICINE
PRONOUNCEMENT

High-Intensity Interval Training for Cardiometabolic Disease Prevention

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ABSTRACT

CAMPBELL, W. W., W. E. KRAUS, K. E. POWELL, W. L. HASKELL, K. F. JANZ, J. M. JAKICIC, R. P. TROIANO, K. SPROW, A. TORRES, K. L. PIERCY, and D. B. BARTLETT, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. High-Intensity Interval Training for Cardiometabolic Disease Prevention. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1220–1226, 2019. **Purpose:** The 2018 Physical Activity Guidelines Advisory Committee systematically searched existing literature reviews to assess the relationship between high-intensity interval training (HIIT) and reduction in cardiometabolic disease risk. **Methods:** Duplicate independent screenings of 260 articles identified from PubMed®, Cochrane Library, and CINAHL databases yielded suitable data from one systematic review and two meta-analyses. Search terms included a combination of "high intensity" "physical activity/exercise" and "interval training" and outcome-specific terms. The quality of the included reviews was assessed using a tailored version of the AMSTARExBP report on quality. Exposure Subcommittee members graded scientific evidence strength based on a five-criteria rubric and assigned one of four grades: strong, moderate, limited, or not assignable. **Results:** Moderate evidence indicates that HIIT can improve insulin sensitivity, blood pressure, and body composition in adults with group mean ages ranging from ~20 to ~77 yr. These HIIT-induced improvements in cardiometabolic disease risk factors are comparable with those resulting from moderate-intensity continuous training, and they are more likely to occur in adults at higher risk of cardiovascular disease and diabetes than in healthy adults. Moderate evidence also indicates that adults with overweight or obesity classification are more responsive than adults with normal weight to HIIT-related improvements in insulin sensitivity, blood pressure, and body composition. Insufficient evidence was available to determine whether a dose–response relationship exists between the quantity of HIIT performed and several risk factors for cardiovascular disease and diabetes, or whether the effects of HIIT on cardiometabolic disease risk factors are influenced by age, sex, race/ethnicity, or socioeconomic status. **Conclusions:** HIIT by adults, especially those with overweight and obesity classification, can improve insulin sensitivity, blood pressure, and body composition, comparable with those resulting from moderate-intensity continuous training. **Key Words:** INSULIN SENSITIVITY, BLOOD PRESSURE, BODY COMPOSITION, OVERWEIGHT, OBESITY, PHYSICAL ACTIVITY

Traditionally, physical activity guidelines have focused on moderate-intensity continuous training (MICT) and, more recently, have included resistance training. However, since the 2008 Physical Activity Guidelines Advisory Committee (PAGAC) Scientific Report (1), there has arisen a resurgence in interest and use of interval training. High-intensity interval training (HIIT) is one type of interval training that has progressively increased in popularity among physically active individuals and has garnered scientific research. The media also presents HIIT as an alternative means by which individuals can achieve health benefits similar to those of MICT. Some have suggested that it might be an

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attractive long-term strategy by which to achieve the health benefits of regular physical activity because HIIT consumes less overall time per week. The 2018 PAGAC considered it prudent to examine scientific evidence regarding the use of HIIT for cardiometabolic health benefits relative to MICT (2).

To this end, the 2018 PAGAC addressed the following: 1) the nature of the relationship between HIIT and reduction in cardiometabolic disease risk, 2) whether a dose–response relationship exists, and 3) what is the shape of any dose–response relationship. Further, the committee was interested in any evidence pointing to whether such relationships might vary by age, sex, race/ethnicity, socioeconomic status, or weight status. Finally, the committee explored the relative rates of adverse events of HIIT programs compared with MICT programs.

Importantly, the term "HIIT" is not precisely defined, and multiple descriptions, exercise protocols, and exertion-related criteria are used among the original studies included in each of the systematic reviews and meta-analyses of literature vetted by the 2018 PAGAC. We retained the descriptions of HIIT stated in each of the manuscripts included in this umbrella systematic review, in part, to avoid misrepresenting or redefining the published research. For this review, we use the following description of HIIT: "episodic short bouts of high intensity exercise separated by short periods of recovery at a lower intensity." On the basis of the literature vetted for this review, the "high intensity" in these bouts may be as low as about 65% of $\dot{V}O_2$ maximum or 60% of $\dot{V}O_2$ reserve (which may be inferior to moderate continuous exercise) and as high as maximal effort, such as during sprinting. The results and conclusions presented in this review encompass a relatively wide range of HIIT exercise intensities, which should be taken into consideration when evaluating these results and using them when developing exercise programs.

METHODS

An umbrella systematic review was conducted to identify existing reviews assessing the association of HIIT to reduction in cardiometabolic disease risk. This review was one of the systematic reviews conducted for the 2018 PAGAC, and the full methods are described elsewhere (3). Briefly, systematic searches were conducted in three electronic databases, including PubMed®, CINAHL, and Cochrane from database inception until May 7, 2017. Subsequently, the search was updated through March 30, 2018, for this manuscript. Search terms included a combination of "high intensity" "physical activity/exercise" and "interval training" and outcome-specific terms.

Final studies were selected using the following inclusion criteria: systematic reviews, meta-analyses, and pooled analyses published in English, including adult populations, assessing PA performed as HIIT, and examining cardiometabolic risk outcomes—all-cause and cardiovascular disease (CVD) mortality, CVD incidence, type 2 diabetes, and CVD risk factors, including blood pressure, blood lipids, and body composition. Reviews exclusively examining patients with existing CVD or athletes were excluded. All articles were independently screened by two reviewers. Data abstraction was conducted by two independent abstractors who also assessed the quality of the included reviews using a tailored version of the AMSTARExBP (3,4). The protocol for this review was registered with the PROSPERO database, registration ID CRD42018093024.

The full literature search strategy is available at https://health.gov/paguidelines/second-edition/report/supplementary_material/pdf/Exposure_Q6_HIIT_Evidence_Portfolio.pdf. Information available here includes the following: 1) evidence summaries of the three articles reviewed (website Table 2); 2) AMSTARExBP-based article review quality assessment chart (website Table 3); 3) systematic review analytical framework (website appendix A); 4) *a priori* strategies for the PubMed®, CINAHL, and Cochrane searches (website appendix B); 5) literature tree detailing the identification, screening, eligibility, and inclusion of vetted articles (website appendix C); 6) search inclusion/exclusion criteria (website appendix D); and 7) the rationale for excluding articles at abstract or full-text triage (website appendix E).

RESULTS

Description of the Evidence

An initial search for systematic reviews, meta-analyses, pooled analyses, and reports identified sufficient literature to adequately address the research questions. The initial search conducted for the 2018 PAGAC resulted in 274 articles identified among the three electronic databases. After removing duplicates, 260 articles were title screened, of which 48 were abstract screened, 11 articles were full-text screened, and three articles used for data extraction. Two additional meta-analyses provide pertinent data from 77 new articles identified in the updated search. Figure 1 outlines the search results from both the original and updated search.

Overview

A total of three existing reviews were included: one systematic review (5) and two meta-analyses (6,7). The reviews were published from 2012 to 2017. The systematic review by Kessler et al. (5) included 24 studies and covered a time frame from database inception to 2011. The meta-analyses included larger numbers of studies. Batacan et al. (6) included 65 studies, and Jelleyman et al. (7) included 50 studies. They covered time frames from 1970 to 2015 and from 1946 to 2015, respectively.

Exposures

The three existing reviews examined physical activity performed as HIIT. There are no universally accepted lengths for the high-intensity period, the recovery period, or the ratio of the two; no universally accepted number of cycles for any HIIT session or the entire duration of the training bout; and no universally accepted relative intensity at which the high-intensity component should be performed. Batacan et al. (6) defined HIIT as "activities with intermittent bouts of activity that were performed at maximal effort, ≥85% $\dot{V}O_2$ max,

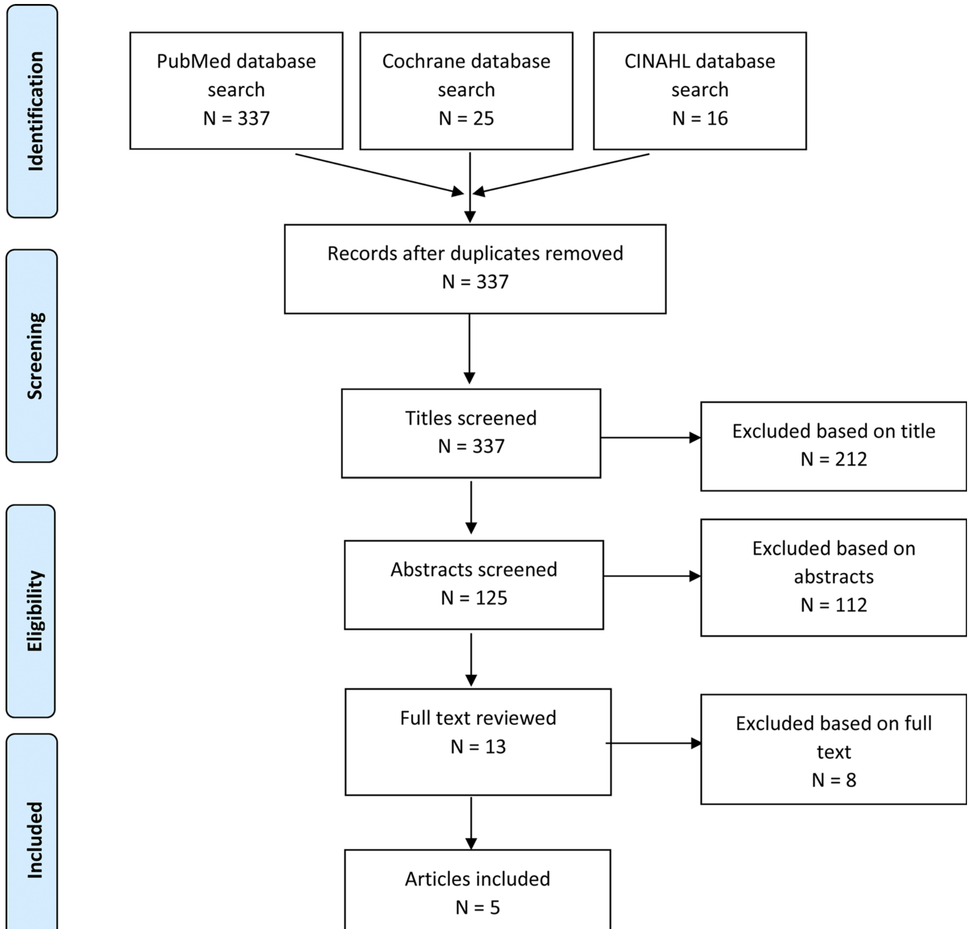

FIGURE 1—Literature Tree Study Selection HIIT Umbrella Review. Includes both original 2018 PAGAC search and updated search results.

≥85% heart rate (HR) reserve or the relative intensity of at least 90% HR max." Jelleyman et al. (7) applied the following description of HIIT to their literature search: "at least two bouts of vigorous or higher intensity exercise interspersed with periods of lower intensity exercise or complete rest." Kessler et al. (5) defined HIIT as "vigorous exercise performed at a high intensity for a brief period interposed with recovery intervals at low-to-moderate intensity or complete rest."

Outcomes

The outcomes initially identified for systematic review included all-cause and CVD mortality, CVD and type 2 diabetes incidences, cardiorespiratory fitness, and cardiometabolic disease risk factors. After extensive discussion, the 2018 PAGAC Exposure Subcommittee members made a conscious decision to exclude cardiovascular fitness as a primary outcome of interest, choosing to focus effort and resources on reviews of literature that included multiple risk factors of CVD and diabetes. The decision to not focus on cardiorespiratory fitness as an outcome of interesting was PAGAC-wide for the entire report; this decision was multifactorial and is addressed in the report. While the Exposure Subcommittee did not vet systematic reviews and meta-analyses of literature exclusively focused on fitness-related parameters, pertinent cardiovascular fitness outcomes contained in the articles reviewed are described in the Review of the Evidence (see below). The 2018 PAGAC Exposure Subcommittee's assessment and evaluation specifically focused on outcomes related to cardiometabolic disease risk factors (blood pressure, fasting blood lipids and lipoproteins, fasting blood glucose and insulin, and body mass index [BMI]) due to a lack of information regarding mortality and cardiometabolic morbidities.

Review of the Evidence

The 2018 Advisory Committee based its conclusions on evidence published before May 2017, specifically from the three existing systematic reviews and/or meta-analyses (5–7). Participants were men and women predominantly with group mean ages ranging from ~20 to ~77 yr. The exposure was predominantly supervised physical activity performed as HIIT using a variety of exercise modalities (mainly stationary cycling or treadmill running/walking, and much less often swimming, track running, or stair climbing).

Evidence on the Overall Relationship

Results from these systematic reviews and/or meta-analyses of clinical intervention studies consistently support that HIIT can improve cardiorespiratory fitness (increase $\dot{V}O_2$ max) in adults with varied body weight and health status (5–7). HIIT-induced improvements in insulin sensitivity (5,7), blood pressure (5,6), and body composition (5–7) more consistently occur in adults with overweight or obesity classification, with or without high risk of CVD and diabetes—especially if these individuals train for 12 or more weeks. These HIIT-induced improvements in cardiometabolic disease risk are comparable with those achievable with MICT (7).

Healthy adults who have normal weight and lower risk of cardiometabolic disease do not typically show improvements in insulin sensitivity, blood pressure, and body composition with HIIT. Blood lipids and lipoproteins apparently are not influenced by HIIT (6). Batacan et al. (6) reported findings based on 65 individual studies involving 2164 participants (including 936 individuals who performed HIIT). Participants were predominantly 18- to 35-yr-old men and women (sex distribution not reported), and group mean ages ranged from ~20 to ~77 yr. This meta-analysis included randomized controlled trials (RCT) and non-RCT and comparative studies in groups of individuals without (46 of 65 studies) or with (19 of 65 studies) a diagnosed, current medical condition.

Batacan et al. (6) defined HIIT "as activities with intermittent bouts of activity that were performed at maximal effort, greater than or equal to 85% $\dot{V}O_{2max}$, greater than or equal to 85% heart rate reserve or the relative intensity of at least 90% maximum heart rate." The modes of exercise included treadmill running, cycling, and swimming. The 65 studies were categorized with respect to exercise training intervention duration and participant BMI classification. Among groups of participants with normal weight (BMI = 18.5–24.9 kg·m^{-2}), short-term (<12 wk) and long-term (≥12 wk) HIIT interventions increased $\dot{V}O_{2max}$ but did not significantly or consistently influence clinical indexes of cardiometabolic disease risk (systolic and diastolic blood pressures; total cholesterol, HDL cholesterol, LDL cholesterol, or triglycerides, fasting glucose, or insulin). Among groups of participants classified with overweight (BMI = 25–29.9 kg·m^{-2}) or obesity (BMI ≥ 30 kg·m^{-2}) status, short-term and long-term HIIT significantly and consistently increased $\dot{V}O_{2max}$ and decreased diastolic blood pressure and waist circumference. Long-term HIIT also decreased resting heart rate, systolic blood pressure, and body fat percentage among groups with overweight or obesity. Batacan et al. (6) presented these results as effect sizes (ES) of the standardized mean differences, not as changes over time in typical units of measure.

Jelleyman et al. (7) conducted a meta-analysis of 50 studies involving 2033 participants (sex distribution not reported)—including 1383 individuals who performed HIIT—to assess the effect of HIIT interventions compared with continuous training or control conditions on indexes of blood glucose control and insulin resistance. Both studies with a control group (n = 36, 72%) and studies without a control group (n = 14, 28%) were included, but the results from studies without a control group were only used for within-group analyses. HIIT was defined as "at least two bouts of vigorous or higher intensity exercise interspersed with periods of lower intensity exercise or complete rest" (7). Participant ages ranged from 18 to 68 yr, and the HIIT interventions ranged from 2 to 16 wk. Among 20 studies (40%) providing data, mean exercise session attendance was 90% ± 10%. Subgroup analyses were performed after stratifying participants by disease status based on a wide range of health characteristics: the categories were labeled healthy (well trained, recreationally active, or sedentary but otherwise healthy), weight status (overweight or obese), metabolic syndrome (metabolic syndrome or type 2 diabetes), or with another chronic disease.

Compared with baseline, $\dot{V}O_{2max}$ increased after HIIT by 0.30 L·min^{-1} (95% confidence interval [CI] = 0.25–0.35, P < 0.001). The increase in $\dot{V}O_{2max}$ was greater for HIIT than for nonexercising control conditions (weighted mean difference [WMD] = 0.28 L·min^{-1}, 95% CI = 0.12–0.44, P = 0.001) and attenuated but still significant compared with continuous training (WMD = 0.16 L·min^{-1}, 95% CI = 0.07–0.25, P = 0.001). HIIT reduced body weight, compared with baseline, by 0.7 kg (95% CI = −1.19 to −0.25, P = 0.002). Compared with nonexercise control, the HIIT-induced weight loss was 1.3 kg (95% CI = −1.90 to −0.68, P < 0.001). HIIT-induced weight loss was not different than weight loss from continuous training. HIIT decreased fasting glucose, compared with baseline, by 0.13 mmol·L^{-1} (95% CI = −0.19 to −0.07, P < 0.001). This response over time was not statistically different compared with nonexercise control or continuous training. In subgroup analysis, for the groups of individuals with metabolic syndrome or type 2 diabetes, fasting glucose was reduced by HIIT compared with nonexercise control by 0.92 mmol·L^{-1} (95% CI = −1.22 to −0.63, P < 0.001). HIIT decreased fasting insulin from baseline by 0.93 μU·L^{-1} (95% CI = −1.39 to −0.48, P < 0.001); however, this response was not statistically different from the nonexercise control. HIIT decreased insulin resistance compared with baseline (change in Homeostasis Model Assessment of Insulin Resistance score = −0.33; 95% CI = −0.47 to −0.18, P < 0.001). Reduction in insulin resistance (results from multiple insulin resistance models combined) was greater for HIIT versus nonexercise control (−0.49; 95% CI = −0.87 to −0.12) and HIIT versus continuous training (−0.35; 95% CI = −0.68 to −0.02). Among all 13 studies reporting data within metabolic syndrome or type 2 diabetes groups, HIIT did not change HbA1c. In subgroup analyses, HIIT reduced HbA1c by 0.25% (95% CI = −0.27 to −0.23, P < 0.001). Among all studies, the HbA1c response over time (no change) was not statistically different among HIIT, continuous training, and control groups. Subgroup analyses based on health (physical activity) status or other chronic diseases were either not significant or inconclusive; this was due, in part, to limited data being available.

Kessler et al. (5) conducted a quasisystematic, qualitative review of 24 RCT with 661 participants (sex distribution not reported) assessing the effects of HIIT interventions on changes in cardiometabolic disease risk factors. Of the

24 trials, 14 included MICT comparison group, which included a wide range of exercise programs, typically performed at 50% to 75% of $\dot{V}O_2$ max for 45 to 60 min per session. The other 14 studies included a nonexercise control group. Participants had various weight statuses (normal weight, overweight, or obese) and health groups (17 studies), CVD (5 studies), metabolic syndrome (1 study), and type 2 diabetes (1 study). Intervention durations ranged from 2 wk to 6 months. HIIT was categorized into two subtypes: aerobic interval training (19 studies) and sprint interval training (SIT; 5 studies). For the subcommittee's assessment, because of the low number of SIT studies included in the Kessler et al. (5) review (n = 3 for glucose metabolism, n = 1 for lipids and lipoproteins, and n = 1 for blood pressures), results from only aerobic interval training studies were considered for strength of evidence grading purposes. Aerobic interval training increased $\dot{V}O_{2max}$ (14 of 14 studies), increased insulin sensitivity (4 of 4 studies), and decreased blood pressure in participants not ingesting antihypertensive medication (5 of 5 studies with intervention periods ≥12 wk). Other indexes of cardiometabolic disease risk were not influenced by aerobic interval training, including fasting glucose, total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides. Results for body weight, BMI, body fat percent, and waist circumference were mixed; improvements more consistently were observed for aerobic interval training interventions of 12 wk or longer in participants with overweight or obesity classification. Collectively, these aerobic interval training responses were comparable with continuous moderate-intensity exercise, except $\dot{V}O_{2max}$, which was greater for aerobic interval training versus continuous moderate-intensity exercise.

The updated search identified two additional pertinent HIIT-related reviews. Keating et al. (8) conducted a systematic review with a meta-analysis of 31 studies directly comparing MICT to HIIT (n = 17) or SIT (n = 14) on body adiposity. For their analyses, HIIT and SIT studies were combined. Of the 28 studies assessed by Keating et al. (8), 19 were not included in the three reviews vetted by the 2018 PAGAC members. A combined 837 individuals (402 women, 402 men, and 33 not reported) were assessed, with ages ranging from 10 to 65 yr, including two studies with a combined 59 adolescent boys and girls. Keating et al. (8) included results from these two studies with adolescents in their overall analyses. Most studies recruited participants classified as untrained (n = 12) or overweight/obese (n = 13), with three recruiting children/adolescents. HIIT was defined as studies using 85%–95% peak heart rate (PHR) or 80%–100% peak work rate for the high intensities, with a minimum duration of 4 wk. Of the 31 studies, 17 (55%) included a HIIT intervention, whereas 14 (45%) included a SIT intervention. Interventions ranged from 4 to 16 wk, with 12 wk the most common (42% of studies). Compared with baseline, both HIIT/SIT and MICT reduced body fat (%) and fat mass (kg). HIIT/SIT reduced body fat (%), on average, by −1.26% (95% CI = −1.80 to −0.72) and fat mass by −1.38 kg (95% CI = −1.99 to −0.77), whereas MICT reduced by −1.48% (95% CI = −1.89 to −1.06) and − 0.91 kg (95% CI = −1.45 to −0.37). When all studies were pooled, no differences between HIIT/SIT and MICT were observed for body fat percent (WMD = 0.15%, 95% CI = −0.57 to 0.88, P = 0.370) or fat mass (WMD = −0.73 kg, 95% CI = −1.81 to 0.35, P = 0.619) changes. Among a subset of studies with protocols having the workload or energy expenditure of each HIIT/SIT session less than the workload or energy expenditure of each MICT session, there was a trend for MICT to have greater reductions in total body fat percentage (P = 0.09). Among a subset of studies with the workload and/or energy expenditure per exercise session matched between exercise types, no differences in body fat percentage were observed between HIIT/SIT and MICT (P = 0.40). Further, no differences were observed for fat mass when workload or energy expenditure was lower for HIIT/SIT versus MICT (P = 0.56) or matched between exercise types (P = 0.38). Collectively, HIIT/SIT was comparable, but not superior, when directly compared with MICT for body fat reductions.

Maillard et al. (9) conducted a meta-analysis of 39 studies, which included 617 individuals (321 women and 296 men) who had completed a HIIT intervention assessing total (n = 35), abdominal (n = 20), and visceral fat mass (n = 14). Of the 39 studies assessed by Maillard et al. (9), 30 were not included in the three reviews vetted by the 2018 PAGAC members. Assessed individuals were adults with a mean age ranging from 20 ± 0.8 to 69 ± 2.8 yr. Except for four studies, which totaled 44 participants, all participants were classified as overweight or obese (mean BMI range, 25.4 ± 2.4 to 38.2 ± 7.9 kg·m^{-2}). Participants were generally healthy, although some studies included patients with type 2 diabetes (n = 6), polycystic ovary syndrome (n = 2), menopausal (n = 2), nonalcoholic fatty liver disease (n = 1), metabolic syndrome (n = 5), and rheumatic disease (n = 1). HIIT was defined as studies using 85%–95% PHR or 80%–100% peak work rate for the high intensities, with a minimum duration of 4 wk. Studies using a SIT protocol were excluded. Interventions ranged from 4 wk to 6 months, with the majority being 12 wk and used either cycling (n = 26) or running (n = 13). Whole-body adiposity was assessed primarily by dual-energy x-ray absorptiometry, with bioelectrical impedance, plethysmography, and skinfolds also used. For the assessment of visceral and abdominal adiposity, computed tomography, magnetic resonance imaging, and dual-energy x-ray absorptiometry were used. HIIT reduced total fat (ES = −0.2, 95% CI = −0.31 to −0.07, I^2 = 0.0%, P = 0.003), abdominal fat mass (ES = −0.19, 95% CI = −0.32 to −0.05, I^2 = 0.0%, P = 0.007), and visceral fat mass (ES = −0.24, 95% CI = −0.44 to −0.04, I^2 = 0.0%, P = 0.018). Stratified analyses suggested that running (P = 0.003) was better than cycling (P = 0.137) for reductions in total fat mass, cycling (P = 0.004) was better than running (P = 0.773) at reducing abdominal fat mass, and only running (P = 0.042) reduced visceral fat mass. The greatest effect on total fat mass was observed with higher-intensity (>90% PHR) protocols (P = 0.017), whereas lower-intensity (<90% PHR) protocols elicited the best effects on abdominal (P = 0.029) and visceral fat mass (P = 0.021). Although HIIT was only successful at reducing total (P = 0.001), abdominal (P = 0.008), and visceral (P = 0.016) fat mass in adults classified as overweight or obese, there were only two studies assessing normal weight in each subgroup.

Dose–Response

Among the three review articles systematically reviewed for the 2018 PAGAC report (5–7), results were not presented from RCT designed to assess dose–response relationships of duration of HIIT to responses in cardiometabolic disease risk factors. Using meta-regression techniques, in the Batacan et al. (6) report, change in $\dot{V}O_{2max}$ was predicted by longer HIIT intervention duration (β coefficient = 0.77, 95% CI = 0.35–1.18) and BMI (β coefficient = 0.84, 95% CI = 0.29–1.38), but not by total time performing HIIT (min) (β coefficient = 0.0002, 95% CI = −0.0017 to 0.0021) among groups of participants with overweight or obesity classification. Intervention duration, total time performing HIIT, and BMI did not predict the improvements observed in systolic blood pressure and diastolic blood pressure among groups with overweight or obesity. Other cardiometabolic risk factors were not assessed due to heterogeneity of responses. Regarding indexes of glucose control, Jelleyman et al. (7) (also using meta-regression techniques) reported that HIIT characteristics, interval intensity, and weekly high-intensity exercise did not predict the improvements over time in insulin resistance, fasting glucose, fasting insulin, or HbA1c.

Evidence on Specific Factors

Age, sex, race/ethnicity, and socioeconomic status. Information on the age, race/ethnicity, and socioeconomic status of participants was limited, inconsistently presented, and not statistically assessed. As a result, no conclusions about these relationships were possible. Only one of the new articles, Maillard et al. (9), assessed differences between sexes for HIIT and found no differences in changes for total, abdominal, or visceral fat mass.

Weight status. Weight status influenced the effect of HIIT on several risk factors of cardiometabolic disease, with groups of adults classified as overweight or obese, but not normal weight, reducing blood pressure and body fat (6) and improving insulin sensitivity (5,7).

Evidence on Participant Safety

Participant safety is central to using HIIT as a tool to reduce the risk of cardiometabolic disease among adults, especially those who have overweight or obesity, with cardiometabolic disease risk factors, diagnosed CVD or type 2 diabetes, or other chronic diseases. Although the committee did not address participant safety among adults performing HIIT, the issue is highly relevant with respect to using HIIT for health promotion. Jelleyman et al. (7) documented adverse events reported in the 50 studies included in their meta-analysis. Among the 19 total adverse events reported from the 17 studies (34% of the total studies), including this type of information, 18 adverse events were attributable to musculoskeletal injuries incurred with exercise; 14 of 18 occurred with HIIT. None of the reported injuries was a serious adverse event or necessitated the participant to discontinue the intervention or drop out of the study. Perhaps consistent with the very low incidence of adverse events, mean participant dropout rate was 10% ± 10% among the 36 (72%) studies documenting attrition. The health and disease characteristics of the participants experiencing an adverse event were not presented or discussed.

For additional details on this body of evidence, visit https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

CONCLUSIONS

HIIT can improve insulin sensitivity, blood pressure, and body composition in adults. These HIIT-induced improvements in cardiometabolic disease risk factors are comparable with those resulting from continuous, moderate-intensity aerobic exercise, and they are more likely to occur in adults at greater risk of CVD and diabetes, compared with healthy adults. The committee considered the strength of evidence to be moderate for this issue. Insufficient evidence was available to determine whether a dose–response relationship exists between HIIT quantity and several risk factors for CVD and diabetes. Insufficient evidence was available to determine whether the effects of HIIT on cardiometabolic risk factors are influenced by age, sex, race/ethnicity, or socioeconomic status. There was moderate evidence indicating that adult weight status influences the effectiveness of HIIT to reduce cardiometabolic disease risk. Adults with overweight or obesity classification are more responsive than adults with normal weight to HIIT's effects on improving insulin sensitivity, blood pressure, and body composition. The committee considered the strength of evidence to be moderate for this conclusion.

Summary, public health impact, and needs for future research. HIIT can improve insulin sensitivity, blood pressure, and body composition in adults. Such improvements in cardiometabolic disease risk factors are comparable with those resulting from continuous, moderate-intensity aerobic exercise and are more likely to occur in adults with overweight and obesity classification.

Research is required in several areas to improve the scientific foundations for long-term effectiveness and safety of HIIT. Specifically, the committee recommends the following:

RCT of at least 6 months should be undertaken to assess the adherence to and the effects of HIIT when compared with other types of physical activity programs on physiological, morphological, and cardiometabolic health outcomes. Such studies should address issues of dose–response and be of at least 6 months in duration. These RCT should include diverse groups of adults, including those with overweight or obesity classification and at high risk of CVD or type 2 diabetes. They should systematically assess adverse events, including musculoskeletal injuries, attributable to HIIT, compared with other types of exercise training, among adults with a wide variety of health and disease characteristics.

Rationale: Most HIIT intervention periods are less than 12 wk, which are likely insufficient time to assess the magnitude and sustainability of clinically important changes in some physiological, morphological, and cardiometabolic health outcomes. The willingness and the ability of individuals to adhere to HIIT currently are not well known. Further research, complementary to the scoping review of the psychological responses to interval exercise that supports "the viability of interval exercise as an alternative to continuous exercise" (10), is warranted. Prescriptively designing these studies to include participants who have overweight or obesity classification and are at high risk of CVD or type 2 diabetes will inform health promotion practitioners and policy leaders on the utility of recommending HIIT for health among a large proportion of the U.S. adult population. At present, the evaluation of the safety of HIIT among adults with varied health and disease characteristics is compromised by the limited availability of relevant data; this is due, in part, to the low proportion of studies reporting adverse events.

Continued research is warranted to assess, compare, and systematically review the effects of specific types of HIIT-related programs on cardiometabolic disease risk factors.

Rationale: There is no universally accepted definition for HIIT. The relatively broad range of HIIT-related exercise protocols and intensities used among studies currently limit physical performance, fitness, and allied health professionals' abilities to optimally plan HIIT programs for health. Yet HIIT protocols generally fall into three categories based on exercise intensities: SIT (intensities greater than $\dot{V}O_2$ maximum), near-maximum interval training (90%–100% of maximum heart rate, oxygen uptake, or other pertinent parameter), and vigorous aerobic intensity (60%–89% $\dot{V}O_2$ reserve or 64%–90% $\dot{V}O_2$ maximum).

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The results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate manipulation. The committee's work was supported by the U.S. Department of Health and Human Services (HHS). Committee members were reimbursed for travel and per diem expenses for the five public meetings; committee members volunteered their time.

HHS staff provided general administrative support to the committee and assured that the committee adhered to the requirements for Federal Advisory Committees. HHS also contracted with ICF, a global consulting services company, to provide technical support for the literature searches conducted by the committee. HHS and ICF staff collaborated with the committee in the design and conduct of the searches by assisting with the development of the analytical frameworks, inclusion/exclusion criteria, and search terms for each primary question; using those parameters, ICF performed the literature searches.

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PRONOUNCEMENT

Sedentary Behavior and Health: Update from the 2018 Physical Activity Guidelines Advisory Committee

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ABSTRACT

KATZMARZYK, P. T., K. E. POWELL, J. M. JAKICIC, R. P. TROIANO, K. PIERCY, and B. TENNANT, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Sedentary Behavior and Health: Update from the 2018 Physical Activity Guidelines Advisory Committee. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1227–1241, 2019. **Purpose:** To provide an overview of relationships between sedentary behavior and mortality as well as incidence of several noncommunicable diseases and weight status reported in the *2018 Physical Activity Guidelines Advisory Committee Scientific Report* (2018 PAGAC Scientific Report), and to update the evidence from recent studies. **Methods:** Evidence related to sedentary behavior in the 2018 PAGAC Scientific Report was summarized, and a systematic review was undertaken to identify original studies published between January 2017 and February 2018. **Results:** The 2018 PAGAC Scientific Report concluded there was strong evidence that high amounts of sedentary behavior increase the risk for all-cause and cardiovascular disease (CVD) mortality and incident CVD and type 2 diabetes. Moderate evidence indicated sedentary behavior is associated with incident endometrial, colon and lung cancer. Limited evidence suggested sedentary behavior is associated with cancer mortality and weight status. There was strong evidence that the hazardous effects of sedentary behavior are more pronounced in physically inactive people. Evidence was insufficient to determine if bout length or breaks in sedentary behavior are associated with health outcomes. The new literature search yielded seven new studies for all-cause mortality, two for CVD mortality, two for cancer mortality, four for type 2 diabetes, one for weight status, and four for cancer; no new studies were identified for CVD incidence. Results of the new studies supported the conclusions in the 2018 PAGAC Scientific Report. **Conclusions:** The results of the updated search add further evidence on the association between sedentary behavior and health. Further research is required on how sex, age, race/ethnicity, socioeconomic status, and weight status may modify associations between sedentary behavior and health outcomes. **Key Words:** SITTING, MORTALITY, COHORT, CHRONIC DISEASE

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Sedentary behavior is defined as any waking behavior characterized by the expenditure of 1.5 METs or less of energy while in a sitting, reclining, or lying posture (1). On an absolute scale of intensity, sedentary behaviors are at the low end of the physical activity continuum; however, the postural component of the definition suggests that sedentary pursuits may represent distinct behaviors (2). In most research studies, sedentary behavior has been operationalized as daily sitting time, television (TV) viewing, or low counts on an activity monitor such as an accelerometer. Representative data collected by accelerometry in the U.S. National Health and Nutrition Examination Survey (NHANES) indicate that children and adults spend approximately 55% of their awake time ($7.7\ h \cdot d^{-1}$) being sedentary (3).

Given that much of the evidence on the negative health effects associated with sedentary behavior has been published in the last decade, the *2008 Physical Activity Guidelines for Americans* (4) did not specifically address this (5). However, given the emerging evidence on the negative health effects and the potential public health burden associated with high levels of sedentary behavior in the population, the 2018 Physical Activity Guidelines Advisory Committee decided to review this evidence. In this regard, the interplay between sedentary behavior and physical activity on health were of particular interest.

The purpose of this article is to summarize the evidence on the associations between sedentary behavior and health reviewed by the 2018 Physical Activity Guidelines Advisory Committee and to perform a systematic review of prospective observational studies published subsequently. In addition to updating the systematic review, we identified articles from the searches to provide evidence on the relationship between changes in sedentary behavior and risk of mortality.

2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE SCIENTIFIC REPORT

The 2018 Physical Activity Guidelines Advisory Committee (Committee) recently conducted a systematic review of the associations between sedentary behavior and several health outcomes (6). The Committee reviewed the scientific evidence on the associations between sedentary behavior and all-cause mortality, cardiovascular disease (CVD) mortality, cancer mortality, type 2 diabetes, weight status, CVD and cancer published through early 2017. Table 1 provides the specific questions addressed by the Committee in its report.

A single literature search was conducted to answer questions 1, 2, and 3. Subsets of the resulting body of evidence were used to answer each question and relevant subquestions. The search strategy included 1) a search for systematic reviews and meta-analyses, 2) reviewing the original research articles contained in the systematic reviews and meta-analyses, and 3) a search for more recent original research studies published after the systematic reviews and meta-analyses. The systematic literature search to address question 4 included 1) a search for systematic reviews and meta-analyses, and 2) a search of more recent original research studies published after the systematic reviews and meta-analyses. The evidence used to address question 5 was obtained from the articles retrieved for question 1.

TABLE 1. Questions related to sedentary behavior and health outcomes in adults addressed by the 2018 physical activity guidelines advisory committee.

Major questions
1. What is the relationship between sedentary behavior and all-cause mortality?
2. What is the relationship between sedentary behavior and cardiovascular disease mortality?
3. What is the relationship between sedentary behavior and cancer mortality?
4. What is the relationship between sedentary behavior and 1) type 2 diabetes, 2) weight status, 3) cardiovascular disease, and 4) cancer?
5. Does the effect of moderate-to-vigorous physical activity on all-cause mortality vary by amount of sedentary behavior?

Subquestions[a]
a) Is there a dose–response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Is the relationship independent of amounts of light, moderate, or vigorous physical activity?
d) Is there any evidence that bouts or breaks in sedentary behavior are important factors?

[a]The subquestions apply to questions 1 through 4 only.

Evidence to inform each question was graded as strong, moderate, limited, or not assignable based on several grading criteria, including applicability, generalizability, risk of bias/study limitations, quantity and consistency of results across studies, and magnitude and precision of effect (See Supplemental Table 1; Supplemental Digital Content 1, 2018 Physical Activity Guidelines Advisory Committee Grading Criteria, http://links.lww.com/MSS/B535) (6). Table 2 provides a summary of the relationships and level of evidence for each health outcome. Overall, there was strong evidence for a direct association between greater amounts of sedentary behavior and higher risk of mortality from all-causes and CVD, and for higher risk of incident type 2 diabetes and CVD. There was moderate evidence for an association between sedentary behavior and incident cancer (especially colon, endometrial, and lung cancer), and limited evidence for associations between sedentary behavior and cancer mortality and weight status. For a detailed summary of the meta-analyses, systematic reviews and original research studies that contributed evidence to these conclusions, please see the PAGAC Scientific Report (Part F, Chapter 2) (6). Specific details on each study can be found in the online supplemental tables (https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx).

There was strong evidence for the existence of dose–response associations between sedentary behavior and all-cause mortality, CVD mortality, and incident CVD, whereas there was limited evidence for cancer mortality, incident type 2 diabetes, weight status, and incident cancer. Two meta-analyses were identified that reported significant dose–response relationships between daily sitting (7), TV viewing (8), and all-cause mortality. Further, 24 of the 29 original studies that tested for the existence of a dose–response relationship with all-cause mortality reported statistical significance (6). Two meta-analyses tested for dose–response associations between sedentary behavior and incident CVD (9,10). Grontved and Hu (9) reported a significant linear dose–response association between TV viewing and

SPECIAL COMMUNICATIONS

TABLE 2. Summary of relationships between sedentary behavior and health outcomes in the *2018 Physical Activity Guidelines Advisory Committee Scientific Report.*

Health Outcomes	Level of Evidence for Association	Level of Evidence for Dose–Response	Level of Evidence for Variation in Association by Physical Activity	Level of Evidence for Variation in Association by Age, Sex, Race/Ethnicity, Socioeconomic Status or Weight Status?	Level of Evidence for Bouts or Breaks as Important Factors
All-cause mortality	Strong	Strong	Strong	Limited for no interaction by age, sex, race/ethnicity and weight status; not assignable for socioeconomic status	Not assignable
CVD mortality	Strong	Strong	Moderate	Limited for no interaction by age, sex, race/ethnicity and weight status; not assignable for socioeconomic status	Not assignable
Cancer mortality	Limited	Limited	Not assignable	Not assignable	Not assignable
Incident type 2 diabetes	Strong	Limited	Not assignable	Not assignable	Not assignable
Weight status	Limited	Limited	Not assignable	Not assignable	Not assignable
Incident CVD	Strong	Strong	Not assignable	Not assignable	Not assignable
Incident cancer	Moderate	Limited	Not assignable	Not assignable	Not assignable

incident fatal and nonfatal CVD, whereas Pandey et al. (10) reported a significant, curvilinear dose–response association with increasing slope of risk for CVD at increasingly higher levels of sedentary time.

An important subquestion addressed by the Committee was the degree to which the observed relationships vary by age, sex, race/ethnicity, socioeconomic status, or weight status. For all outcomes, there was insufficient evidence to inform the degree to which socioeconomic status was an effect modifier in the associations with sedentary behavior. For both all-cause and CVD mortality, studies generally reported no significant effect modification by age, sex, race/ethnicity, or weight status. Further age-, sex-, race/ethnicity-, and weight status-stratified analyses were generally significant in all strata examined. Evidence was insufficient for other outcomes to determine whether the relationships varied by these factors.

A bout of sedentary behavior can be operationalized as a period of uninterrupted sedentary time, whereas a break in sedentary behavior can be operationalized as a nonsedentary bout in between two sedentary bouts (1). The degree to which bouts and breaks in sedentary behavior are related to health outcomes is of interest. Unfortunately, there was insufficient evidence to inform the degree to which bouts and breaks in sedentary behavior are important factors in the major questions addressed by the Committee. At the time of the review, only one study was identified that included bouts of sedentary time as a variable in a latent class analysis prediction of all-cause mortality (11); no studies could be identified for the other health outcomes. This resulted in a grade of "not assignable" for this subquestion.

The degree to which sedentary behavior and physical activity interact in their associations with health outcomes was of particular interest to the Committee. There was evidence that the associations between sedentary behavior and all-cause mortality (strong) and CVD mortality (moderate) vary by level of moderate-to-vigorous physical activity. The effect of sedentary behavior on all-cause and CVD mortality is stronger among people who have low amounts of moderate-to-vigorous physical activity. In the meta-analysis of Biswas et al. (12), the summary hazard ratio (HR) for all-cause mortality associated with sedentary time was 1.16 (95% confidence interval [CI, 0.84–1.56) among those with high physical activity and 1.46 (95% CI, 1.22–1.75) among those with low physical activity. Further, Ekelund et al. (13) conducted a harmonized meta-analysis using individual-level data from more than 1 million adults and reported that increasingly higher amounts of moderate-to-vigorous physical activity attenuated the relationships between sedentary behavior and all-cause and CVD mortality. At the highest amounts of moderate-to-vigorous physical activity, the HR for all-cause mortality associated with the four levels of sedentary behavior appear to converge at about 1 (reference value). The number of minutes per day needed to achieve this estimated volume of moderate-to-vigorous physical activity (35.5 $\text{MET}\cdot\text{h}\cdot\text{wk}^{-1}$) varies inversely with the MET value of the activity, ranging from approximately 40 $\text{min}\cdot\text{d}^{-1}$ at 8 METs to 50 $\text{min}\cdot\text{d}^{-1}$ at 6 METs to 100 $\text{min}\cdot\text{d}^{-1}$ at 3 METs. According to data from the 2015 National Health Interview Survey, the prevalence of people participating in more than 300 $\text{min}\cdot\text{wk}^{-1}$ (~43 $\text{min}\cdot\text{d}^{-1}$) of moderate-to-vigorous physical activity is approximately 33%, whereas the prevalence of people participating in more than 700 $\text{min}\cdot\text{wk}^{-1}$ (~100 $\text{min}\cdot\text{d}^{-1}$) is approximately 11% (2018 PAGAC Scientific Report, Figure D1 (6,14)).

Evidence to inform question 5 was largely derived from the meta-analysis of Ekelund et al. (13). The overall shape of the dose–response relationships between moderate-to-vigorous physical activity and all-cause mortality are generally similar when stratified by level of sitting or TV viewing. However, the relative risks are consistently higher in the high sitting and high TV viewing groups. The reduction in risk of all-cause mortality associated with moderate-to-vigorous physical activity is relatively greater for those who are the most sedentary. This is especially apparent at the lower amounts of moderate-to-vigorous physical activity.

To visually describe the joint associations among sedentary behavior, moderate-to-vigorous physical activity and all-cause mortality, the Committee developed a heat map figure which depicts the risk of all-cause mortality associated with various combinations of sitting time and moderate-to-vigorous physical activity (Fig. 1). Linear and nonlinear regression techniques were used to interpolate the hazard ratios between four levels of sitting time and four levels of moderate-to-vigorous physical activity reported in Ekelund et al. (13). In the heat map, red represents higher risk of all-cause mortality, and green represents lower risk. The greatest risk of mortality is borne by those who sit the most and who do the least moderate-to-vigorous physical activity, whereas the lowest risk of mortality is achieved

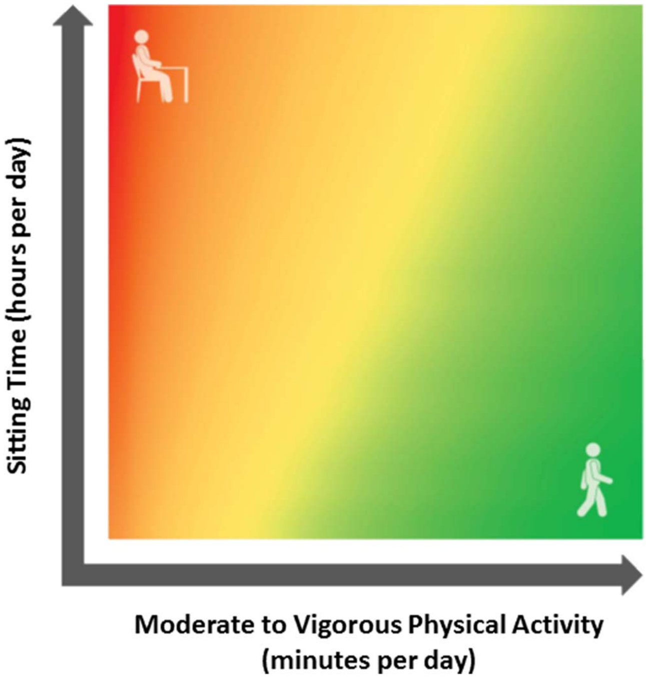

FIGURE 1—Joint associations of sitting time and moderate-to-vigorous physical activity with risk of all-cause mortality. From the *2018 Physical Activity Guidelines Advisory Committee Scientific Report* (6), and based on data presented by Ekelund et al. (13).

by individuals who sit the least and do the most moderate-to-vigorous physical activity.

METHODS FOR UPDATED LITERATURE SEARCH

This systematic review is reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines (15). The systematic review followed an established protocol, and was registered prospectively at PROSPERO (CRD42018092817). Our aim was to update the systematic review conducted by the 2018 Physical Activity Guidelines Advisory Committee and to additionally examine the association between changes in sedentary behavior and risk of all-cause mortality.

Literature search strategy. We searched the PubMed, Cochrane, and CINAHL bibliographic databases for studies published in English between January 1, 2017, and February 28, 2018. Two separate searches were conducted for 1) all-cause, CVD and cancer mortality, and 2) type 2 diabetes, weight status, CVD and cancer. Our search strategy was similar to that employed by the 2018 Physical Activity Guidelines Advisory Committee, and included a comprehensive list of search terms including several combinations of sedentary, sitting, screen time, television, TV, inactivity, physically inactive, sedentarism, and so on, along with relevant terms to identify the mortality and disease outcomes of interest (see *2018 Physical Activity Guidelines Advisory Committee Scientific Report* (6) for a full list of specific search terms).

Study selection criteria. The inclusion criteria were predefined, and studies were considered potentially eligible if they were original prospective observational studies, only involved adults 18 yr and older, were published in English, and investigated the association between sedentary behavior and one of the health outcomes of interest. Studies of nonambulatory adults, hospitalized patients, or samples with preexisting health conditions were excluded. A sample size of at least 1000 people was required for the mortality outcomes. Two authors independently reviewed the titles, abstracts and full-text articles, and disagreements about eligibility were resolved through consensus. Although intervention studies that examine changes in chronic disease risk factors in response to alterations in sedentary behavior provide valuable information about potential mechanisms, this type of evidence was beyond the scope of this review which focused on mortality and noncommunicable disease outcomes.

The systematic search for the mortality outcomes (all-cause, CVD, cancer) identified 780 unique records after duplicates were removed. Of these, 770 were excluded after a review of the titles and abstracts. Based on full-text reviews, four were excluded for all-cause mortality, nine were excluded for CVD mortality, and nine were excluded for cancer mortality. One additional study that was relevant for CVD and cancer mortality was identified in the search for disease outcomes, and was added at this stage. Thus, the final number of eligible studies was seven for all-cause mortality, two for CVD mortality, and two for cancer mortality (see Supplemental Figure 1, Supplemental Digital Content 2, article selection process for mortality studies, http://links.lww.com/MSS/B536). The systematic search for disease outcomes identified 922 unique records after duplicates were removed. Of these, 910 were excluded after a review of the titles and abstracts. Based on full-text reviews, an additional five studies were excluded, leaving a total of two studies of type 2 diabetes, one study for weight status, and four studies for incident cancer; no studies were identified for incident CVD (see Supplemental Figure 2, Supplemental Digital Content 3, article selection process for incident condition studies, http://links.lww.com/MSS/B537).

Data extraction and quality assessment. The following information was extracted from each eligible article: name of the first author, year of publication, study sample, sample size, age (range or mean), definition of sedentary behavior, dates and length of follow-up, risk estimates with corresponding 95% CI comparing levels of sedentary behavior, and whether the study tested and reported a dose–response association. If a study provided several risk estimates, we used the fully adjusted estimate. Extraction of data was performed by one author, and the resulting table was checked by another author.

Quality assessment and risk of bias in the eligible studies was done using the USDA Nutrition Evidence Library (NEL) Bias Assessment Tool (BAT) (16). The NEL BAT uses a domain-based evaluation to help determine whether any systematic error exists that could either over- or underestimate the study results. Selection, performance, detection, and attrition bias are addressed in the NEL BAT. The results of studies' risk of bias assessments were used to develop a risk of bias summary chart (see Supplemental Table 2, Supplemental Digital Content 4, original research bias assessment chart, http://links.lww.com/MSS/B538). The NEL BAT assessment was performed by one author, and the resulting table was checked by another author.

RESULTS

Study characteristics. The main characteristics of the eligible studies identified in the updated search are presented in Table 3 for all-cause, CVD and cancer mortality, and in Table 4 for incident type 2 diabetes, weight status, incident CVD and incident cancer. All studies used prospective cohort designs, with follow-up periods ranging from 2.3 to 19.4 yr. The sedentary exposures varied across studies: five studies used self-reported sitting time (19,26,28–30), seven studies used self-reported TV viewing time (18,21,24–26,28,31), and five studies used accelerometer-derived estimates of sedentary time (17,20,22,23,27). All studies included an estimate of duration of sedentary behavior (sedentary time) as an exposure, whereas three studies also included a marker of bouts or breaks in sedentary time as an exposure (17,22,27).

Mortality outcomes. Seven studies reported on the association between sedentary behavior and all-cause mortality (Table 3) (17–23). Six of the studies reported a statistically significant association (17–22). For example, an analysis from the Women's Health Initiative reported a significant ($P < 0.05$) association between self-reported daily sitting time and all-cause mortality (odds ratio for dying before age 85 yr for $\geq 10\ h \cdot d^{-1}$ vs $< 5\ h \cdot d^{-1}$ = 1.16; 95% CI, 1.04–1.29) over 13.7 yr of follow-up (19). Two additional studies, one from the United Kingdom and one among African Americans, demonstrated significant associations between daily TV viewing and all-cause mortality (18,21). Hamer et al. (18) reported a HR for all-cause mortality of 1.98 (95% CI, 1.25–3.15) comparing $\geq 6\ h \cdot d^{-1}$ versus $< 2\ h \cdot d^{-1}$ of TV viewing, whereas Imran et al. (21) reported a HR for all-cause mortality of 1.48 (95% CI, 1.19–1.83) comparing $\geq 4\ h \cdot d^{-1} < 2\ h \cdot d^{-1}$ of TV viewing. Three studies that used accelerometer-derived estimates of sedentary time as the exposure reported a significant association with all-cause mortality (17,20,22), whereas one did not (23). The three positive studies were in samples of US and UK adults and had follow-up period ranging from 4.0 to 6.5 yr, whereas the negative study was conducted among older US women (mean age, 72 yr), with a mean follow-up time of 2.3 yr (Table 3). Among the three positive studies, Diaz et al. (17) and Jefferis et al. (22) reported HR of 2.63 (95% CI, 1.60–4.30) and 2.73 (95% CI, 1.50–4.95), respectively, for the upper versus lowest quartiles of sedentary time, whereas Theou et al. (20) reported an HR of 1.15 (95% CI, 1.11–1.20) per each additional hour of sedentary time.

In addition to total duration of sedentary behavior, two studies examined the effects of bouts or breaks in sedentary behavior in relation to all-cause mortality (17,22). Diaz and colleagues reported a significant association (P for trend <0.001) between bout duration and all-cause mortality in US adults, and participants classified as both highly sedentary ($\geq 12\ h \cdot d^{-1}$) and with high bout duration (≥ 10 min per bout) had the highest risk of death (17). On the other hand, Jefferis and colleagues reported that neither breaks in sedentary behavior nor sedentary bout duration were related to all-cause mortality in a sample of older men (ages 71–92 yr) from the UK (22).

Two studies reported on the association between sedentary behavior and CVD mortality (18,24). Grace and colleagues reported a significant association between TV viewing and CVD mortality among smokers (but not nonsmokers) after adjustment for age and sex in the Australian Diabetes, Obesity and Lifestyle Study (AusDiab) (24). However, this association was no longer significant after the inclusion of additional covariates in the model. On the other hand, Hamer and colleagues reported a multivariable-adjusted HR of 1.22 (95% CI, 1.00–1.49) per standard deviation of daily TV viewing for CVD mortality in the English Longitudinal Study of Ageing (18).

Two studies reported on the association between sedentary behavior and cancer mortality (18,24). Hamer and colleagues reported a nonsignificant HR of 1.16 (95% CI, 0.96–1.39) per standard deviation of daily TV viewing for cancer mortality in the English Longitudinal Study of Ageing (15). Results from the AusDiab study indicated a significant association between TV viewing and cancer mortality among smokers (P for trend = 0.02) but not among nonsmokers (P for trend = 0.52) (24).

A total of six of seven studies reported a dose–response association between sedentary behavior and all-cause mortality (Table 3). Only one of two studies of CVD mortality and one of two studies of cancer mortality reported dose–response associations. Few studies formally tested for interactions between sedentary behavior and demographic characteristics on mortality outcomes; however, Rillamas-Sun et al. (19) reported no interaction by race/ethnicity on all-cause mortality in the Women's Health Initiative (19). Diaz and colleagues reported that the positive associations of sedentary time and bout duration with all-cause mortality did not vary by age, sex, race, body mass index (BMI) or moderate-to-vigorous physical activity (17). Further, Imran et al. (21) reported that in African Americans the results were similar when they excluded those with high and low BMI, those with low leisure physical activity, and those without a high school diploma. Theou and colleagues (20) reported a significant association between accelerometer-derived sedentary time and all-cause mortality in NHANES; the association was statistically significant in physically inactive adults but not in physically active adults.

Diseases and conditions. Two studies were identified that examined the association between sedentary behavior and incident type 2 diabetes (25,26). Stamatakis and colleagues (26) reported a significant association of TV sitting and total sitting with incident diabetes in UK adults enrolled in the Whitehall II study in models adjusting for several covariates, but the results were attenuated and were no longer significant after adjustment for BMI. Joseph and colleagues reported no associations between self-reported TV viewing and incident diabetes in African American adults in the

TABLE 3. Summary of original research studies on sedentary behavior and all-cause, CVD and cancer mortality published between January 1, 2017, and February 28, 2018.

References	Year of Publication	Population	Sample Size	Age	Definition of Sedentary Behavior	Mortality Follow-up Period	Main Results	Dose–Response
All-cause mortality								
Diaz et al. (17)	2017	U.S. Adults; Reasons for Geographic and Racial Differences in Stroke (REGARDS)	7985	≥45 yr	Actical waist accelerometry Total sedentary time: <50 counts per minute Sedentary bout: consecutive minutes <50 counts per minute	2009–13 to 2015 Median of 4.0 yr	HR (95% CI) across quartiles of total sedentary time in fully adjusted model: Q1: 1.00 (reference) Q2: 1.22 (0.74–2.02) Q3: 1.61 (0.99–2.63) Q4: 2.63 (1.60–4.30) *P* for trend <0.001 HR (95% CI) across quartiles of total sedentary bout duration in fully adjusted model: Q1: 1.00 (reference) Q2: 1.03 (0.67–1.60) Q3: 1.22 (0.80–1.85) Q4: 1.96 (1.31–2.93) *P* for trend <0.001 Participants classified as high for both high sedentary time [≥12.5 $h \cdot d^{-1}$] and high bout duration [≥10 min per bout]) had the greatest risk for death. Associations of sedentary time and bout duration did not vary by age, sex, race, BMI or moderate-to-vigorous physical activity ($P > 0.10$).	Yes
Hamer et al. (18)	2017	U.K. Adults: The English Longitudinal Study of Ageing (ELSA)	8451	Mean of 64.8 yr	Self-reported TV viewing	2008–09 to 2012 Mean of 4 yr	HR (95% CI) across levels of TV viewing time in fully adjusted model: <2 $h \cdot d^{-1}$: 1.00 (reference) 2–<4 $h \cdot d^{-1}$: 1.63 (1.02–2.61) 4–<6 $h \cdot d^{-1}$: 1.49 (0.92–2.39) ≥6 $h \cdot d^{-1}$: 1.98 (1.25–3.15) Per SD increase: 1.17 (1.06–1.28)	Yes
Rillamas-Sun et al. (19)	2017	U.S. Women: Women's Health Initiative Observational Study	29,090	62–81 yr	Self-reported daily sitting time	1993–98 to 2015 Mean of 13.7 yr	OR (95% CI) of dying before age 85 yr across daily sitting categories in fully adjusted model: ≤5 $h \cdot d^{-1}$: 1.00 (reference) 6–9 $h \cdot d^{-1}$: 1.02 (0.94–1.11) ≥10 $h \cdot d^{-1}$: 1.16 (1.04–1.29) *P* for trend ≤0.05 No interaction by race/ethnicity.	Yes

Theou et al. (20)	2017	U.S. Adults; 2003–04 & 2005–06 U.S. NHANES	3141	≥50 yr	ActiGraph waist accelerometry (≤100 counts per minute)	2003–2006 to 2011 Mean of 6.5 yr	HR (95% CI) per hour of sedentary time in fully adjusted model: 1.15 (1.11–1.20) HR (95% CI) per hour of sedentary time in fully adjusted models, stratified by physical activity level: Physically Inactive 1.20 (1.12–1.29) Physically Active 0.98 (0.78–1.24) HR (95% CI) per hour of sedentary time in fully adjusted models including physical activity, stratified by level of frailty: Frailty Index Score ≤ 0.1 0.90 (0.70–1.15) Frailty Index Score 0.1 to ≤0.2 1.13 (1.00–1.28) Frailty Index Score 0.2 to ≤0.3 1.27 (1.11–1.46) Frailty Index Score ≥ 0.3 1.36 (1.22–1.52)	Yes
Imran et al. (21)	2018	U.S. African American Adults: Jackson Heart Study (JHS)	5289	Mean of 55 yr	Self-reported TV viewing	Baseline in 2000–04 Median of 9.9 yr	HR (95% CI) across levels of TV viewing time in fully adjusted model: <2 $h \cdot d^{-1}$: 1.00 (reference) 2–<4 $h \cdot d^{-1}$: 1.08 (0.86–1.37) ≥4 $h \cdot d^{-1}$: 1.48 (1.19–1.83) *P* for trend = 0.002 The results were similar in models which excluded those who died in the first 2 yr of follow-up, those with low or high BMI, those with low leisure physical activity, those with low eGFR, and those without a high school diploma.	Yes
Jefferis et al. (22)	2018	U.K. Older Men: British Regional Heart Study	1181	71–92 yr	ActiGraph waist accelerometry Total sedentary time: <100 counts per minute Sedentary breaks: interruption of a sedentary bout lasting >1 min	2010–11 to 2016 Median of 5.0 yr	HR (95% CI) across quartiles of total sedentary time in fully adjusted model: Q1: 1.00 (reference) Q2: 1.14 (0.69–1.91) Q3: 1.55 (0.91–2.64) Q4: 2.73 (1.50–4.95) HR per 30 $min \cdot d^{-1}$: 1.15 (1.06–1.26) HR (95% CI) across quartiles of sedentary breaks per hour in fully adjusted model: Q1: 1.00 (reference) Q2: 1.22 (0.81–1.82) Q3: 0.95 (0.56–1.61) Q4: 1.01 (0.50–2.02) The numbers of minutes spent in sedentary bouts lasting 1–15 min, 16–30, 31–60 and >61 min were all similarly associated with mortality.	Yes

(continued next page)

TABLE 3. *(Continued)*

References	Year of Publication	Population	Sample Size	Age	Definition of Sedentary Behavior	Mortality Follow-up Period	Main Results	Dose–Response
Lee et al. (23)	2018	U.S. Women; Women's Health Study	16,741	Mean of 72 yr	ActiGraph waist accelerometry Total sedentary time: <200 counts per minute	2011–15 to 2015 Mean of 2.3 yr	HR (95% CI) across quartiles of total sedentary time in fully adjusted model: Q1: 1.00 (reference) Q2: 0.97 (0.62–1.50) Q3: 1.18 (0.77–1.82) Q4: 0.92 (0.56–1.50) *P* for trend = 0.99	No
CVD mortality								
Grace et al. (24)	2017	Australian Adults: Australian Diabetes, Obesity and Lifestyle Study (AusDiab)	8907	≥25 yr	Self-reported TV viewing	1999–2000 to 2013 Median of 13.6 yr	HR (95% CI) across levels of TV viewing time in fully adjusted model: <u>Nonsmokers</u> <2 $h \cdot d^{-1}$: 1.00 (reference) 2–<4 $h \cdot d^{-1}$: 0.93 (0.69–1.26) ≥4 $h \cdot d^{-1}$: 1.04(0.69–1.57) *P* for trend = 0.99 <u>Current Smokers</u> <2 $h \cdot d^{-1}$: 1.00 (reference) 2–<4 $h \cdot d^{-1}$: 1.11 (0.46–2.63) ≥4 $h \cdot d^{-1}$: 2.02 (0.80–5.12) *P* for trend = 0.16	No
Hamer et al. (18)	2017	U.K. Adults: The English Longitudinal Study of Ageing (ELSA)	8451	Mean of 64.8 yr	Self-reported TV viewing	2008–09 to 2012 Mean of 4 yr	HR per SD increase in daily TV viewing: 1.22 (1.00–1.49).	Yes
Cancer mortality								
Grace et al. (24)	2016	Australian Adults: Australian Diabetes, Obesity and Lifestyle Study (AusDiab)	8907	≥25 yr	Self-reported TV viewing	1999/2000 to 2013 Median of 13.6 yr	HR (95% CI) across levels of TV viewing time in fully adjusted model: <u>Nonsmokers</u> <2 $h \cdot d^{-1}$: 1.00 (reference) 2–<4 $h \cdot d^{-1}$: 0.92 (0.72–1.19) ≥4 $h \cdot d^{-1}$: 0.91(0.61–1.34) *P* for trend = 0.52 <u>Current Smokers</u> <2 $h \cdot d^{-1}$: 1.00 (reference) 2–<4 $h \cdot d^{-1}$: 1.44 (0.77–2.69) ≥4 $h \cdot d^{-1}$: 2.27 (1.11–4.67) *P* for trend = 0.02	Yes: in current smokers only
Hamer et al. (18)	2017	U.K. Adults: The English Longitudinal Study of Ageing (ELSA)	8451	Mean of 64.8 yr	Self-reported TV viewing	2008–09 to 2012 Mean of 4 yr	HR per SD increase in daily TV viewing: 1.16 (0.96–1.39).	No

eGFR, estimated glomerular filtration rate; OR, odds ratio; SD, standard deviation.

TABLE 4. Summary of original studies on sedentary behavior and type 2 diabetes, weight status, and cancer published between January 1, 2017 and February 28, 2018.[a]

Reference	Year of Publication	Population	Sample Size	Age	Definition of Sedentary Behavior	Follow-up Period	Main Results	Dose–Response
Type 2 diabetes								
Joseph et al. (25)	2017	U.S. African American Adults; Jackson Heart Study (JHS)	3252	21–94 yr	Self-reported TV viewing	2000–04 to 2005–12 Median of 7.5 yr	IRR (95% CI) across levels of daily TV viewing time in fully adjusted models: ≥4 h·d^{-1}: 1.00 (reference) 1–3.9 h·d^{-1}: 0.99 (0.82–1.18) <1 h·d^{-1}: 0.95 (0.72–1.25) Continuous IRR = 0.98 (0.86–1.11)	No
Stamatakis et al. (26)	2017	U.K. Adults: Whitehall II Study	4811	Mean of 44 yr	Self-reported work-related sitting time, TV viewing time, non-TV leisure time sitting, total leisure sitting time, total sitting time, non-TV total sitting time	1997–99 to 2011 Mean of 13.0 yr	HR (95% CI) across levels of sedentary behavior in fully adjusted models: Work Sitting <15 h·wk^{-1}: 1.00 (reference) 15–<35 h·wk^{-1}: 1.14 (0.87–1.51) ≥35 h·wk^{-1}: 1.17 (0.89–1.53) *P* for trend = 0.48 TV Sitting <11 h·wk^{-1}: 1.00 (reference) 11–<16 h·wk^{-1}: 1.33 (1.00–1.77) ≥16 h·wk^{-1}: 1.39 (1.03–1.88) *P* for trend = 0.05 Non-TV Leisure Sitting at Home <8 h·wk^{-1}: 1.00 (reference) 8–<16 h·wk^{-1}: 0.78 (0.57–1.05) ≥16 h·wk^{-1}: 0.98 (0.70–1.36) *P* for trend = 0.15 Leisure Sitting at Home <15 h·wk^{-1}: 1.00 (reference) 15–<25 h·wk^{-1}: 1.26 (0.97–1.64) ≥25 h·wk^{-1}: 1.27 (0.98–1.66) *P* for trend = 0.15 Total Sitting <15 h·wk^{-1}: 1.00 (reference) 15–<25 h·wk^{-1}: 0.87 (0.67–1.13) ≥25 h·wk^{-1}: 1.26 (1.00–1.62) *P* for trend = 0.01 Total Sitting Excluding TV <15 h·wk^{-1}: 1.00 (reference) 15–<25 h·wk^{-1}: 0.93 (0.68–1.27) ≥25 h·wk^{-1}: 1.23 (0.91–1.66) *P* for trend = 0.15 After additional adjustment for BMI the results were attenuated and no longer significant for TV sitting and total sitting.	Yes – for TV sitting and total sitting before adjustment for BMI No – after adjustment for BMI

(continued next page)

TABLE 4. (Continued)

Reference	Year of Publication	Population	Sample Size	Age	Definition of Sedentary Behavior	Follow-up Period	Main Results	Dose–Response
Weight status								
Barone Gibbs et al. (27)	2017	U.S. Adults; Coronary Artery and Risk Development in Young Adults (CARDIA)	1826	38–50 yr	ActiGraph waist accelerometry (<100 counts per minute) Total sedentary time and bouts of ≥10 min	2005–06 to 2010–11 ~5 yr	Higher total sedentary time at baseline was not associated with 5-yr changes in BMI and waist circumference. Each hour of sedentary time at baseline accumulated in bouts of ≥10 min was associated with 0.077 $kg \cdot m^{-2}$ higher gain in BMI (P = 0.033) and 0.198 cm higher gain in waist circumference (P = 0.028).	Yes
Cancer								
Eaglehouse et al. (28)	2017	Chinese Adults Living in Singapore: Singapore Chinese Health Study	61,321	45–74 yr	Self-reported TV viewing and “other” sitting activities	1993–1998 to 2014 Mean of 16.8 yr	HR (95% CI) for incident colorectal cancer across levels of TV viewing in fully adjusted model: <2 $h \cdot d^{-1}$: 1.00 (reference) ≥3 $h \cdot d^{-1}$: 1.04 (0.95–1.14) HR (95% CI) for incident colorectal cancer across levels of “other” sitting activities in fully adjusted model: None: 1.00 (reference) <1 $h \cdot d^{-1}$: 0.99 (0.87–1.13) 1–2 $h \cdot d^{-1}$: 1.00 (0.87–1.15) ≥3 $h \cdot d^{-1}$ 0.99 (0.84–1.17) P for trend = 0.99	No
Gorczca et al. (29)	2017	U.S. Women: Women's Health Initiative Observational Study	74,870	50–79 yr	Self-reported daily sitting time	Median of 13.4 yr	HR (95% CI) for incident colorectal cancer across levels of daily sitting time in fully adjusted model: ≤5 $h \cdot d^{-1}$: 1.00 (reference) 5.1–9.9 $h \cdot d^{-1}$: 1.10 (0.95–1.26) ≥10 $h \cdot d^{-1}$: 1.12 (0.92–1.35) P for trend = 0.29 HR (95% CI) for incident rectal cancer across levels of daily sitting time in fully adjusted model: ≤5 $h \cdot d^{-1}$: 1.00 (reference) 5.1–9.9 $h \cdot d^{-1}$: 1.08 (0.78–1.51) ≥10 $h \cdot d^{-1}$: 0.94 (0.59–1.48) P for trend = 0.74 HR (95% CI) for incident colon cancer across levels of daily sitting time in fully adjusted model: ≤5 $h \cdot d^{-1}$: 1.00 (reference) 5.1–9.9 $h \cdot d^{-1}$: 1.10 (0.95–1.28) ≥10 $h \cdot d^{-1}$: 1.14 (0.92–1.40) P for trend = 0.25 No interaction between sitting time and physical activity (P = 0.62), age group (P = 0.97), BMI (P = 0.66) or employment status (P = 0.99).	No

Nomura et al. (30)	2017	U.S. Women; Women's Health Initiative Observational Study	70,233	50–79 yr	Self-reported daily sitting time and total sedentary time	1994–98 to 2015	HR (95% CI) for incident postmenopausal breast cancer across levels of daily sitting time in fully adjusted model: ≤5 $h \cdot d^{-1}$: 1.00 (reference) 6–9 $h \cdot d^{-1}$: 1.03 (0.96–1.11) ≥10 $h \cdot d^{-1}$: 1.00 (0.92–1.09) *P* for trend = 0.88 Continuous HR ($h \cdot d^{-1}$) = 1.00 (0.98–1.02). No interactions between sitting and race/ethnicity, hormone receptor status, BMI, weight gain since age 18, waist circumference, or waist-to-hip ratio.	No
Ukawa et al. (31)	2018	Japanese Women; Japan Collaborative Cohort Study for Evaluation of Cancer Risk (JACC Study)	34,758	40–79 yr	Self-reported TV viewing	1988–90 to 2009 Median of 19.4 yr	HR (95% CI) for incident ovarian cancer across levels of TV viewing time in fully adjusted model: <2 $h \cdot d^{-1}$: 1.00 (reference) 2–2.9 $h \cdot d^{-1}$: 1.03 (0.70–1.50) 3–3.9 $h \cdot d^{-1}$: 1.18 (0.82–1.70) 4–4.9 $h \cdot d^{-1}$: 0.81 (0.54–1.21) ≥5 $h \cdot d^{-1}$: 2.15 (1.54–2.99)	Not tested

[a]No studies were identified for incident CVD.

Jackson Heart Study, both before and after including BMI as a covariate (25).

A single study was identified that examined the association between sedentary behavior and weight status (27). Among adults in the CARDIA Study, there was no association between total duration of sedentary behavior and 5-yr changes in BMI or waist circumference. However, each additional hour of sedentary time accumulated in bouts of greater than or equal to 10 min was associated with greater gain in BMI ($P = 0.033$) and waist circumference ($P = 0.028$) (Table 4).

Four studies were identified that addressed the association between sedentary behavior and incident cancer: two studied colorectal cancer (28,29), one studied breast cancer (30), and one studied ovarian cancer (31). Neither of the two studies of colorectal cancer reported a significant effect of sedentary behavior (TV viewing or sitting time) on cancer incidence (Table 4). Nomura and colleagues (30) reported no significant association between sedentary behavior and incident breast cancer in post-menopausal US women in the Women's Health Initiative Observational Study (30). On the other hand, Ukawa and colleagues reported that Japanese women who watched TV for greater than or equal to 5 $h \cdot d^{-1}$ were more likely to develop ovarian cancer than those who watched TV for less than 2 $h \cdot d^{-1}$ (HR, 2.15; 95% CI, 1.54–2.99). Two studies tested for interactions, and reported no interactions between sedentary behavior and race/ethnicity, age, hormone receptor status, BMI, weight gain since age 18 yr, waist circumference, waist-to-hip ratio, employment status or physical activity (29,30).

A total of six of the seven studies of sedentary behavior, disease incidence or weight status tested for dose–response associations (25–30). Only Barone-Gibbs and colleagues reported significant dose–response associations - between sedentary time and weight status (BMI and waist circumference) (27).

Changes in sedentary behavior and risk of mortality. We identified several papers from the original systematic review search (32–35) and the updated search (36) that addressed changes in sedentary behavior over time and risk of mortality ($n = 4$ for all-cause mortality, $n = 1$ for CVD mortality) (Table 5). In each of the studies, mortality rates were compared across categories of changes in sitting time (consistently sedentary, increased or decreased sedentary time, or consistently nonsedentary). Changes in sedentary time were evaluated over approximately 2 to 11 yr, and the mean or median follow-up time for mortality surveillance ranged from approximately 5 to 9 yr after the second assessment of sedentary behavior. In all studies, the risk of mortality was significantly lower in those who were consistently nonsedentary over time, compared to those who were consistently sedentary. In general, those who decreased sedentary behavior over time had an intermediate risk of mortality, compared to those who were consistently sedentary or nonsedentary. Three studies reported lower risk of mortality associated with increased sedentary behavior over time, compared to those who were consistently sedentary (32,33,36), whereas two studies reported an increased risk of mortality among those who increased sedentary

TABLE 5. Summary of original studies on changes in sedentary behavior and mortality.

Authors	Year of Publication	Population	Sample Size	Age (yr)	Definition of Sedentary Behavior	Mortality Follow-up Period	Main Results
Leon-Munoz et al. (32)	2013	Spanish Adults	2635	≥60 yr	Changes in daily sitting time between 2001–2003	2003 to 2011	HR (95% CI) for all-cause mortality across categories of sitting time in fully adjusted model: Consistently sedentary: 1.00 (reference) Newly sedentary: 0.91 (0.76–1.10) Formerly sedentary: 0.86 (0.70–1.05) Consistently nonsedentary: 0.75 (0.62–0.90)
Lee et al. (33)	2015	U.S. Women; Women's Health Initiative (WHI)	77,801	50–79 yr	Changes in daily sitting time from baseline and year 6	1998 to 2008 Mean of 5.1 yr	HR (95% CI) for all-cause mortality across categories of sitting time in fully adjusted model: Consistently high sitting: 1.00 (reference) Increased sitting: 0.79 (0.58–1.07) Decreased sitting: 0.71 (0.54–0.95) Consistently low sitting: 0.49 (0.39–0.63)
Keadle et al. (34)	2015	U.S. Adults; NIH-AARP Diet and Health Study	165,087	50–71 yr	Changes in TV viewing time between 1994–96 and 2004–06	2004–2006 to 2011 Mean of 6.6 yr	HR (95% CI) for all-cause mortality across categories of TV viewing in fully adjusted model: Consistent 5+ $h \cdot d^{-1}$: 1.28 (1.21–1.34) Decreased from 5+ to 3–4 $h \cdot d^{-1}$: 0.85 (0.80–0.91) Decreased from 5+ to <3 $h \cdot d^{-1}$: 0.88 (0.79–0.97) Increased from <3 to 3.4 $h \cdot d^{-1}$: 1.17 (1.10–1.24) Increased from <3 to 5+ $h \cdot d^{-1}$: 1.45 (1.32–1.58) Consistent <3 $h \cdot d^{-1}$: 1.0 (reference)
Grunseit et al. (35)	2017	Norwegian Adults; Nord-Trondelag Health Study (HUNT)	25,651	≥20 yr	Changes in daily sitting time between 1995–97 and 2006–08	2006–2008 to 2013 Mean of 6.2 yr	HR (95% CI) for all-cause mortality across categories of sitting time in fully adjusted model: Consistently high sitting: 1.26 (1.06–1.51) Increased sitting: 1.51 (1.28–2.78) Decreased sitting: 1.03 (0.88–1.20) Consistently low sitting: 1.00 (reference)
Cabanas-Sanchez et al. (36)	2017	Spanish Adults	2657	≥60 yr	Changes in daily sitting time between 2001 and 2003	2003 to 2014 Mean of 9.2 yr	HR (95% CI) of CVD mortality across categories of sitting time in fully adjusted model: Consistently sedentary: 1.00 (reference) Newly sedentary: 1.18 (0.87–1.59) Formerly sedentary: 0.77 (0.56–1.07) Consistently nonsedentary: 0.67 (0.46–0.96)

behavior over time, compared to those who were consistently sedentary (34,35). It is plausible that using two measurements of sedentary behavior over a period of time may be a better marker of long-term levels of sedentary behavior rather than a measure of precise changes over time given the self-reported nature of the data. Two concordant responses may classify participants more accurately than two discordant responses over time, making the later more susceptible misclassification and inconsistent findings.

DISCUSSION

The results from the updated search provide further evidence of an association between sedentary behavior and all-cause mortality. Further, the new results from studies of changes in sedentary behavior and mortality suggest that individuals who maintain sedentary behavior over time have the highest risk of mortality, those with sustained low levels of sedentary behavior have lowest risk, and those who report changes in sedentary behavior have an intermediate mortality risk. The updated results obtained for CVD mortality (18,24) do not alter the strength of evidence for the strong association with sedentary behavior. Although Grace and colleagues did not find a significant multivariable-adjusted association between TV viewing and CVD mortality when the AusDiab sample was stratified by smoking status (24), these results are in contrast with an earlier report from that cohort that reported a HR of 1.80 (95% CI, 1.00–3.25) between high amounts of TV viewing ($\geq$4 h·d^{-1} vs <2 h·d^{-1}) and CVD mortality in the full sample (8). The smaller sample size and small number of events in the sub-group analyses likely contributed to the nonsignificant results. The two new studies identified for cancer mortality (18,24) do not alter the conclusion of the Committee that the evidence for an association between sedentary behavior and cancer mortality is limited. Associations between sedentary behavior and cancer mortality are affected by cancer screening and treatment availability and efficacy. A limitation of most studies is a failure to take these factors into account.

Similar to the results of previous studies on the association between sedentary behavior and type 2 diabetes, the observed associations in the updated review are not statistically significant in fully-adjusted models where BMI is included as a covariate (25,26). The effects of sedentary behavior on risk of type 2 diabetes may be operating, in part, through its association with BMI; however, whether or not BMI is in the causal pathway between sedentary behavior and type 2 diabetes is not known. The extent to which sedentary behavior and BMI represent independent risk factors will require further research to disentangle the effects of BMI and sedentary behavior on risk of incident disease, especially type 2 diabetes.

Strong evidence demonstrates that the association between sedentary behavior and all-cause mortality is more pronounced among physically inactive people. In addition, individuals who are highly sedentary appear to require higher amounts of physical activity to achieve the same level of absolute mortality risk as those who are less sedentary (37). Therefore, moderate-to-vigorous physical activity should be part of every adult's lifestyle, especially for those who are sedentary for large portions of the day. These results also illustrate the need to individualize and tailor lifestyle recommendations for maximum benefit to the individual, which in turn will have a greater impact on population health. Further, the finding that the association between physical activity and health varies by level of sedentary behavior also highlights the importance of integrating sedentary behavior and physical activity guidelines.

US adults spend a large portion of each day engaging in sedentary behavior (3). Therefore, limiting excessive time spent sitting would reduce the population health impact associated with premature mortality and several major chronic diseases such as type 2 diabetes, CVD, and several cancers. For physically inactive adults, replacing sedentary behavior with light intensity physical activities is likely to produce some health benefits; however, among all adults, replacing sedentary behavior with higher intensity physical activities may produce even greater benefits (38–41). The updated systematic review identified several new papers addressing the relationship between sedentary behavior and health outcomes. However, the new studies did not provide results that would change the levels of evidence that addressed the Committee's questions.

Several research recommendations were generated by this work. As described in the introduction, the current consensus definition of sedentary behavior has both an energy expenditure component ($\leq$1.5 METs) and a postural component (sitting, reclining, or lying) (1). There is a pressing need to develop objective field methods to simultaneously assess these two components of the definition that can be applied in both surveillance and research settings to properly quantify time spent in sedentary behavior. Analysis strategies to identify different bout lengths as well as breaks in sedentary behavior vary among studies and are also an important area for future research. Further, research using prospective cohorts is required 1) on the interactive effects of physical activity (especially light intensity activity) and sedentary behavior on mortality and incident CVD, 2) on the role of bouts and breaks in sedentary behavior in relation to mortality and other health outcomes, and 3) on disentangling the independent effects of sedentary behavior and adiposity on risk of type 2 diabetes, and the degree to which adiposity may be in the causal pathway in this association. Further research is also required to determine how sex, age, race/ethnicity, socioeconomic status, and weight status relate to the association between sedentary behavior and CVD incidence and mortality. Finally, randomized controlled trials are required to test the health effects of interventions to replace time spent in sedentary behaviors with standing and light, moderate, and vigorous intensity activity.

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HHS staff provided general administrative support to the Committee and assured that the Committee adhered to the requirements for Federal Advisory Committees. HHS also contracted with ICF, a global consulting services company, to provide technical support for the literature searches conducted by the Committee. HHS and ICF staff collaborated with the Committee in the design and conduct of the searches by assisting with the development of the analytical frameworks, inclusion/exclusion criteria, and search terms for each primary question; using those parameters, ICF performed the literature searches.

This paper is being published as an official pronouncement of the American College of Sports Medicine. This pronouncement was reviewed for the American College of Sports Medicine by members-at-large and the Pronouncements Committee. *Disclaimer:* Care has been taken to confirm the accuracy of the information present and to describe generally accepted practices. However, the authors, editors, and publisher are not responsible for errors or omissions or for any consequences from application of the information in this publication and make no warranty, expressed or implied, with respect to the currency, completeness, or accuracy of the contents of the publication. Application of this information in a particular situation remains the professional responsibility of the practitioner; the clinical treatments described and recommended may not be considered absolute and universal recommendations.

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PRONOUNCEMENT

Physical Activity, Cognition, and Brain Outcomes: A Review of the 2018 Physical Activity Guidelines

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ABSTRACT

ERICKSON, K. I., C. HILLMAN, C. M. STILLMAN, R. M. BALLARD, B. BLOODGOOD, D. E. CONROY, R. MACKO, D. X. MARQUEZ, S. J. PETRUZZELLO, and K. E. POWELL, FOR 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Physical Activity, Cognition, and Brain Outcomes: A Review of the 2018 Physical Activity Guidelines. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1242–1251, 2019. **Purpose:** Physical activity (PA) is known to improve cognitive and brain function, but debate continues regarding the consistency and magnitude of its effects, populations and cognitive domains most affected, and parameters necessary to achieve the greatest improvements (e.g., dose). **Methods:** In this umbrella review conducted in part for the 2018 Health and Human Services Physical Activity Guidelines for Americans Advisory Committee, we examined whether PA interventions enhance cognitive and brain outcomes across the life span, as well as in populations experiencing cognitive dysfunction (e.g., schizophrenia). Systematic reviews, meta-analyses, and pooled analyses were used. We further examined whether engaging in greater amounts of PA is associated with a reduced risk of developing cognitive impairment and dementia in late adulthood. **Results:** Moderate evidence from randomized controlled trials indicates an association between moderate- to vigorous-intensity PA and improvements in cognition, including performance on academic achievement and neuropsychological tests, such as those measuring processing speed, memory, and executive function. Strong evidence demonstrates that acute bouts of moderate- to vigorous-intensity PA have transient benefits for cognition during the postrecovery period after exercise. Strong evidence demonstrates that greater amounts of PA are associated with a reduced risk of developing cognitive impairment, including Alzheimer's disease. The strength of the findings varies across the life span and in individuals with medical conditions influencing cognition. **Conclusions:** There is moderate-to-strong support that PA benefits cognitive functioning during early and late periods of the life span and in certain populations characterized by cognitive deficits.
Key Words: ACUTE EXERCISE, ACADEMIC ACHIEVEMENT, BRAIN, COGNITIVE FUNCTION, DEMENTIA, FITNESS

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Scientific, educational, and public health communities have demonstrated immense interest in investigating approaches that might enhance cognitive and brain function throughout the life span. Indeed, improvements in cognitive and brain health may have profound consequences for shaping quality of life, educational and career opportunities, and decision-making abilities. Physical activity (PA), defined as bodily movement produced by skeletal muscles that results in energy expenditure (1), has emerged as one of the most promising methods for positively influencing cognitive function across the life span and reducing the risk of age-related cognitive decline. The 2018 Physical Activity Guidelines Advisory Committee (PAGAC) reviewed evidence on these effects to inform federal policy.

The possibility that PA might favorably influence cognitive and brain health is based on the fundamental neurobiological principle that cellular and molecular events in the brain are amenable to modification by environmental enrichment. The pioneering work on environmental enrichment demonstrated that rodents housed in impoverished cages have a substantially different neurobiology than rodents housed in enriched cages and that this neurobiological effect translated to enhanced learning and memory (2,3). Access to a running wheel was shown to be a critical feature of an enriched environment (4).

Demonstration of the positive effects of PA on the brain in rodents has guided questions about its potential for positive effects in humans. Indeed, studies in humans have found associations between PA and cognitive and brain outcomes across the life span (5). However, several reviews and meta-analyses of this literature have concluded that the effect PA on cognitive and brain health remains unclear because of the inconsistencies in the parameters of PA used across studies, the ways in which cognition was measured, the assessment of moderators and mechanisms that could explain heterogeneity of the results, and the quality of the study designs (5). More recent reviews and meta-analyses have found that PA training results in modest improvements in cognitive and brain outcomes across the life span, but many of these reviews have not closely interrogated quality (6,7).

The 2018 PAGAC reviewed the scientific literature of this field, and the results from that analysis are partially described herein. We aimed to address several questions. First, by integrating the literature across ages and health conditions and by providing a bird's-eye perspective to the field, can we determine whether there is sufficient evidence that PA positively influences cognitive and brain outcomes in humans? Second, at which age or in which population is the scientific literature the strongest and in which the weakest? Third, are there cognitive domains that are especially responsive to PA? Fourth, is PA associated with a reduced risk of cognitive impairment? Finally, is there sufficient evidence to indicate which parameters of PA may be important for modulation of cognitive and brain health?

METHODS

The methods used to conduct the reviews that informed the 2018 PAGAC Scientific Report have been described in detail elsewhere (8).

The searches were conducted in electronic databases (PubMed®, CINAHL, and Cochrane) and supplemented by additional articles identified by experts. The inclusion criteria were predefined, and studies were considered potentially eligible if they were systematic reviews (SR), meta-analyses, or pooled analyses published in English from 2003 to February 2017. Studies published in 2017 or 2018 (i.e., after data extraction for the PAGAC report) are also included as the search was updated for this manuscript (N = 44). For the sake of this review, we used a relatively broad definition of PA based on that provided by Casperson et al. (1) to include play and recess activities in children, structured exercise programs for adults, and experimental manipulations of acute bouts of exercise. All types and intensities of PA, including free-living activities and play, were included in the search as interventions/exposures. Although not a form of PA, the term "physical fitness" was also included in the search, and, if relevant, these studies were described separately. Studies of nonambulatory people, hospitalized patients, or animals were excluded. The full search strategy is available at https://health.gov/paguidelines/second-edition/report/supplementary_material/pdf/Brain_Health_Q1_Cognition_Evidence_Portfolio.pdf.

Titles, abstracts, and full-text articles were independently screened by two reviewers. Disagreement between reviewers was resolved by discussion or by a third person. The protocol for this review was registered at PROSPERO #CRD42018095774. Figure 1 shows the search strategy and study selection process.

A total of 76 articles (35 meta-analyses; 41 SR) were identified that examined the effects of randomized controlled trials (RCT) and prospective longitudinal studies with cognitive outcomes. These reviews included results from younger (18–50 yr; n = 5) (9–13) adults, older adults (n = 7) (6,14–19), children (n = 13) (20–32), and adolescents (n = 6) (33–38), as well as populations with impaired cognition, such as attention deficit/hyperactivity disorder (ADHD) (n = 3) (39–41), mild cognitive impairment or dementia (n = 13) (42–54), multiple sclerosis (MS) (n = 1) (55), Parkinson's disease (n = 2) (56,57), schizophrenia (n = 1) (58), HIV (n = 1) (59), type 2 diabetes (n = 2) (60,61), cancer (n = 2) (62,63), and stroke (n = 2) (53,64). We also included articles on acute exercise and cognitive outcomes (n = 4) (65–68), sedentary behavior and cognitive outcomes (n = 1) (69), and biomarkers of brain health (n = 9) (70–78). We further included one meta-analysis examining resistance training and episodic memory (79) and three articles on interval training and exergaming (80–82). We summarized the outcomes of our review with the following "grades": 1) grade not assignable, 2) limited, 3) moderate, and 4) strong (see the 2018 Physical Activity Guidelines Committee [8] for an in-depth description and the defining characteristics of these categories).

RESULTS

Table 1 presents a summary of the results in each of the following domains.

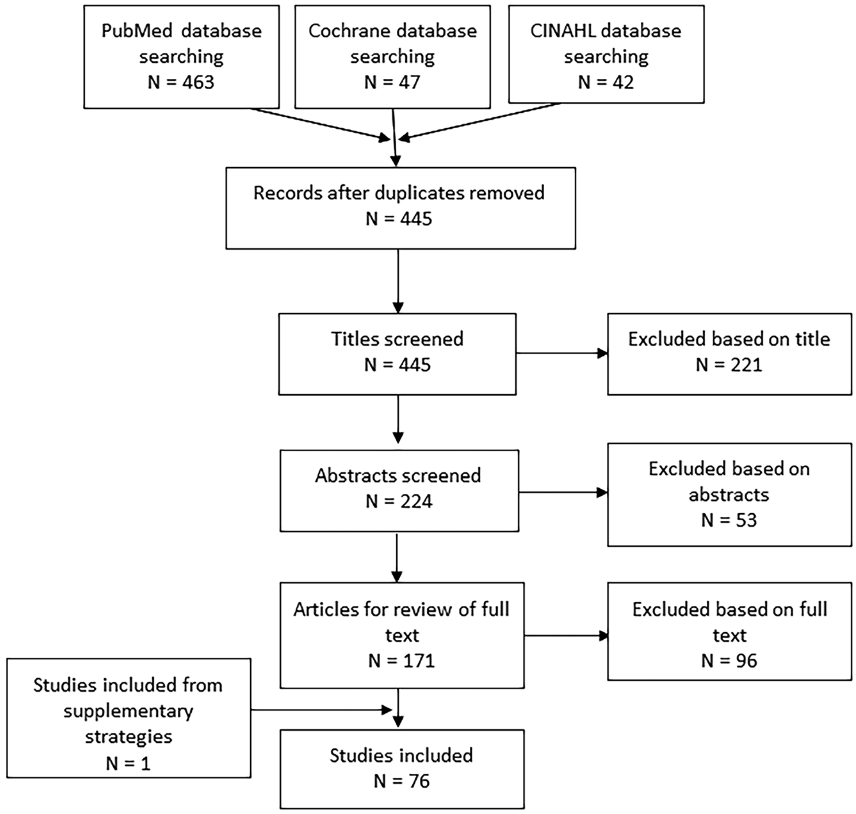

FIGURE 1—Flow diagram of search strategy and study selection.

Chronic PA behavior. In the following subsections, we refer to chronic PA behavior as PA that is repeated and lasts longer than a single session or episode. Thus, acute PA research reflects the immediate (transient) response to a single bout of PA, whereas chronic PA reflects a true change in an individual's baseline (i.e., a prolonged/permanent shift in activity). In the case of chronic PA, the change is not as tightly coupled in time to the last bout of PA. The effects of single-session, or acute, PA are discussed in a separate section below. Most of the work on chronic PA includes studies that examine

TABLE 1. Committee-assigned grades for the effects of PA on various ages and clinical outcomes.

Population or Measure	Outcome	Grade
Children <6 yr	Insufficient evidence to determine the effects of moderate- to vigorous-intensity PA on cognition	Not assignable
Children 6–13 yr	Both acute and chronic moderate- to vigorous-intensity PA interventions improve brain structure and function, as well as cognition, and academic outcomes	Moderate
Children 14–18 yr	Limited evidence to determine the effects of moderate- to vigorous-intensity PA on cognition	Limited
Young and middle-age adults 18–50 yr	Insufficient evidence to determine the effects of moderate- to vigorous-intensity PA on cognition	Not assignable
Older adults >50 yr	Both acute and long-term moderate- to vigorous-intensity PA interventions improve brain structure and function, as well as cognition	Moderate
Adults with dementia	Evidence suggests that PA may improve cognitive function	Moderate
Risk of dementia and cognitive impairment	Greater amounts of PA reduce the risk for cognitive impairment	Strong
Other clinical disorders (i.e., ADHD, schizophrenia, MS, Parkinson's, stroke)	Evidence that moderate- to vigorous-intensity PA has beneficial effects on cognition in individuals with diseases or disorders that impair cognition	Moderate
Biomarkers of brain health	Moderate- to vigorous-intensity PA positively influences biomarkers, including MRI-based measures of function, brain volume, and white matter	Moderate
Acute bouts	Short, acute bouts of moderate- to vigorous-intensity PA transiently improves cognition during the postrecovery period	Strong
Overall	There is a consistent association between chronic MVPA and improved cognition, including performance on academic achievement tests, neuropsychological tests, and risk of dementia. Effects are demonstrated across a gradient of normal to impaired cognitive health status	Moderate

PA behavior and engagement over a span of weeks, months, or years.

Children ≤6 yr. In preschool-age children, little published research has examined the relationship between regular PA and cognitive outcomes. In fact, only two SR have appeared to date (24,32). Carson and colleagues (24) reviewed seven observational and experimental studies of PA in typically developing children and reported that six of the studies yielded a beneficial effect of greater PA on at least one cognitive outcome, with the most notable findings observed for executive function (67% of the outcomes assessed) and language (60% of the outcomes assessed). No studies demonstrated that PA was related to poorer cognition. However, the authors rated six of the seven studies as having weak experimental quality and a high risk of reporting bias using PRISMA guidelines. Further, Zeng et al. (32) reviewed five RCT of PA on cognitive development in children 4–6 yr old. Four (80%) of the five studies observed a positive effect of PA on attention, memory, language, and academic achievement. Similarly, they concluded that there is only preliminary evidence to support a positive effect of PA on cognition during early childhood. Because of insufficient evidence, the subcommittee decided a grade was *not assignable* regarding the effect of PA on cognitive development in the early, preschool years.

Children 6 to 13 yr. The greatest wealth of evidence for an effect of PA on cognitive outcomes in children was found for preadolescents. Several SR and meta-analyses report beneficial effects (using SR criteria, Cohen's *d*, or Hedges' *g*) of PA on cognitive and academic outcomes (20,21,23,25,26,29–31,35,36). Specifically, consistent benefits of PA were observed for executive function (21,23,26), attention (25), and academic achievement (20,26), including academic behaviors (e.g., time on task) (30). Across the included articles, there were consistent findings indicating a small to moderate effect (effect sizes = 0.13–0.30) of PA on cognitive and academic outcomes. Such findings were observed across several cognitive domains (and assessments within domains), highlighting the robustness of this relationship despite the heterogeneity of approaches for investigating the influence of PA on cognition.

Additional support for the relationship for PA on cognition in preadolescence stemmed from the use of neuroimaging tools in this population. Two SR (23,26) have described differences in brain structure and function as a result of PA in RCT, with additional support from cross-sectional comparisons of higher and lower fit groups of preadolescents. Briefly, findings have demonstrated differences in brain structure, including greater integrity in specific white matter tracts after PA interventions (23,26). Functional brain changes resulting from PA interventions have also been noted in preadolescent children. Such studies have indicated PA intervention-induced benefits to the neuroelectric system as well as changes in functional magnetic resonance imaging signals (23,26). Collectively, there is *moderate* evidence that PA is beneficial to cognition and brain structure and function during preadolescence.

Children 14 to 18 yr. Relative to preadolescence, significantly fewer reports (i.e., six SR and meta-analyses) have been published in adolescent children. In adolescents, there were fewer rigorous experimental studies with control groups, studies with well-described parameters and definitions of PA, and well-described measures of cognitive function or academic achievement. Despite these limitations, a recent meta-analysis reported a positive effect (Cohen's $d = 0.37$) for PA on academic outcomes across 10 studies (38). In addition, two SR (both with ~20 studies) focused on PA and cognitive outcomes. Esteban-Cornejo et al. (33) observed mixed results, such that 70% of the studies observed a positive relationship of PA (broadly defined as physical education, sport, athletic participation, and exercise behavior) with cognitive or academic outcomes, 20% observed no relationship, and 10% observed a negative relationship. Similarly, Ruiz-Ariza et al. (37) observed a generally beneficial relationship of several metrics of fitness with cognitive outcomes. Given the limited number of rigorous experimental studies with randomized designs, these findings should be considered preliminary. Four new reports emerged in 2017 and 2018 after the PAGAC search was completed (34–37), and collectively these reports have demonstrated consistency in their conclusions of a positive association between PA and cognition in adolescence. However, given the heterogeneity of findings in this age-group, we determined there is *limited* but promising evidence for the positive effects of PA on cognition in adolescent children. Note that this grade was changed from the 2018 PAGAC Report, where there was insufficient evidence available at the time for even a limited grade.

Young and middle-age adults. Relative to studies of children and older adults, there is a dearth of SR and meta-analyses on the relationship of PA and cognition in young and middle-age adults (18–50 yr). Several reports have investigated PA on cognition across the adult life span; however, the samples were weighted toward older adults (>60 yr) or included individuals with various clinical disorders (11,12). Other reports in middle-age adults only included 1–2 studies aimed at chronic, or long-term, PA participation, with the majority of studies focused on acute PA effects (79). Of the few studies reported, the findings were mixed for the effects of moderate- to vigorous-intensity PA on cognition, indicating the need for additional research during young and middle adulthood. We determined that a grade was *not assignable* regarding the effects of PA on cognition and brain outcomes in this age range.

Older adults (>50 yr). The most significant body of research (i.e., seven SR and meta-analyses) examining the effects of PA on cognitive function has been conducted in older adults, which the PAGAC defined at those over the age of 50 yr. This work indicates that there is *moderate* evidence for an effect of long-term moderate- to vigorous-intensity PA on cognitive outcomes in adults 50 yr and older. In cognitively normal older adults, effect sizes (Hedges' *g*) ranged from nonsignificant (15) to 0.20 (18) to 0.48 (6) or higher (14) in favor of PA. Effect sizes were greatest for measures of executive function (6), global cognition (18), and attention (15). In one meta-analysis of 39 RCT, PA training improved executive function, episodic memory, visuospatial function, word fluency, processing speed, and global cognitive function (14). Some of these effects were large (Hedges' $g = 2.06$ for aerobic training effects on executive functions) but were moderated by the mode of activity with larger effect sizes for aerobic training compared with resistance or multi-modal (i.e., resistance and aerobic) interventions. Other studies have also reported effects of resistance training. For example, measures of reasoning were significantly improved across 25 RCT, but this effect was specific to resistance exercise (15), whereas others reported the largest effect sizes for combined resistance and aerobic training (6,19). Other modes of activity like exergaming (e.g., Wii Fit) might also improve cognitive function (17). In addition, for executive functions, larger effect sizes have been reported for studies with a greater percentage of women, suggesting sex is an important moderator of the effect of PA on cognition (6,14). In another meta-analysis of 39 RCT examining the effects of PA on cognitive function in individuals over the age of 50, PA improved cognition with an effect size of 0.29 (16). In sum, despite heterogeneity across studies, the majority of SR and meta-analyses reported small- to moderate-sized effects of RCT on cognitive performance in older adults, which were moderated by both sex and the cognitive domain assessed.

Neuroimaging research has provided another level and type of support for the effects of PA in older adults. These results have been summarized across several reviews (83). In one meta-analysis of 14 studies, 9 of which were in older adults, aerobic exercise increased right and left anterior hippocampal volumes (71,76). Yet, despite these promising results, few large-scale studies with sufficient sample sizes have examined the effects of PA interventions on hippocampal volume in older adults, leading to ambiguity about the long-term effects (75). Other studies have reported positive effects on other brain biomarkers of morphology and function (71,77,78), whereas others are more equivocal (72).

In summary, there are promising effects of PA on cognitive and brain outcomes in older adults, but more research is needed to disambiguate the age ranges most affected, sex differences, dose–response parameters necessary to optimize PA effects, and brain biomarkers for better understanding pathways leading to improvements in cognition. These remaining open questions led us to grade the evidence as *moderate* for this age range.

Mild cognitive impairment and dementia. The evidence for this question was based on prospective observational research designs that followed people over periods of time ranging from 1 to 12 yr (i.e., two SR and meta-analyses). There is *strong* evidence indicating that greater amounts of PA are associated with a reduced risk of cognitive decline (51) and dementia, including AD (42). In this literature, prospective observational studies are conducted on cognitively normal individuals who are then subsequently followed over time to determine whether PA is associated with risk for developing cognitive impairment. For example, a meta-analysis of 15 prospective studies ranging from 1 to 12 yr in duration with more than 33,000 participants found that greater amounts of PA were associated with a 38% reduced risk of cognitive decline (51). Another meta-analysis of 10 prospective studies with more than 20,000 participants reported that greater amounts of PA were associated with a 40% reduced risk of developing AD (42). One additional SR published after the PAGAC search was completed examined the effects of PA interventions (of any type) lasting at least 6 months on delaying cognitive impairment in currently undiagnosed individuals (44). The authors concluded that there was insufficient evidence that PA could be used for dementia prevention. However, the heterogeneous nature of the interventions (e.g., with many including both PA and diet components) and cognitive test measures, small and underpowered studies, and inability to assess the clinical significance of cognitive test outcomes were common limitations of the included studies.

PA is also a possible approach for managing the symptoms of dementia, indicating that PA interventions may help to improve cognition in individuals with a clinical dementia diagnosis, including AD (45,47,49,50,52,84). For example, one meta-analysis of 18 RCT from 802 dementia patients reported an overall standardized mean difference of 0.42; this effect was also significant for individuals with AD (n = 8 studies) or in studies that combined AD and non-AD dementias (n = 7) (47). These positive effects were found for interventions that were both high-frequency and low-frequency PA (defined as an average of 213 or 93 $\text{min}\cdot\text{wk}^{-1}$, respectively), although it is important to note that consensus in the literature has not been reached regarding the effects of RCT of PA on reducing the risk for developing cognitive impairment many years later (43,44). Despite these findings, there is considerable heterogeneity in the cognitive assessment methods, description of the PA interventions, and a moderate risk for bias noted across studies.

In sum, given the significant heterogeneity in study design, lack of appropriate reporting of important PA parameters, and significant variability in cognitive tests used, there is *moderate evidence* that PA interventions improve cognitive performance in populations with a current diagnosis of dementia. However, there is *strong evidence* from observational prospective studies that engaging in greater amounts of PA is associated with a reduced risk of developing cognitive impairment.

Other clinical populations. There is *moderate* evidence, largely based on RCT, indicating that PA improves cognitive function in individuals with diseases or disorders that impair cognitive function, including ADHD (39), schizophrenia (58), MS (55), Parkinson's disease (56), and stroke (53,64). Results in MS are conflicting, but executive function, learning, memory, and processing speed show the largest effects (55). Individuals with Parkinson's disease show improvements in cognition after PA (56,57), with the largest effect sizes in general cognitive function and executive function. In schizophrenia, moderate- to vigorous-intensity PA interventions improve global cognition, working memory, and attention, with an average Hedges' g of 0.43 (58). Further, increases in brain volume and connectivity and elevated levels of serum BDNF are observed after 8 wk to 6 months of PA in individuals with schizophrenia (70). In patients with both acute and chronic stroke, PA improves global cognition, attention, memory, and visuospatial abilities (53,64).

In studies examining the effects of PA in ADHD, the effect sizes (Hedges' *g*) ranged from 0.18 to 0.77 in favor of PA improving cognitive performance (39–41). The cognitive domains most commonly affected included attention and executive function (e.g., inhibition and impulsivity) (39,41). Such findings have been extended to children with social, emotional, and behavioral disabilities (22). In autism spectrum disorder (ASD), Tan et al. (41) reported a small to moderate effect (Hedges' $g = 0.47$) for improvement in some aspects of cognition. However, the meta-analysis included children with ASD, ADHD, or both disorders (overall Hedges' $g = 0.24$), and as such, it is difficult to interpret the effects of PA on ASD alone (41).

The study of PA as an adjuvant treatment for cancer-related cognitive deficits is in its early stages (62,63). Myers et al. (63) reported that 7 of 11 RCT indicated improved cognitive function because of PA (aerobic, resistance, mindfulness-based exercise, or a combination of PA modes). However, only two of the studies used objective measures of cognition (63). The remaining trials used subjective cognitive outcomes (e.g., ratings of cognitive slips or failures in daily activities). A similar conclusion was reached by Furmaniak et al. (62).

There are also promising, but preliminary results, showing that cognition in individuals with HIV (59) or type 2 diabetes (60,61) was improved by PA. For example, a recent SR of 16 studies in HIV suggests that PA may influence cognitive health across a variety of self-report, executive function, memory, and processing speed measures (59). Similar benefits have been suggested for type 2 diabetes (60), but another review failed to establish a benefit of PA on cognitive health in this population (61).

Dose–response effects of PA. Unfortunately, little is known about the dose of PA—volume, duration, frequency, or intensity—needed to improve cognitive function. One meta-analysis in older adults (6) reported that larger effects were observed in RCT in which PA bouts lasted 46–60 min (compared with bout lasting 15–30 and 31–45 min) and in interventions lasting for at least 6 months. Similarly, Northey et al. (16) reported that moderate-intensity PA for 45–60 min per session was associated with benefits to cognition in adults over the age of 50 yr. Despite these preliminary findings, heterogeneity in the dose parameters across studies makes it difficult to draw firm conclusions about the frequency, duration, or intensity of activity needed to achieve cognitive improvements for any age-group or population.

Acute bouts of PA. Although the research described in the above sections has focused on the effects of longer-term (i.e., more than a single episode), or chronic, PA, it is important to acknowledge that a single brief session of PA (i.e., acute PA) also influences cognition. Studies demonstrate a small, transient improvement in cognition after the cessation of a single, acute bout of PA, with effect sizes (Cohen's *d*, Cohen's k, and Hedges' *g*) ranging from 0.014 to 0.67 across six SR and meta-analyses that summarized 12–79 studies (27,65–68). Reported effects were most consistent for domains of executive function (65–68), but significant benefits were also realized for processing speed, attention (although see Janssen et al. [27] for a discrepant finding), and memory (65,66,68). Although effects were observed across the life span, larger effects (Hedges' *g*) were realized for preadolescent children (0.54 [0.21–0.87]) and older adults (0.67 [0.40–0.93]) relative to adolescents (0.04 [−0.14 to 0.23]) and young adults (0.20 [0.07–0.34]) for executive function (67). Similar age differences in effect sizes were reported for other aspects of cognition.

Studies have reported that PA intensity affects cognition, although the pattern of effect has been inconsistent. Some findings suggest an inverted U–shaped curve, with moderate-intensity PA demonstrating a larger effect than light- and vigorous-intensity PA (66,68), and other studies indicate that very light-, light-, and moderate-intensity PA benefited cognition, but hard-, very hard-, and maximal-intensity PA demonstrated no benefit (65,80). The timing of the assessment of cognition relative to the cessation of the acute bout also demonstrated differential effects. PA bouts lasting 11–20 min demonstrated the greatest benefits, with bouts lasting less than 11 min or more than 20 min having smaller effects on cognition (65).

The investigation into biological or physiological pathways leading to changes in cognition after an acute bout of PA is in its early stages. Despite several empirical reports assessing acute PA effects on brain function using neuroimaging approaches (65,85), no SR or meta-analysis has appeared. However, a meta-analysis examining a blood-based biomarker has indicated higher concentrations of peripheral blood BDNF after an acute bout of PA (both aerobic and resistance bouts). Findings further indicated that increased BDNF concentrations were observed after longer bout durations (>30 min relative to ≤30 min) in those who had higher cardiorespiratory fitness (i.e., $>\dot{V}O_2$ peak), and that the findings were selective to males (although 75% of participants across studies were male) (74). Such findings suggest that BDNF may serve as a marker for the acute effects of PA on brain function in healthy adult males.

Overall, the findings strongly indicate that transient cognitive benefits may be derived after single acute bouts of PA. Such effects appear strongest for preadolescent children and older adults and for a PA dose of moderate intensity (65–68), with further evidence supporting 11–20 min in duration as the optimal range for enhancing cognitive function (65). These findings are important and relevant to the Physical Guidelines for Americans because they suggest that the benefits of engaging in PA can be seen immediately (i.e., after an acute bout) and accumulate over time (i.e., after more chronic PA behavior).

DISCUSSION

In regard to our first aim, we concluded from this umbrella review that there is overall *moderate evidence* that PA positively influences cognition in humans. The "moderate" grade emerged because there were noticeable gaps in some populations (e.g., adolescents, young, and middle-age adults) as well as significant heterogeneity in study designs, cognitive instruments used, lack of consistent reporting of blinding and adherence/compliance, and poor descriptions of whether the interventions were successful at maintaining moderate-intensity PA through the course of the intervention. Similarly, there is also considerable variability in the type and quality of PA measurements used across studies (86). Yet, despite these limitations and heterogeneity, we argue that the consistency of effects and of effect sizes across populations (16,26), durations of PA (including acute bouts), intensities, comorbid conditions (58), and ages (12) is truly remarkable and demonstrates that sufficient evidence exists to conclude that PA positively influences cognitive function in humans.

Our second aim was to examine whether there was a particular age or population that showed the strongest or weakest associations with PA. Most studies have been conducted in preadolescent children and older adults, so conclusions about the effects of PA across the life span are inherently limited because of the lack of high-quality data available in other age-groups. Nonetheless, this research in children and older adults suggests that benefits might be obtained across the life span. Yet, clearly more research is needed to determine the effects in other age-groups and to examine whether the magnitude of the benefit is greater at some ages (or in some populations) relative to others.

Our third aim was to examine whether there were cognitive domains especially susceptible to a PA intervention. Executive functions emerged as the most consistent cognitive domain affected. However, this conclusion should be interpreted cautiously. Many studies have prioritized the assessment of executive functions over that of other cognitive domains, and there is considerable variability in the type and quality of instruments used to test executive (and all other) cognitive domains. In addition, many of the instruments used to assess executive functioning are traditional neuropsychological tools that were primarily developed to aid in clinical diagnosis rather than to assess individual variation in normative cognitive functioning. As such, their sensitivity to detect changes as a function of an intervention (especially in the context of a normative sample) remains questionable.

Our fourth aim was to examine whether PA was associated with reducing risk for cognitive impairment in late adulthood. Here the prospective observational literature was unequivocal—engaging in greater amounts of PA was associated with a reduced risk of cognitive decline and impairment. It is important to note the methodological differences in the studies that make up this literature compared with the scientific literature discussed in other sections. In other sections of this review, the meta-analyses and SR were primarily focused on RCT, whereas in the context of MCI and dementia, the studies were prospective and observational and typically used self-reported measures of PA. Such methodological differences are important when reflecting on the strength and weaknesses of the literature examining cognitive outcomes as well as the populations, parameters, and measures that might be most sensitive to improvements with PA.

Finally, we asked whether there are parameters of PA (e.g., intensity) that are more important for the modulation of cognitive and brain health. Unfortunately, we conclude that there is insufficient data about the optimal dose parameters. Moderate-intensity PA is the most commonly reported dose, yet there is a consistent lack of clarity across studies about how moderate intensity is defined and measured. Several reports find that moderate-intensity interventions of longer durations had larger effect sizes than lighter intensity and shorter duration studies. Yet, the lack of specificity on dose and the variability in the dose delivered across studies, populations, and age ranges led to a conclusion of *grade not assignable*. Because of this between-study heterogeneity, similar ambiguity exists about the optimal dosage of PA necessary to achieve cardiovascular disease outcomes (87). Similarly, there are few studies examining the effect of sedentary behavior or light-intensity activity on cognitive outcomes as most RCT manipulate moderate-intensity activity and not light-intensity or sedentary behaviors. The most likely outcome is that the appropriate dose of PA will be moderated by age, population, and other factors sensitive to both cognitive function and PA.

Although most studies reported beneficial associations of PA on cognition, others reported less robust or even absent effects. In such instances, it is important to consider the factors that may have led to these discrepant findings. Not all SR and meta-analyses were conducted using the same set of guiding principles and criteria, with some using stronger theoretical and methodological approaches than others. Among the more poorly constructed SR and meta-analyses, one obvious limitation was the inclusion of empirical reports with poor adherence and compliance, imprecise measurement of PA, insensitive cognitive measurements, or poor descriptions of PA parameters. In addition, the considerable variability in how PA is measured and quantified across studies can often lead to heterogeneity of results and erroneous conclusions (85). Many of these design and measurement issues are not captured by PRISMA guidelines and, thus, could be influencing effect sizes and conclusions from meta-analyses and SR.

For more effective translation and adoption of PA, it is important to understand the possible mechanisms by which PA influences brain and cognition. Mechanisms can be conceptualized at multiple levels of analysis (88). On the molecular and cellular level, PA directly influences the expression of neurotransmitter and neurotrophic factors, which in turn influence synaptic plasticity and cell proliferation and survival. PA might also influence cognitive and brain health by modifying insulin/glucose signaling, oxidative stress, inflammatory pathways, hormonal regulation, or cerebrovasculature (2,83). Indeed, it is likely that all of these factors are enhancing different aspects of brain health. In addition, there might be multiple mediators at other levels of analysis. For example, PA might be modifying sleep behaviors, which in turn improve cognitive function. In short, there are many possible mechanisms by which PA influences brain health; more research across these diverse levels is required to better elucidate the primary pathways driving effects and how those pathways interact.

The meta-analyses and SR reviewed in this report predominantly focused on RCT or experimental manipulations

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of exercise (in the context of acute bout studies). However, this contrasts with many of the studies on MCI and dementia, which were observational and prospective. In these observational studies, PA was often measured by self-report, whereas in RCT, it was generally controlled and experimentally manipulated. These methodological differences could be contributing to the differences in effect sizes and consistency between these studies. It will be important for future research to conduct longer RCT with larger sample sizes and with sufficiently protracted post-intervention follow-up assessments over many years to determine whether engaging in a PA treatment reduces the incident rate of MCI and dementia.

Given the findings herein and the noted limitations, this field would benefit from a better understanding of the underlying mechanisms of these relationships, including central and peripheral biomarkers. Further, understanding of potential moderators of the PA–cognition relationship is needed, as reports suggest that the relationship may differ as a function of body composition, fitness level, sex, and health status, among other factors. Relatedly, reporting parameters of the intervention (i.e., compliance and adherence) is important to better understand the execution and quality of the intervention. One reason for the excitement surrounding PA effects on childhood cognition is the ability to link such findings to scholastic performance. Thus, there is a need to identify other ecologically valid outcomes, not only in children but also in adults who have the potential to strengthen the external validity of research on PA. Finally, future research needs greater consistency and harmonization in the cognitive instruments used.

In summary, there are positive effects of PA on a broad array of cognitive outcomes. This evidence comes from a variety of assessments that measure changes in brain structure and function, cognition, and applied academic outcomes. Accordingly, such findings may serve to promote better cognitive function in healthy individuals and to improve cognitive function in those experiencing certain cognitive and brain disorders. These findings may lead to more informed policies about using PA to improve and shape cognitive function across the life span.

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AMERICAN COLLEGE of SPORTS MEDICINE.
PRONOUNCEMENT

Physical Activity in Cancer Prevention and Survival: A Systematic Review

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ABSTRACT

MCTIERNAN, A., C. M. FRIEDENREICH, P. T. KATZMARZYK, K. E. POWELL, R. MACKO, D. BUCHNER, L. S. PESCATELLO, B. BLOODGOOD, B. TENNANT, A. VAUX-BJERKE, S. M. GEORGE, R. P. TROIANO, and K. L. PIERCY, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Physical Activity in Cancer Prevention and Survival: A Systematic Review. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1252–1261, 2019. **Purpose:** This article reviews and updates the evidence on the associations between physical activity and risk for cancer, and for mortality in persons with cancer, as presented in the *2018 Physical Activity Guidelines Advisory Committee Scientific Report*. **Methods:** Systematic reviews of meta-analyses, systematic reviews, and pooled analyses were conducted through December 2016. An updated systematic review of such reports plus original research through February 2018 was conducted. This article also identifies future research needs. **Results:** In reviewing 45 reports comprising hundreds of epidemiologic studies with several million study participants, the report found strong evidence for an association between highest versus lowest physical activity levels and reduced risks of bladder, breast, colon, endometrial, esophageal adenocarcinoma, renal, and gastric cancers. Relative risk reductions ranged from

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approximately 10% to 20%. Based on 18 systematic reviews and meta-analyses, the report also found moderate or limited associations between greater amounts of physical activity and decreased all-cause and cancer-specific mortality in individuals with a diagnosis of breast, colorectal, or prostate cancer, with relative risk reductions ranging almost up to 40% to 50%. The updated search, with five meta-analyses and 25 source articles reviewed, confirmed these findings. **Conclusions:** Levels of physical activity recommended in the 2018 Guidelines are associated with reduced risk and improved survival for several cancers. More research is needed to determine the associations between physical activity and incidence for less common cancers and associations with survival for other cancers. Future studies of cancer incidence and mortality should consider these associations for population subgroups, to determine dose–response relationships between physical activity and cancer risk and prognosis, and to establish mechanisms to explain these associations. **Key Words:** EXERCISE, CANCER RISK, CANCER SURVIVORSHIP

In 2018, 1,735,350 new cancer cases and 609,640 cancer deaths are projected to occur in the United States (1). In 2018, there are expected to be over 18 million cancer cases worldwide and over 9.5 million deaths (2). An estimated one in three Americans will be diagnosed with an invasive cancer over their lifetimes (1), and the number of cancer survivors is expected to exceed 20 million by 2026 (3).

Most cancers arise from a complex etiology involving genetic, environmental and lifestyle factors, and their interactions (4), and there is great need and opportunity for cancer prevention through lifestyle change. Increasingly, recognition of the role of host factors in cancer survival has supported the increased focus on lifestyle changes to improve these factors (5).

Decades of epidemiologic research have identified a physically active lifestyle as protective against the occurrence of some common cancers, but comprehensive reviews were lacking. The US Department of Health and Human Services 2018 Physical Activity Guidelines Advisory Committee (PAGAC) therefore addressed the following question: What is the relationship between physical activity and specific cancer incidence? (6) The PAGAC then investigated the presence and shape of dose–response relationships, whether the relationships varied by age, sex, race/ethnicity, socioeconomic status, or weight status, whether the relationship varies by specific cancer subtypes, and whether the relationship is present in individuals at high risk, such as those with familial predisposition to cancer. The PAGAC also examined the role of sedentary behaviors in the etiology of cancer (presented in Katzmarzyk et al.) (7).

In addition to the questions related to the primary prevention of cancer, the PAGAC also investigated the following question: Among cancer survivors, what is the relationship between physical activity and 1) all-cause mortality, 2) cancer-specific mortality, or 3) risk of cancer recurrence or second primary cancer? Further, the PAGAC considered the presence and shape of dose–response relationships, and whether the relationships vary by age, sex, race/ethnicity, socioeconomic status, or weight status. Finally, the PAGAC explored whether the relationships vary based on frequency, duration, intensity, type (mode), and how physical activity is measured. The PAGAC also considered current knowledge gaps and priorities for future research.

The purpose of this article is to summarize and update epidemiologic evidence on the associations between physical activity and risk of cancer incidence and survival as reviewed by the PAGAC (6).

METHODS

This systematic review is reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines (8). The systematic review followed an established protocol, and was registered at PROSPERO (CRD42018096729). The purpose of the PAGAC systematic review was to identify systematic reviews, meta-analyses, and pooled analyses that examined the relationship between physical activity and risks of cancer incidence, and risks of mortality among persons diagnosed with cancer. The purpose of the updated systematic search was to determine whether additional meta-analyses were published after the *2018 Physical Activity Guidelines Advisory Committee Scientific Report* (2018 Scientific Report) search, and whether individual source studies had been published after the dates of the latest meta-analyses.

Search Strategy and Selection Criteria

For the 2018 Scientific Report, systematic literature searches were conducted using PubMed, Cochrane, and CINAHL databases through December 2016 (see Supplemental Table 1, Supplemental Digital Content 1, 2018 Physical Activity Guidelines Advisory Committee search terms for epidemiologic literature on relationships between physical activity and risk for cancer, http://links.lww.com/MSS/B524; and Supplemental Table 2, Supplemental Digital Content 2, 2018 Physical Activity Guidelines Advisory Committee search terms for epidemiologic literature on relationships between physical activity and mortality in persons diagnosed with cancer, http://links.lww.com/MSS/B525). (6) Studies were considered potentially eligible if they were systematic reviews, meta-analyses, reports, or pooled analyses published in English through December 2016, and investigated the relationship between all types and intensities of physical activity and risk of invasive cancer of any type in adults, or the relationship between all types and intensities of physical activity and mortality in persons of any age with a diagnosis of cancer.

For the present article, updated systematic literature searches were conducted for the inclusive dates January 2016 through February 2018 using the same search terms, including systematic reviews, meta-analyses, and pooled analyses, and more recent original prospective cohort studies published after the inclusion dates for the cancer-specific systematic reviews/meta-analyses.

Data Extraction and Methodological Study Quality Assessment

The titles, abstracts, and full-text of the identified articles were independently screened, and data were abstracted by two reviewers. Disagreement between reviewers was resolved by discussion or a third person review. For the 2018 Scientific Report, data were extracted for systematic reviews, meta-analyses, and pooled analyses regarding years of source studies inclusion, numbers of studies, type of studies included (e.g., cohort, case-control), whether dose–response relationships were addressed, adjustment for confounders, evaluation of effect modifiers, and effect sizes and statistical significance. For the updated search, two reviewers independently screened the titles, abstracts, and full-text of the identified articles, and abstracted data to determine if new information would change the conclusions of the 2018 Scientific Report.

Grading of Evidence

Grading criteria were established before the review of the evidence was conducted (see Supplemental Table 3, Supplemental Digital Content 3, 2018 Physical Activity Guidelines Advisory Committee grading criteria, http://links.lww.com/MSS/B526). (6) These criteria were used to evaluate the epidemiologic evidence included in the systematic reviews and meta-analyses considered by the PAGAC members. The criteria included the applicability, generalizability, risk of bias and study limitations, quantity and consistency of the results across studies as well as the magnitude and precision of the effects. The PAGAC members undertook careful deliberations when reviewing the evidence and consensus on the grade to be assigned to each cancer site was sought through discussion among the PAGAC members in subcommittees and through regular reports during public PAGAC meetings.

RESULTS

For the 2018 Scientific Report, 45 systematic reviews, meta-analyses, or pooled analyses were reviewed related to associations between physical activity and cancer risk; 18 systematic reviews, meta-analyses, or pooled analyses were reviewed on the associations between physical activity and cancer survival (6). For the updated search, 145 systematic reviews, meta-analyses, or pooled analyses were identified as potentially relevant, of these, five were included in the updated review (exclusions were primarily because of not focusing on cancer etiology or survival). In addition, 25 original source articles were included, of 1256 identified from the updated search (exclusions were primarily for already being included in the meta-analyses or pooled analyses, or for not focusing on cancer etiology or survival).

In the studies included in the meta-analyses, systematic reviews, and pooled analyses, physical activity was measured by self-report, with different types of physical activity questionnaires. In many studies, participants were presented with a list of typical activities (e.g., walking, running, biking) and asked to indicate the frequency and duration of each activity. Other studies used more general questions about time spent in moderate- or vigorous-intensity activities. Most studies collected information on recreational activities, several also included occupational activities, and only a few included household activities. Some studies added up all of these activities to estimate total physical activity; most limited estimation of total physical activity to leisure time activity. Most of the meta-analyses estimated MET-hours per week of moderate-to-vigorous intensity physical activities where data were available, but the cutpoints for "highest" versus "lowest" activity levels varied across studies.

Most of the meta-analyses, as well as a large pooled study (9), were restricted to prospective cohort studies. However, for some of the rarer cancers, meta-analyses or pooled analyses did include case-control studies. Observational studies on cancer survival were restricted to prospective cohort studies of cancer survivors.

For the review of cancer survivors, PAGAC recognized that the definition of cancer recurrence was heterogeneous, rarely examined as an outcome, and therefore eliminated recurrence outcomes from this review. Furthermore, only postdiagnosis physical activity was included in the review of cancer survival.

Cancer Primary Prevention

The PAGAC evaluated 45 systematic reviews, meta-analyses, and pooled analyses comprising hundreds of epidemiologic studies with several million participants. The PAGAC determined that, when comparing the incidence among individuals in the highest category of physical activity with individuals in the lowest, strong evidence demonstrated reduced risks of bladder, breast, colon, endometrial, esophageal adenocarcinoma, renal and gastric cancers, with relative risk reductions ranging from approximately 10% to 20% (Table 1). The PAGAC also found moderate evidence that individuals in the highest category of physical activity had lower risk for lung cancer compared with those in the lowest category of physical activity. The number of available meta-analyses for each cancer type ranged from one to seven. Below are the main results from the most recent, or most

TABLE 1. 2018 physical activity guidelines advisory committee evidence on relationship between physical activity and risk of developing invasive cancer.

Cancer	Overall Evidence Grade	Approximate % RR Reduction	Dose–Response? Grade
Bladder	Strong	15%	Yes, moderate
Breast	Strong	12%–21%	Yes, strong
Colon	Strong	19%	Yes, strong
Endometrium	Strong	20%	Yes, moderate
Esophagus (adenocarcinoma)	Strong	21%	No, limited
Gastric	Strong	19%	Yes, moderate
Renal	Strong	12%	Yes, limited
Lung	Moderate	21%–25%	Yes, limited
Hematologic	Limited	Variable effect sizes	Not assignable
Head & Neck	Limited	Variable effect sizes	Not assignable
Ovary	Limited	8%	Yes, limited
Pancreas	Limited	11%	No, limited
Prostate	Limited	Variable effect sizes	Not assignable
Brain	Grade not assignable	Variable effect sizes	Not assignable
Thyroid	Limited	0	Not assignable
Rectal	Limited	0	Not assignable

comprehensive, meta-analyses reviewed for the 2018 Scientific Report (6) for individual cancers for which the PAGAC found strong or moderate grade evidence of an association between increased physical activity and reduced cancer risk (see also Table 1).

Bladder cancer. The PAGAC identified two meta-analyses/systematic reviews and one pooled analysis on the association between bladder cancer and physical activity. Of these reports, the most comprehensive was a 2014 meta-analysis that found bladder cancer risk was significantly lower for individuals engaging in the highest versus lowest categories of recreational or occupational physical activity level (relative risk [RR], 0.85; 95% confidence interval [CI], 0.74–0.98) (10). The other meta-analysis and pooled analysis found similar results (6). No new reports were identified in our updated search.

Breast cancer. A total of four meta-analyses/systematic reviews and two pooled analyses were identified that focused on physical activity and breast cancer risk. The most recent and comprehensive report was a 2016 meta-analysis that examined risk of breast cancer by all types of physical activity in which a statistically significant reduction for breast cancer incidence was found when comparing the highest versus the lowest amounts of all types of physical activity combined (odds ratio [OR], 0.88; 95% CI, 0.85–0.91) (11). When examining the associations by type of activity, these authors reported risk reductions for nonoccupational physical activity (OR, 0.88; 95% CI, 0.85–0.92 from 30 studies) and occupational physical activity (OR, 0.87; 95% CI, 0.83–0.90) based on 11 studies). Premenopausal and postmenopausal women had very similar risk reductions for highest versus lowest levels of physical activity (RR, 0.87; 95% CI, 0.78–0.96 and RR, 0.88; 95% CI, 0.85–0.91, respectively). The other meta-analyses and pooled analyses found similar results (6). The updated search identified two meta-analyses on the associations between physical activity and breast cancer risk, both of which reported reduced breast cancer risk comparing high versus low levels of physical activity for the total population (12,13), although one meta-analysis found no association of physical activity with breast cancer occurring before menopause (12). The updated search identified five publications of cohort studies (14–18) that investigated the associations of physical activity with breast cancer risk. One cohort study observed that strenuous activity was inversely and significantly associated with reduced breast cancer risk, particularly in certain molecular subtypes (14). Another study found that increased total, leisure, and occupational physical activity were inversely and significantly associated with reduced breast cancer risk (15). One study found that increased physical activity in childhood and teenage years was associated with lower risk for breast cancer development (16), whereas another found no association between physical activity between menarche and first pregnancy on later breast cancer risk (17). Finally, a study found statistically significant associations between high versus low levels of physical activity and reduced risk for postmenopausal breast cancer (18).

Colon cancer. A total of eight meta-analyses/systematic reviews and one pooled analysis on physical activity and colon cancer were identified in the PAGAC literature review. The most recent was a 2016 meta-analysis which reported that risk of colon cancer is significantly reduced for individuals engaging in the highest versus lowest categories of physical activity level (RR = 0.81, 95% CI: 0.83–0.93) (19). These findings were similar to those reported in the other meta-analyses (6). Our updated literature search yielded two additional meta-analyses, both of which supported these findings (20,21). The updated search also identified three original research reports of cohort studies that had not been included in any reviewed meta-analyses, which found that high versus low levels of physical activity decrease risk for colon cancer (22–24).

Endometrial cancer. The PAGAC used information from four meta-analyses/systematic reviews and one pooled analysis on physical activity and endometrial cancer risk with the most recent one published in 2015. That meta-analysis found a statistically significant reduction for endometrial cancer incidence when comparing the highest versus the lowest amounts of all types of physical activity combined (OR, 0.80; 95% CI, 0.75–0.85) (25). The meta-analysis further reported risk reductions for recreational (OR, 0.84; 95% CI, 0.78–0.91), occupational (OR, 0.81; 95% CI, 0.75–0.87), and household (OR, 0.70; 95% CI, 0.47–1.02) activities as well as for walking (OR, 0.82; 95% CI, 0.69–0.97). Risk was decreased with all intensity levels of physical activity (light, moderate-to-vigorous, and vigorous). The other meta-analyses and pooled analysis found similar results (6). Two cohort studies identified in the updated search found statistically significant associations between high versus low levels of physical activity and reduced risk of endometrial cancer (26,27).

Esophageal cancer. The PAGAC identified three meta-analyses/systematic reviews and one pooled analysis on physical activity and esophageal cancer risk. The most comprehensive was a 2014 meta-analysis (28) that included 24 individual studies of which nine were cohort and 15 were case-control studies. Risk of esophageal adenocarcinoma was statistically significantly reduced for individuals engaging in highest versus lowest levels of activity (RR, 0.79; 95% CI, 0.66–0.94). Conversely, physical activity was not related to risk of squamous cell carcinoma of the esophagus. The other meta-analyses and pooled analysis found similar results (6). No new reports were identified in our updated search.

Gastric cancer. There were five meta-analyses and one pooled analysis that reported on physical activity and its association with gastric cancer risk. In a 2016 meta-analysis (29), the risk of gastric cancer was statistically significantly reduced for individuals engaging in highest versus lowest levels of activity (RR, 0.81; 95% CI, 0.73–0.89). The other meta-analyses and pooled analysis found similar results (6). No new reports were identified in our updated search.

Renal cancer. The PAGAC identified one meta-analysis/systematic review and one pooled analysis of physical activity and renal cancer. The meta-analysis, published in 2013, reported that the risk of renal cancer was significantly lower for individuals engaging in the highest versus lowest categories of physical activity level (RR, 0.88; 95% CI, 0.79–0.97) (30). The pooled analysis found similar results (6). No new reports were identified in our updated search.

Lung cancer. The PAGAC used information from six meta-analyses and one pooled analysis on physical activity and risk of lung cancer. Using data from the most recent and comprehensive meta-analysis, the PAGAC found evidence of a 25% relative reduction in lung cancer risk with highest versus lowest levels of physical activity (RR, 0.75; 95% CI, 0.68–0.84) (31). The other meta-analyses and pooled analysis found similar results (6). The PAGAC could not rule out effect modification by tobacco use and therefore considered the evidence to be of a moderate grade. The updated search yielded two publications of cohort studies on physical activity and risk of lung cancer (32,33). Both studies assessed the association between physical activity and risk for lung cancer within categories of smoking (e.g., current, former, or never smoker), and both found lack of association of physical activity with reduced lung cancer in some or all smoking status categories.

Other cancers. For some other cancer sites, very few meta-analyses and systematic reviews had been published at the time of the original review for the 2018 Scientific Report. Hence, the PAGAC determined that limited evidence suggested an association between higher physical activity and decreased risks of hematologic, head and neck, ovarian, pancreatic, and prostate cancers. No grade could be assigned for brain cancer given the paucity of evidence. The PAGAC found limited evidence of no association of physical activity with risk of thyroid or rectal cancer. Finally, for all remaining cancer sites, there were no published studies that could be considered for this report.

Six publications on the associations between physical activity and risk of hematologic cancers were identified in the updated literature search. One study found that high versus low levels of physical activity were associated with reduced risk for myeloid neoplasms (myelodysplastic syndromes, acute myeloid leukemia, myeloproliferative neoplasms), chronic lymphocytic leukemia, small lymphocytic lymphoma, and mature B-cell lymphomas, but not plasma cell disorders (34). Three studies found varying associations of physical activity with non-Hodgkin lymphoma or B-cell non-Hodgkin lymphoma: one found no association with either (35), one finding a nonsignificant reduced risk of non-Hodgkin lymphoma (36), and one no association with B-cell non-Hodgkin lymphoma (37). Finally, one study of physical activity and risk of multiple myeloma was identified, which found no statistically significant associations (38). One report on the association between physical activity and risk of head and neck cancer found statistically significant decreases in risk with increasing hours per week spent in vigorous activity (39). The updated literature search identified two cohort studies of physical activity and ovarian cancer; one found no association between physical activity and reduced risk for ovarian cancer (40), and one suggested increased risk for ovarian cancer with high physical activity levels (41). Two publications presented results of cohort studies that examined the association between physical activity and risk of pancreatic cancer: one found a negative association in men but not women (42), whereas the other found a negative association in persons younger than 60 yr but not in older individuals (43).

In 2018, a meta-analysis of leisure-time physical activity and risk of prostate cancer was published, focusing on dose–response effects; it found no association of leisure time physical activity with risk of total, local, or advanced prostate cancer (44). Two cohort studies of prostate cancer risk in relation to physical activity were identified; one found no statistically significant associations between physical activity and risk (45), and one observed a statistically significant reduction only in risk of advanced prostate cancer in active versus inactive men (46).

The updated search also found publications focused on hepatobiliary, (47) carcinoid tumors of the small intestine (48), squamous cell skin cancer (49), and testicular cancers (50) that the PAGAC did not review for the 2018 Scientific Report. None provided enough evidence to reverse the PAGAC decision that evidence is lacking on the role of physical activity in risk for any of these cancers.

Associations of Physical Activity with Cancer by Dose–Response and Subgroups

Dose–response. A dose–response relationship between physical activity and specific cancer risk was evident for several cancers (Table 1), but given the inconsistent methods of measuring and categorizing physical activity levels in the various studies, meta-analyses, and pooled analyses, it was not possible to determine exact levels of physical activity that provide given levels of effect.

Cancer subtypes. Investigation by cancer subtype showed that increased physical activity is associated with reduced risk of breast cancer regardless of hormone receptor status and of colon cancer originating both proximally and distally. Conversely, although high levels of physical activity were associated with reduced adenocarcinoma of the esophagus, no statistically significant effect was observed for squamous cell cancer of the esophagus. Little information was available for other subtypes of cancer.

Population subgroups. Effects of physical activity on specific cancer risk were seen for both women and men for colon and renal cancers, whereas for other cancers, such as bladder, esophageal, gastric, lung, and pancreatic, differences by sex could not be ruled out. Little information was available on differences in physical activity effect on cancer risk by age or socioeconomic status. Few estimates were available for specific racial/ethnic groups other than whites. For several cancers, individuals of Asian ancestry appeared to have similar protection from physical activity as do non-Asian individuals. The pooled analysis suggested that, similar to whites, physical activity reduces risks of lung, colon, and breast cancers in African Americans (9). For some US populations (Latino, Native American, Pacific Islander), data are so sparse that systematic reviews, meta-analyses, and pooled analyses have not presented data on these racial/ethnic populations. Weight status affected the association between physical activity and risk of several cancers, including breast, endometrial, lung, ovarian, and thyroid, and possibly for esophageal adenocarcinoma and gastric cardia cancers.

Mortality in Persons Diagnosed with Cancer

The National Cancer Institute states that an individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life (51). Systematic reviews and meta-analyses on the relationship between physical activity and mortality among cancer survivors were available only for three cancers: breast, colorectal, and prostate cancer (Table 2).

Breast cancer. Data from six meta-analyses show a consistent inverse association between amounts of physical activity after diagnosis and cancer-specific and all-cause mortality in breast cancer survivors. Estimates from a 2015 meta-analysis of eight cohorts found that highest versus lowest levels of physical activity were associated with a 48% reduction in risk for all-cause mortality (RR, 0.52; 95% CI, 0.43–0.64) (52). A 2016 meta-analysis of 10 cohorts found that highest versus lowest levels of postdiagnosis physical activity were associated with a 38% reduction in risk of breast cancer-specific mortality (RR, 0.62; 95% CI, 0.48–0.80) (53). A pooled analysis addressed the association between meeting the 2008 Physical Activity Guidelines (54) recommended activity levels and breast cancer survival. The project found that engaging in ≥10 MET·h·wk^{-1} was associated with a 27% reduction in all-cause mortality (hazard ratio [HR], 0.73; 95% CI, 0.66–0.82) and a 25% reduction in breast cancer-specific mortality (HR, 0.75; 95% CI, 0.65–0.85) (55). The updated literature search identified two additional prospective cohort studies of breast cancer that examined the association between postdiagnosis physical activity and overall survival (56) and breast cancer-specific survival (57). In both of these cohort studies, higher levels of physical activity were associated with improved survival outcomes.

Colorectal cancer. Data from six meta-analyses found a consistent inverse association between amounts of physical activity after diagnosis and all-cause mortality and colorectal cancer-specific mortality in colorectal cancer survivors. A 2016 meta-analysis including seven cohort studies showed a 42% reduced risk of all-cause mortality in survivors with highest versus lowest levels of physical activity (RR, 0.58; 95% CI, 0.49–0.68) (58). A different 2016 meta-analysis of six cohorts found that highest versus lowest levels of postdiagnosis physical activity were associated with a 38% reduction in risk of colorectal cancer-specific mortality (RR, 0.62; 95% CI, 0.45–0.86) (53). One meta-analysis assessed dose–response using five cohort studies (59). In comparisons of less active to more active individuals, each 5, 10, or 15 MET·h·wk^{-1} increase in postdiagnosis physical activity was associated with a 15% (95% CI, 10%–19%), 28% (95% CI, 20%–35%), and 35% (95% CI, 28%–47%) lower risk for all-cause mortality. Results for colorectal cancer-specific mortality were virtually identical. The updated literature review identified two additional prospective cohort studies on physical activity and colorectal cancer survival. The first cohort study noted a 25% reduction in mortality associated with highest versus lowest levels of leisure time physical activity (HR, 0.75; 95% CI, 0.61–0.91) (60). The second cohort study found an approximate 50% reduced risk of overall mortality associated with highest versus lowest postdiagnosis total physical activity (HR, 0.53; 95% CI, 0.36–0.80) (61).

TABLE 2. 2018 physical activity guidelines advisory committee evidence on relationship.

Cancer	Evidence Grade	Approximate % RR Reduction
All-cause mortality		
Breast	Moderate	48%
Colorectal	Moderate	42%
Prostate	Limited	37%–49%
Cancer-specific mortality		
Breast	Moderate	38%
Colorectal	Moderate	38%
Prostate	Moderate	38%

Between physical activity and mortality in cancer survivors.

Prostate cancer. Data from three available meta-analyses show an inverse association between amounts of physical activity after diagnosis and cancer-specific mortality in prostate cancer survivors. Estimates from a 2016 meta-analysis of three cohort studies found that highest versus lowest levels of physical activity were associated with a 38% reduction in risk for prostate cancer-specific mortality (RR, 0.62; 95% CI, 0.47–0.82) (53). A review of the articles included in the systematic reviews indicates that highest versus lowest levels of total, recreational, nonsedentary occupational, and vigorous physical activity, as well as greater MET-hours per week or greater numbers of hours per week, were statistically significantly related to reduced risk for all-cause mortality (62–64). One additional cohort study that included assessment of physical activity that was done at least 1 yr postdiagnosis was found in the updated literature review (65). Higher levels of physical activity significantly reduced prostate cancer-specific mortality in this study.

The PAGAC assigned grades of only Moderate or lower to the associations for all three of these cancers, because of the considerable chance of reverse causation. That is, individuals who have cancer may feel more fatigue and be less physically active as a result.

DISCUSSION

We found strong evidence that physical activity reduces the risk of cancers of the breast, colon, endometrium, bladder, stomach, esophagus (adenocarcinoma) and kidney and moderate evidence for an association with lung cancer risk, with 10% to 20% reductions in RRs. We found limited evidence that physical activity is associated with reduced risk for prostate cancer overall. The evidence for an association with hematologic, head and neck, ovary, and pancreas cancers remains limited mainly because of the lack of research that has been done on these cancers. Furthermore, for brain cancer and other cancer sites not listed here, there is insufficient evidence to determine the nature of the association with physical activity at this time.

The epidemiologic evidence on the association between physical activity and survival after cancer is still emerging with preliminary results supporting 40% to 50% RR reductions for mortality for breast, colon, and prostate cancers with high levels versus low levels of physical activity.

There were several limitations to our work. The evidence relied on epidemiologic studies, with a lack of clinical trial evidence in either preventing cancer or improving survival in persons with cancer. Furthermore, most of the studies in persons diagnosed with cancer did not control adequately for treatment type or completion, nor for undiagnosed progression of disease, all of which can interfere with physical activity ability and therefore could have been major confounders of the relationships between physical activity and cancer survival.

Given the varying methods of physical activity ascertainment and classification in source articles and meta-analyses, the PAGAC could not determine the specific levels of physical activity that correspond to the reported levels of risk reduction. Furthermore, although dose–response associations were estimated in some articles and meta-analyses, the results varied such that exact dose–response relationships cannot be described even for individual cancers. Nevertheless, for several cancers, dose–response relationships were evident. Most importantly, there did not appear to be a lower threshold below which no effect was evident. In other words, almost any level of physical activity likely confers some benefit.

Almost all epidemiologic data on physical activity and cancer risk and survival focus on aerobic activity. The PAGAC, therefore, was only able to consider this type of activity. Furthermore, several of the studies provided information only on leisure time, recreational activity. The effects of occupational, household, transportation and other activities on cancer risk and survival have therefore not been established.

The data in meta-analyses were not consistent enough or classified with sufficient precision for the PAGAC to determine the exact nature of physical activity-cancer relationships across population subgroups, such as by age, race/ethnicity, socioeconomic status, or weight status. Nevertheless, where data were available, they pointed to likely benefit of physical activity across a wide range of population groups.

The PAGAC did not perform its own meta-analyses, and therefore relied on the methods of classifying data on physical activity, cancers, and covariates in the published meta-analyses. All physical activity data in the observational studies were collected via self-report, with resulting potential for measurement error due to recall error and reporting bias. Very few observational studies have included device-based measures of physical activity.

The PAGAC recommended future research in the areas of cancer prevention. There is a need for large prospective epidemiologic studies of the associations of physical activity on risk for specific cancers that have not been adequately studied. More epidemiologic studies of effects of physical activity on risk of cancer in specific age, racial, ethnic, and socioeconomic groups are needed. The methods of data collection and classification of activity amount varied across studies. Greater consistency and data harmonization across studies is needed, so that dose–response relationships can be established. Defining dose–response relationships will be critical to develop physical activity guidelines for cancer prevention. Most of the data available in meta-analyses and pooled analyses were on aerobic physical activity, typically added together into total leisure-time activity. Therefore, there is need for epidemiologic studies to determine effects of specific types of physical activity on cancer risk and survival.

Finally, to reduce the chance of confounding and error in testing the effect of physical activity on cancer risk, there remains a need for randomized controlled clinical trials testing exercise effects on cancer incidence. Randomized trials in high-risk individuals could be more cost-effective, as trials with smaller sample sizes or shorter follow-up durations are more feasible than trials in the general, at-risk population. Furthermore, randomized clinical trials testing the effects of physical activity on biomarkers of cancer, as well as animal models, have provided important mechanistic information to support the relationship between physical activity and reduced cancer risk (66–69).

For cancer survival, the PAGAC identified several research needs. Because of the increasing length of cancer survivorship, there is need to continue long-term follow-up of cohorts of cancer survivors, with repeated self-report and device-based measures of physical activity, to determine long-term associations of physical activity with recurrence and survival. In addition, continued follow-up of established large epidemiologic cohorts will allow for identification of individuals with less common cancers, to determine associations between physical activity level and survival from these other cancers. Given the strong potential for confounding by cancer treatment, stage, and progression, there is need for randomized controlled trials and cohort studies of physical activity and cancer survival and recurrence, aimed at eliminating effects of possible confounders. There is also need for prospective cohort studies and randomized controlled trials to determine effects of physical activity on cancer survival and recurrence in understudied groups, such as survivors from diverse ages, races, ethnicities, and socioeconomic groups; individuals with metastatic cancer; individuals with cancers other than colorectal, prostate, and female breast cancer; and patients treated with cardiotoxic drugs, radiotherapy, and hormonal treatments. Although the original and updated searches identified only studies of cancers in adults, the authors are aware that at least one study in childhood survivors was published after our updated search was completed (70); more research is needed in this population. Of note, two ongoing randomized clinical trials will provide more definitive data on the dose and type of physical activity needed for improved survival in persons diagnosed with colon and prostate cancers (71,72).

In summary, levels of physical activity recommended in the 2018 guidelines (73) are associated with reduced risk for several cancers, notably some of the most common cancers. The PAGAC also recognizes the potential benefit of these levels of physical activity in improving survival for individuals diagnosed with some common cancers. Given the significant impact of cancer on quality of life, financial stability, and mortality, the reduction in risk, and improved prognosis, of common cancers from high levels of physical activity could have a large public health impact. Substantial reductions in the incidence of cancer, mortality from cancer, and cancer-related costs would be expected if currently inactive individuals became more physically active. Therefore, the PAGAC suggests that all individuals should be encouraged to engage in recommended levels of physical activity to reduce risk for developing cancer and for improving cancer prognosis.

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PRONOUNCEMENT

Physical Activity and the Prevention of Weight Gain in Adults: A Systematic Review

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ABSTRACT

JAKICIC, J. M., K. E. POWELL, W. W. CAMPBELL, L. DIPIETRO, R. R. PATE, L. S. PESCATELLO, K. A. COLLINS, B. BLOODGOOD, and K. L. PIERCY; FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Physical Activity and the Prevention of Weight Gain in Adults: A Systematic Review. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1262–1269, 2019. **Purpose:** To conduct a systematic literature review to determine if physical activity is associated with prevention of weight gain in adults. **Methods:** The primary literature search was conducted for the 2018 Physical Activity Guidelines Advisory Committee and encompassed literature through June 2017, with an additional literature search conducted to include literature published through March 2018 for inclusion in this systematic review. **Results:** The literature review identified 40 articles pertinent to the research question. There is strong evidence of an association between physical activity and prevention of weight gain in adults, with the majority of the evidence from prospective cohort studies. Based on limited evidence in adults, however, there is a dose–response relationship and the prevention of weight gain is most pronounced when moderate-to-vigorous intensity physical activity (≥3 METs) is above 150 min·wk^{-1}. Although there is strong evidence to demonstrate that the relationship between greater time spent in physical activity and attenuated weight gain in adults is observed with moderate-to-vigorous intensity physical activity, there is insufficient evidence available to determine if there is an association between light-intensity activity (<3 METs) and attenuated weight gain in adults. **Conclusions:** The scientific evidence supports that physical activity can be an effective lifestyle behavior to prevent or minimize weight gain in adults. Therefore, public health initiatives to prevent weight gain, overweight, and obesity should include physical activity as an important lifestyle behavior. **Key Words:** OBESITY, OVERWEIGHT, EXERCISE, PHYSICAL ACTIVITY, WEIGHT GAIN

Excessive body weight is associated with numerous negative health outcomes that include, but are not limited to cardiovascular disease, diabetes, some forms of cancer, and musculoskeletal disorders (1,2). Recent estimates indicate that the prevalence of overweight (body mass index [BMI], 25–≤30 kg·m^{-2}) in the United States for adult men is approximately 39% and 27% for adult women (3), with estimates of obesity (BMI ≥30 kg·m^{-2}) for men being approximately 38% and for women being 40% (4).

Given the high prevalence of overweight and obesity, there is an ongoing need for effective treatment and prevention methods. The 2008 Physical Activity Guidelines Advisory Committee (PAGAC) Report concluded physical activity was associated with modest weight loss of approximately ≤3 kg, prevention of weight gain following weight loss, and reductions in total

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and regional adiposity (5). Moreover, professional organizations have also identified physical activity as an important behavior that contributes to body weight regulation (6–8).

Evidence from the CARDIA Study has demonstrated that the average weight gain across a 25-yr period was approximately 0.5 to 0.8 $kg \cdot yr^{-1}$. This magnitude of weight gain has the potential to lead to overweight and obesity as individuals transition from young (18–30 yr of age) to middle-age (43–55 yr of age) adults (9), and therefore weight gain prevention efforts may be of importance. The 2018 PAGAC, recognizing the public health importance of the prevention of weight gain, examined the existing literature regarding the relationship between physical activity and prevention of weight gain in adults (10). In addition, within the context of this overall examination of the literature, the PAGAC also examined whether the relationship between physical activity and weight gain varied by age, sex, race/ethnicity, socioeconomic status, or weight status, and whether the relationship varied based on levels of light (<3 METs: moderate [3 to <6 METs], vigorous [≥6 METs], or the combination of moderate-to-vigorous [≥3 METs]) physical activity.

METHODS

The overarching methods used to conduct systematic reviews informing the 2018 PAGAC Scientific Report are described in detail elsewhere (10,11). The searches were conducted using electronic databases (PubMed®, CINAHL, and Cochrane). An initial search to identify systematic reviews, meta-analyses, and pooled analyses examining the relationship between physical activity and weight gain did not identify sufficient literature to answer the proposed research question. Therefore, a *de novo* search of original research was conducted through June 2017 for the 2018 PAGAC Report. This *de novo* search of original research was expanded to include literature though March 2018 for inclusion in this manuscript. Eligibility criteria for the *de novo* search included original research studies published in English; study designs that included randomized trials and prospective cohort studies; studies that were at least 1 yr in duration; and outcomes of weight, weight change, weight control, weight gain, weight maintenance, weight regulation, weight stability, and weight status. Physical activity included all types and intensities of physical activity including lifestyle activities, leisure activities, and sedentary behavior. The full search strategy is available at https://health.gov/paguidelines/second-edition/report/supplementary_material/pdf/Cardiometabolic_Q1_Weight_Status_Evidence_Portfolio.pdf.

The titles and abstracts of the identified articles were independently screened by two reviewers who were members of the 2018 PAGAC. The full-text of relevant articles were also reviewed by at least two members of the PAGAC to identify and include those meeting the inclusion criteria. Discrepancies in article selection or data abstractions were resolved by discussion between the two reviewers or by a third reviewer, if needed, to achieve agreement. The protocol for this review was registered with the PROSPERO database registration (CRD42018096694).

For the 2018 PAGAC Report, 33 original studies published through June 2017 that examined the relationship between physical activity and weight gain were included as sources of evidence (12–44). The additional search conducted through March 2018 resulted in an additional seven original research studies being included in the literature review (45–51). Thus, 40 original research studies were included, and a summary of the articles included in this review is shown in Figure 1.

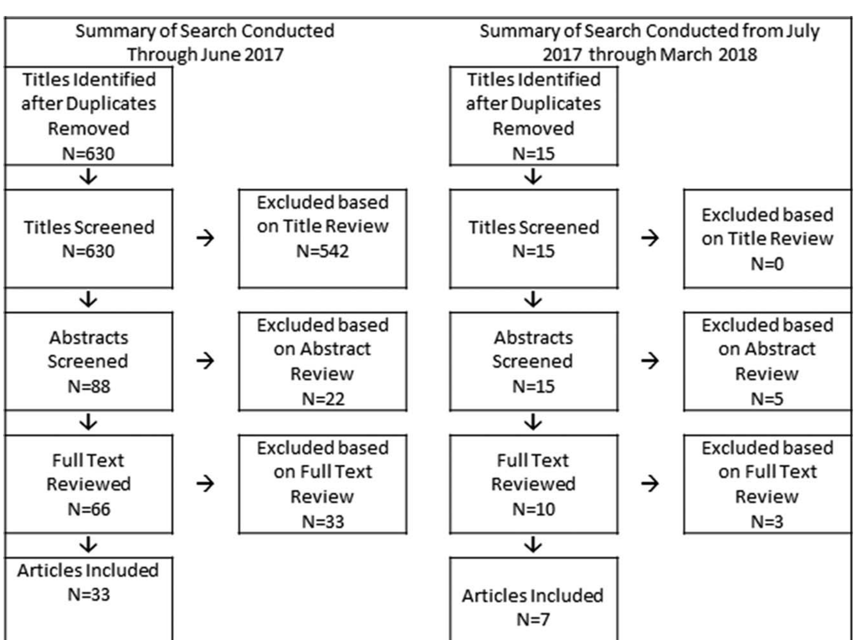


FIGURE 1—Summary of literature search.

RESULTS

The studies reviewed provided substantial information to allow for evaluation of an overall association between physical activity and either weight gain, increase in BMI, or development of obesity. Although data were available to examine whether these associations were influenced by sex and age, very limited information was provided within the studies reviewed to examine the influence of race/ethnicity, socioeconomic status, initial weight status, or dietary intake and eating behaviors, on the relationship between physical activity and weight gain. Moreover, although substantial information was provided for moderate-to-vigorous intensity physical activity, few studies provided data for light-intensity physical activity.

Overall Association between Physical Activity and Attenuation of Weight Gain

Most (n = 29) of the studies showing an association between greater physical activity and attenuated weight gain were prospective cohort studies (12,13,15,16,18,20–22,25–29,32–34,36–44,49–51), with follow-up periods ranging from 1 to 22 yr and one study involving 6-yr follow-up after a block randomized controlled trial (14). For the studies not showing an effect (n = 11), cohort studies had a follow-up period ranging from 1 to 20 yr (17,19,23,24,30,31,35,45–48), with three of these studies having follow-up periods of two or fewer years (19,22,23,31), and one was a secondary analysis of data from a randomized study (24).

Of studies showing an inverse association with weight gain, eight studies assessed physical activity at one time point to examine the association with weight gain (15,20,25,26,29,33,39,51), whereas 21 studies assessed physical activity at two or more time points to allow physical activity to be examined using individual time points or between time points across the observation period (12–14,16,18,21,22,27,28,32,34,36–38,40–44,49,50). There were studies that examined the association with weight gain but did not show an effect, with some studies measuring physical activity at one time point (19,30,31,45–48) and other studies measuring physical activity at multiple time points (17,23,24,35).

Physical Activity Volume and Dose–Response

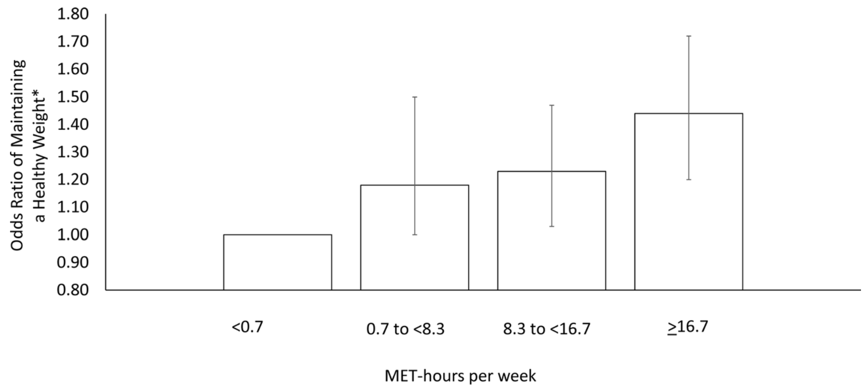
There were 12 studies that reported data for the volume of physical activity where the effect on prevention of weight gain was observed (15,18,25,27,28,32,34,38,39,41,44,52). The evidence, however, for a specific volume threshold of physical activity that is associated with prevention of weight gain in adults is inconsistent. For example, some evidence supports the need to achieve at least 150 min·wk^{-1} of moderate intensity physical activity (27,28) or achieve 10,000 steps per day (41) to minimize weight gain or to prevent increases in BMI. However, other studies support greater amounts physical activity to prevent or minimize weight gain, with some studies reporting this effect with greater than 150 min·wk^{-1} at a moderate intensity (3 METs, similar to brisk walking) (≥450 MET·min·wk^{-1} at a 3-MET intensity) (34), at least 167 min·wk^{-1} (≥500 MET·min·wk^{-1}) (18,39), or more than 300 min·wk^{-1} (>900 MET·min·wk^{-1}) (15,25,32).

The amount of physical activity necessary to prevent weight gain and the development of obesity may depend on the intensity of the physical activity. For example, at least 1 h·wk^{-1} of moderate intensity physical activity was shown to reduce the risk of developing obesity in both normal weight women (incidence rate ratio [IRR], 0.81; 95% confidence interval [CI], 0.71–0.93) and overweight women (IRR, 0.88; 95% CI, 0.81–0.95) (37); however, a lower duration of physical activity may be necessary for vigorous intensity rather than moderate intensity. For example, Williams and Wood (44) have reported that running equivalent to 4.4 km·wk^{-1} (~2.8 mile·wk^{-1} (~28 min·wk^{-1} at a 10-min·mile^{-1} pace) in men and 6.2 km·wk^{-1} (~3.8 mile·wk^{-1} (~38 min·wk^{-1} at a 10-min·mile^{-1} pace) in women may be sufficient to prevent weight gain associated with aging.

Preventing or minimizing weight gain. Some of the reviewed studies provided data on the dose–response relationship of physical activity and weight gain (15,25,34,39). Sims et al. (39) reported a trend (P < 0.08) for minimized weight gain in women engaging in more than 8.3–20 MET·h·wk^{-1} (>167–400 min·wk^{-1} at a 3-MET intensity) or more than 20 MET·h·wk^{-1} (>400 min·wk^{-1} at a 3-MET intensity) of physical activity, compared with those engaged in less than 1.7 MET·h·wk^{-1} (<33 min·wk^{-1} at a 3-MET intensity). A physical activity volume of 1.7–8.3 MET·h·wk^{-1} (33–≤167 min·wk^{-1} at a 3-MET intensity) was not protective against weight gain.

Two studies provide evidence of a dose–response to prevent weight gain of approximately 2 kg. Moholdt et al. (34) identified four groups based on physical activity ("Inactive": no leisure-time physical activity; "Below Recommended": active <150 min·wk^{-1} in moderate intensity or <60 min·wk^{-1} in vigorous intensity leisure-time physical activity; "Recommended": active at 150 min·wk^{-1} in moderate intensity or 60 min·wk^{-1} in vigorous intensity leisure-time physical activity; "Above Recommended": active >150 min·wk^{-1} in moderate intensity or >60 min·wk^{-1} in vigorous intensity leisure-time physical activity). For men, compared with those in the "Inactive" category, the risk of gaining ≥2.3 kg was 0.97 (95% CI, 0.87–1.08) for those in the "Recommended" category and 0.79 (95% CI, 0.69–0.91) for those in the "Above Recommended" category. A similar pattern was observed in women, with the risk of 0.97 (95% CI, 0.88–1.07) for those in the "Recommended" category and 0.69 (95% CI, 0.59–0.82) for those in the "Above Recommended" category. Gebel et al. (25) reported a 10% reduction in the odds of ≥2 kg weight gain with 300 min·wk^{-1} or more of moderate-to-vigorous intensity physical activity compared with less than 150 min·wk^{-1} of moderate-to-vigorous intensity physical activity; however, 150 to 249 min·wk^{-1} was not predictive of weight change.

Blanck et al. (15) reported relatively high levels of physical activity may be needed to reduce the odds of gaining 10 or more pounds (≥4.5 kg). In women, with the reference group defined as those with an activity level of 0 to <4 MET·h·wk^{-1},



*Maintaining a Healthy Weight defined as Body Mass Index of ≥18.5 to <25 kg/m².

Source: Adapted from data found in Brown et al., 2016.

FIGURE 2—Odds of maintaining a healthy weight by level of physical activity.

the odds of gaining 10 or more pounds (≥4.5 kg) was significantly lower with ≥18 MET·h·wk^{-1} (0.88; 95% CI, 0.77–0.99). Compared to the reference, however, the odds of gaining this magnitude of weight did not differ with 0 MET·h·wk^{-1} (1.01; 95% CI, 0.82–1.01), 4 to less than 10 MET·h·wk^{-1} (0.93; 95% CI, 0.80–1.08), and 10 to less than 18 MET·h·wk^{-1} (0.99; 95% CI, 0.87–1.14).

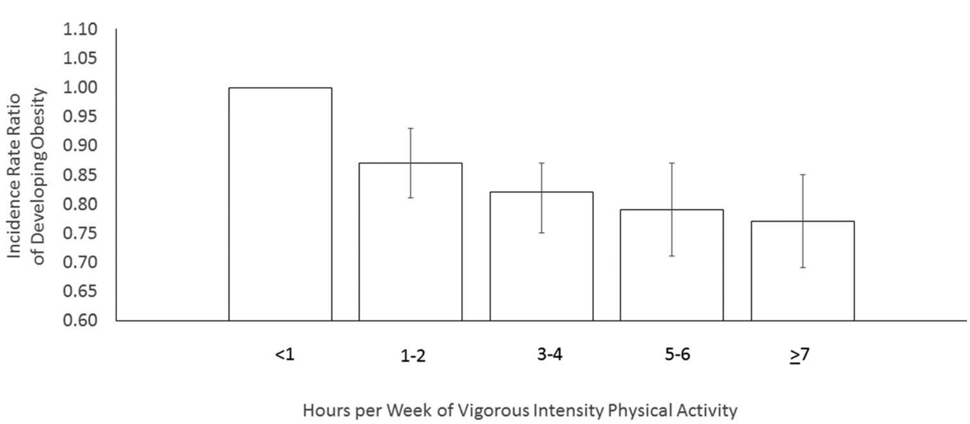
Maintaining a healthy weight. Brown et al. (18) report on a dose–response relationship for physical activity and the odds of maintaining a healthy weight (i.e., BMI of ≥18.5 to <25 kg·m^{-2}). Compared with less than 0.7 MET·h·wk^{-1}, the odds ratio for maintaining a normal BMI was 1.18 (95% CI, 1.00–1.40) for 0.7 to less than 8.3 MET·h·wk^{-1}, 1.23 (95% CI, 1.03–1.47) for 8.3 to less than 16.7 MET·h·wk^{-1}, and 1.44 (95% CI, 1.20–1.72) for 16.7 or more MET-h·wk^{-1} (18) (Fig. 2).

Overweight or obesity. Su et al. (50) reported on the dose–response relationship leisure-time physical activity (MET·h·wk^{-1}) and the odds of overweight and obesity in the China Health and Nutrition Survey. The reference category was defined as ≥15 MET·h·wk^{-1}, which was then compared to 7.5 to <15 MET·h·wk^{-1}, >0 to 7.5 MET·h·wk^{-1}, and 0 MET·h·wk^{-1}. In men, the odds ratio of overweight and obesity were 1.0, 1.54 (95% CI, 0.97–1.99), 1.88 (95% CI, 1.15–2.51), and 2.01 (95% CI, 1.41–3.03) in these physical activity categories, respectively. For women, the odds ratio of overweight and obesity were 1.0, 1.24 (95% CI, 0.94–1.62), 1.63 (95% CI, 1.29–2.21), and 1.69 (95% CI, 1.37–2.27) in these physical activity categories, respectively.

Rosenberg et al. (37) reported on the dose–response relationship for vigorous intensity physical activity (e.g, basketball, swimming, running aerobics) and the likelihood of developing obesity. In women with normal weight and overweight, when compared to less than 1 h·wk^{-1}, the incidence of developing obesity was significantly reduced in a graded manner, with vigorous intensity activity of 1 to 2 h·wk^{-1} (0.87; 95% CI, 0.81–0.93), 3 to 4 h·wk^{-1} (0.82; 95% CI, 0.75–0.88), 5 to 6 h·wk^{-1} (0.79; 95% CI, 0.71–0.87), and 7 h·wk^{-1} or more (0.77; 95% CI, 0.69–0.85) (Fig. 3).

Evidence on Specific Factors

Age. In general, the studies in which a significant inverse association between physical activity and weight gain was



Source: Adapted from data found in Rosenberg et al., 2013.

FIGURE 3—IRR of developing obesity at various levels of vigorous physical activity.

observed encompassed a broad age range that included young, middle-age, and older adults. Six studies analyzed the data specifically by age, with the evidence suggesting attenuation of this association with increasing age in some (32,33,39,42), but not all studies (34,43).

Macinnis et al. (33) reported a significant inverse association between physical activity and magnitude of weight gain across a mean follow-up of approximately 12 yr in adults ages 40 to 49 yr, with this association not observed in adults ages 50 to 59 yr or 60 to 69 yr. Williams (42) reported that running attenuated weight gain in men younger than 55 yr of age and in women younger than 50 yr of age.

These results are not consistent with the finding of Moholdt et al. (34), who reported that physical activity was significantly associated with reduced odds of gaining ≥2.3 kg in both men and women, but the odds of a ≥2.3 kg weight gain in physically active adult men was significant for those 40 yr or older but not in those younger across a follow-up period of approximately 22 yr. In contrast, the inverse association between physical activity and odds of a ≥2.3 kg weight gain was observed across the age spectrum (younger than age 40 yr, age 40 to 59 yr, and age 60 yr and older) in women.

Williams and Thompson (43) reported that the weight gain associated with the cessation of running, across a follow-up period of approximately 7 yr, was consistent between men less than 45 yr of age and 45 yr or older. However, among women, weight gain was greater in women ages 45 yr or older compared with their younger counterparts. Two studies examined the association between physical activity and weight gain only in women. Lee et al. (32) examined data from the Women's Health Initiative study and reported a trend for greater weight gain, across a follow-up period of approximately 13 yr, with lower levels of activity in women younger than age 64 yr, but not in women ages 65 yr and older. Similar findings were reported by Sims et al. (39) in a study of post-menopausal women ages 50 to 79 yr, which showed attenuated weight gain across a follow-up period of 8 yr with greater amounts of physical activity in women ages 50 to 59 yr, but not in those of ages 60 to 69 yr or 70 to 79 yr.

Sex. The studies in which a significant inverse association between physical activity and weight gain was observed included either women (12,14,15,18,20,26,29,32,37,39) or both men and women (13,16,21,22,25,27,38,41–44,49,50). Of the studies that included both men and women, some did not analyze the data separately by sex (16,22,25,27,38,41). Of the studies that presented findings separately by sex, some reported that the association between physical activity and weight gain was consistent for both men and women (13,21,28,33,34,36,40,42–44,50).

Race/ethnicity. In general, the studies in which a significant inverse association between physical activity and weight gain was observed encompassed diverse races and ethnicities. When specified, for studies conducted based on adults residing in the United States, a broad range of races and ethnicities appeared to be represented in the study samples (16,22,28,29,39) or the sample included only black/African Americans (37,45). Some of the studies were conducted in countries outside of the United States, including Australia (18,25,33,41), China (50), France (40), Great Britain (36), Norway (34), South Africa (26), Spain (13), Sweden (21), and the Philippines (12,20). Although some studies included race or ethnicity as a covariate in the analyses, none of them presented data separately by race or ethnicity to allow for comparisons.

Socioeconomic status. Of those studies showing an inverse association between physical activity and weight gain, some studies provided a measure of socioeconomic status as a descriptive variable or as a covariate in analyses. Only one study isolated the effect of socioeconomic status on the association between physical activity and weight gain, and it was reported that socioeconomic status attenuated this association even though it remained statistically significant (16).

Weight status. The studies in which a significant inverse association between physical activity and weight gain was observed included adults of normal, overweight, and obese weight status. However, studies do not show a consistent pattern of findings that favor one category of initial weight status over others. Some studies reported that the association did not differ by weight status (39,53), some reported the association to be more favorable in adults who had normal weight versus overweight or obesity (15,29,32), and some studies reported results showing a more favorable pattern in adults with overweight or obese compared to those with normal weight (13,34).

Physical Activity Intensity and Mode

In the studies in which a significant inverse association between physical activity and weight gain was reported, data were reported for a number of physical activity domains. These included leisure-time/recreational activity, occupational activity, household activity, walking, and total steps of physical activity, with some studies also reporting on various intensities of physical activity (light, moderate, vigorous, moderate-to-vigorous).

Total leisure-time physical activity was consistently inversely associated with weight change across the studies reviewed (15,21,32,33,36,39,40). Studies reporting on moderate intensity (13,22), vigorous intensity (16,26,27,33,37,42–44), and moderate-to-vigorous intensity (18,25–29,34,38) physical activity showed consistent patterns of inverse associations with weight gain. Light-intensity physical activity, however, was not associated with prevention of weight gain (22,23,27).

Walking was not consistently associated with change in weight or BMI (26,33) or with the incidence of developing obesity (37). Smith et al. (41), however, reported that achieving 10,000 steps or more per day attenuated weight gain compared with not achieving 10,000 steps per day. These results may suggest that high volumes of walking need to be achieve to attenuate weight gain.

Studies also examined occupational and household activity. Moderate-to-vigorous occupational activity was inversely associated with weight gain (12,33), but not with light-intensity occupational activity (12). In studies of household activity, the evidence does not support that this mode of physical activity minimizes weight gain (20,33).

DISCUSSION

Summary and public health impact. The evidence contained in this review expands the information contained in the 2008 PAGAC Report (5) by summarizing the literature related to the association between physical activity and weight gain, incidence of obesity, and maintenance of BMI within a range of ≥18.5 to <25 kg·m^{-2}. The literature includes primarily evidence from prospective observational studies that met the inclusion criteria for this review. The evidence supports the following conclusions:

1. There is strong evidence to demonstrate a relationship between greater amounts of physical activity and attenuated weight gain in adults. There is also some evidence to support that this relationship is most pronounced when physical activity exposure is above 150 min·wk^{-1}.
2. There is limited evidence to support a dose–response relationship between physical activity and the risk of weight gain in adults.
3. There is limited evidence suggesting that the relationship between greater amounts of physical activity and attenuated weight gain in adults varies by age, with the effect diminishing with increasing age.
4. There is moderate evidence to indicate that the relationship between greater amounts of physical activity and attenuated weight gain in adults does not appear to vary by sex.
5. There is insufficient evidence available to determine whether the relationship between greater amounts of physical activity and attenuated weight gain in adults varies by race/ethnicity, socioeconomic status, or initial weight status.
6. With regard to intensity of physical activity, there is strong evidence to demonstrate that the relationship between greater time spent in physical activity and attenuated weight gain in adults is observed with moderate-to-vigorous intensity physical activity. There is, however, insufficient evidence available to determine if there is an association between light-intensity activity and attenuated weight gain in adults.

Public health impact. Weight gain that results in overweight or obesity is associated with increased risk for numerous chronic conditions. This is a significant health concern in the United States due to the high prevalence of both overweight and obesity. Thus, while it is important to focus on effective treatments for overweight and obesity, there is also a need to implement effective public health strategies to prevent the approximately 0.5–1 kg of annual weight gain in adults (9) and the onset of both overweight and obesity. The scientific evidence supports that physical activity can be an effective lifestyle behavior to prevent or minimize weight gain in adults. Therefore, public health initiatives to prevent weight gain, overweight, and obesity should include physical activity as an important lifestyle behavior.

Needs for future research. The evidence from this review supports that physical activity contributes to the prevention of weight gain and obesity, and the maintenance of a healthy body weight. The review of evidence also has identified a number of areas for additional research, and these research needs are described below.

Conduct longitudinal research in observational or randomized controlled trials that include objective measures of physical activity and that are specifically designed to examine the association between physical activity and prevention of weight gain. The majority of the studies included in this review were from observational prospectives studies with physical activity measured using questionnaires or other self-reported measures. Thus, confirming these findings with additional study designs and with objective measures of physical activity would provide clarity on the role of physical activity to prevent weight gain and obesity.

Conduct longitudinal research on lower exposure levels of physical activity to allow for an enhanced understanding of the dose–response associations between physical activity and weight gain across a wider spectrum of exposure. There is limited evidence available on the effect of physical activity of less than 150 min·wk^{-1} on prevention of weight gain. This knowledge will inform public health recommendations regarding the minimum physical activity exposure that can be effective for preventing weight gain or the development of obesity.

Conduct large research trials with ample sample sizes to allow for stratum-specific analyses to determine whether the influence of physical activity on the prevention of weight gain varies by age, sex, race/ethnicity, socioeconomic status, or initial weight status. Based on the literature reviewed, there is limited evidence on whether the influence of physical activity on weight gain varies by age, sex, race/ethnicity, socioeconomic status, weight status. Moreover, little is known about whether the influence of physical activity varies when the exposure to physical activity is consistent across individuals with different demographic characteristics. Thus, adequately designed and statistically powered studies are needed to allow for comparisons across the various strata of demographic characteristics to examine whether the influence of physical activity on weight gain and obesity prevention varies by these factors. This may require multiple studies to be conducted that allow for these characteristics to be examined in a feasible manner rather than one large comprehensive study.

Conduct experimental research on varying intensities (light, moderate, and vigorous) of physical activity, while holding energy expenditure constant, to determine the independent effects of physical activity intensity on weight gain. Limited evidence is available on whether the influence of physical activity on weight gain is consistent across intensities (light, moderate, vigorous) when total energy expenditure is held constant, and only limited evidence is available on the influence of light-intensity physical activity on weight gain. This information will inform public health recommendations regarding whether the emphasis to prevent weight gain should be on total volume of physical activity regardless of intensity, or whether the emphasis needs to be on volume of physical activity that is performed at a specific intensity.

Conduct observational and experimental research that quantifies energy intake and eating behavior to determine whether these factors influence the association between physical activity and weight gain. The majority of the literature reviewed either did not report that diet and eating behavior were measured or considered in the analysis. It is important to understand whether the physical activity exposure necessary to limit weight gain will vary based on diet or eating behavior patterns.

Conduct studies to examine the relationship of physical activity to other indices of unhealthy weight or fat gain. This review used the following search terms: weight, weight change, weight control, weight gain, weight maintenance, weight regulation, weight stability, and weight status. Thus, measures of adiposity (total body, visceral) were not a focus of this search or review. However, measures of adiposity, particularly visceral and abdominal adiposity, may provide important information beyond what is obtained solely when considering body weight.

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Role of the Funder/Sponsor: HHS staff provided general administrative support to the Committee and assured that the Committee adhered to the requirements for Federal Advisory Committees. HHS also contracted with ICF, a global consulting services company, to provide technical support for the literature searches conducted by the Committee. HHS and ICF staff collaborated with the Committee in the design and conduct of the searches by assisting with the development of the analytical frameworks, inclusion/exclusion criteria, and search terms for each primary question; using those parameters, ICF performed the literature searches.

This paper is being published as an official pronouncement of the American College of Sports Medicine. This pronouncement was reviewed for the American College of Sports Medicine by members-at-large and the Pronouncements Committee. This paper serves as an update to the topics covered in the 2009 ACSM position stand, "Appropriate Physical Activity Intervention Strategies for Weight Loss and Prevention of Weight Regain for Adults" [*Med. Sci. Sports Exerc*. 2009; 41(2):459–71]. *Disclaimer:* Care has been taken to confirm the accuracy of the information present and to describe generally accepted practices. However, the authors, editors, and publisher are not responsible for errors or omissions or for any consequences from application of the information in this publication and make no warranty, expressed or implied, with respect to the currency, completeness, or accuracy of the contents of the publication. Application of this information in a particular situation remains the professional responsibility of the practitioner; the clinical treatments described and recommended may not be considered absolute and universal recommendations.

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PRONOUNCEMENT

Physical Activity, All-Cause and Cardiovascular Mortality, and Cardiovascular Disease

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ABSTRACT

KRAUS, W. E., K. E. POWELL, W. L. HASKELL, K. F. JANZ, W. W. CAMPBELL, J. M. JAKICIC, R. P. TROIANO, K. SPROW, A. TORRES, and K. L. PIERCY, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Physical Activity, All-Cause and Cardiovascular Mortality, and Cardiovascular Disease. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1270–1281, 2019. **Purpose:** Conduct a systematic umbrella review to evaluate the relationship of physical activity (PA) with all-cause mortality, cardiovascular mortality, and incident cardiovascular disease (CVD); to evaluate the shape of the dose–response relationships; and to evaluate these relationships relative to the 2008 *Physical Activity Guidelines Advisory Committee Report*. **Methods:** Primary search encompassing 2006 to March, 2018 for existing systematic reviews, meta-analyses, and pooled analyses reporting on these relationships. Graded the strength of evidence using a matrix developed for the *Physical Activity Guidelines Advisory Committee*. **Results:** The association of self-reported moderate-to-vigorous physical activity (MVPA) on all-cause mortality, CVD mortality, and atherosclerotic CVD—including incident coronary heart disease, ischemic stroke and heart failure—are very similar. Increasing MVPA to guidelines amounts in the inactive US population has the potential to have an important and substantial positive impact on these outcomes in the adult population. The following points are clear: the associations of PA with beneficial health outcomes begin when adopting very modest (one-third of guidelines) amounts; any MVPA is better than none; meeting the 2008 PA guidelines reduces mortality and CVD risk to about 75% of the maximal benefit obtained by physical activity alone; PA amounts beyond guidelines recommendations amount reduces risk even more, but greater amounts of PA are required to obtain smaller health benefits; and there is no evidence of excess risk over the maximal effect observed at about three to five times the amounts associated with current guidelines. When PA is quantified in terms of energy expenditure (MET·h·wk^{-1}), these relationships hold for walking, running, and biking. **Conclusions:** To avoid the risks associated with premature mortality and the development of ischemic heart disease, ischemic stroke, and all-cause heart failure, all adults should strive to reach the 2008 Physical Activity Guidelines for Americans. **Key Words:** ALL-CAUSE MORTALITY, CARDIOVASCULAR MORTALITY, CARDIOVASCULAR DISEASE, HEART FAILURE, STROKE

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The *2008 Physical Activity Guidelines Advisory Committee Report* concluded that the amount of moderate-to-vigorous physical activity (MVPA) obtained per week is inversely associated with all-cause mortality, cardiovascular disease (CVD) mortality, and incident CVD (1). The 2008 Physical Activity Guidelines for Americans recommended a target range that could be achieved by 150 to 300 min·wk^{-1} of moderate-intensity physical activity, 75 to 150 min of vigorous physical activity, or an equivalent volume from a combination of moderate and vigorous physical activity (2). All of the dose–response data used to develop the physical activity targets for the *2008 Physical Activity Guidelines* were developed using epidemiologic data from longitudinal cohort studies—with moderate-to-vigorous aerobic physical activity as the lone physical activity exposure. Unfortunately, little literature has appeared addressing the influence of strength or resistance training on these outcomes; this continues to be a significant limitation of the field.

In 2008, the Advisory Committee relied mostly on primary literature to perform its work regarding all-cause mortality, CVD mortality, and CVD. Since then, there have continued to be published studies on the relationship of MVPA to these outcomes. In 2008, the assessment of CVD as an outcome was principally limited to coronary artery disease. Since then, meta-analyses have been published on additional cardiovascular outcomes, including incident cerebrovascular disease—primarily ischemic stroke—and incident heart failure. In addition, now available is a large volume of studies, reviews, pooled analyses, and meta-analyses with many component studies and large sample sizes on the relationship of MVPA with all-cause mortality, CVD mortality, and CVD. The abundance of meta-analyses permitted the members of the 2018 Physical Activity Guidelines Advisory Committee (Committee) to solely use meta-analyses to perform an updated review of the literature on this topic.

In 2008, the Advisory Committee began to define a dose–response relationship among MVPA and both all-cause and CVD mortality as a curvilinear one, with an early decrease in risk with greater amounts of MVPA, and with continuing benefit through obtaining greater amounts of physical activity. While undertaking the current review, the Committee believed it was important to confirm whether this relationship still holds with new data, and whether it extends to the various CVD outcomes of incident CVD, cerebrovascular disease (ischemic stroke), and incident heart failure.

For the *2018 Physical Activity Guidelines Advisory Committee Report* (3), the Committee chose to address update and expand upon the 2008 report (1): by address the relationships of physical activity and 1) all-cause mortality; 2) CVD mortality; and 3) incident CVD. In this new report, we address stroke and heart failure for the first time. Specifically, for each of these outcomes, the Committee was interested in whether there is a dose–response relationship; what is the shape of the relationship; and does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status? The Committee was also interested in compiling data within this framework on whether new CVD syndromes—for instance, heart failure and ischemic stroke—had enough new data to make statements about the relationships to physical activity. Finally, the Committee was interested in understanding whether the relationships of physical activity to disease outcomes might be modified from 2008, based on the fact that our lives are becoming increasingly sedentary.

METHODS

The overarching methods used to conduct systematic reviews informing the *2018 Physical Activity Guidelines Advisory Committee Scientific Report* have been described in detail elsewhere (3,4). An umbrella systematic review was conducted to identify studies investigating the association between all types and intensities of physical activity and the health outcomes of interest: all-cause mortality, CVD mortality, or CVD incidence. Studies were restricted to those in adults and addressing mortality and disease incidence. An umbrella review is in essence a review of meta-analyses; there is no formal means yet developed to perform meta-analyses of meta-analyses. The searches for meta-analyses addressing our questions were conducted in electronic databases (PubMed®, CINAHL, and Cochrane). One search and triage process was conducted for these three outcomes. Studies were considered eligible if they were systematic reviews, meta-analyses or pooled analyses published in English from 2006 until March 2018. The titles, abstracts, and full-text articles of the identified articles were independently screened by two reviewers. Disagreement between reviewers was resolved by discussion with a third member of the Committee, when necessary. Two independent abstractors extracted relevant data from all the studies eligible at full text triage to minimize abstraction errors. Abstractors also used a tailored version of AMSTARExBP to grade the quality of the reviews and select them for analysis (5). The full search strategies and AMSTARExBP grading assessments for our three questions are available at the Physical Activity Guidelines website: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx. The review was registered in PROSPERO CRD42018092743.

RESULTS

Physical Activity and All-Cause Mortality

A literature tree summarizing the selection of systematic reviews, meta-analyses, and pooled analyses for this outcome is contained in Supplemental Digital Content (see Figure, Supplemental Digital 1, literature search tree for all-cause mortality, http://links.lww.com/MSS/B527). The Committee determined that the initial umbrella search identified sufficient literature to answer the primary research questions. Additional searches for original research were not needed.

Articles collected from 2006 to 2017 often assessed each of the three outcomes of all-cause mortality, CVD mortality, and incident CVD. Therefore, the systematic reviews and meta-analyses contributing to the understanding of the relation of physical activity to these three outcomes had significant overlap. Similarly, many of the same studies appeared in the systematic reviews and meta-analyses identified in our searches. One additional article was identified in a supplemental search from 2017 to April 2018.

A total of 13 reviews were included in the analysis of the relation of physical activity to all-cause mortality: two systematic reviews (6,7), seven meta-analyses (8–14), and four pooled analyses (15–18). Follow-up for these studies ranged from 3.8 to more than 20 yr, and up to 3.9 million participants in total were studied across these reviews and meta-analyses.

The two systematic reviews included a large number of contributing studies: 121 (6) and 254 (7). However, in Milton et al. (4), only seven addressed all-cause mortality, nine addressed CVD, and three addressed stroke. For Warburton (5), 70 component studies addressed all-cause mortality, 49 addressed CVD, and 25 addressed stroke. The total numbers for each outcome were not reported. The studies covered extensive timeframes: from 1990 to 2013 and from 1950 to 2008, respectively.

The meta-analyses ranged from 9 to 80 studies. Most meta-analyses covered an extensive timeframe: from inception of the database to 1 yr before publication (8,10,13,14), from 1945 to 2013 (11), and from the 1960s and 1970s to 2007 and 2006 (9,12). Three of the pooled analyses included data from six prospective cohort studies ((15,17) used the same six studies) and from 11 cohorts (18). The pooled analysis from the Asia Cohort Consortium (14) included nine cohort studies, with 467,729 East Asians who experienced 65,858 deaths over a mean follow-up period of 13.6 yr. Incident ischemic heart disease and stroke were also assessed.

The majority of the included reviews examined self-reported leisure time MVPA as determined at face value in the contributing articles. Most reviews also established specific physical activity dose categories in metabolic equivalents of task (MET) for minutes or hours per week using quartiles or a variety of categories such as inactive and low, medium, and high amounts of physical activity, or high versus low amounts of physical activity.

Three reviews addressed specific types of physical activity. Kelly et al. (11) studied cycling and walking. Samitz et al. (13) studied domain-specific physical activity defined into leisure-time physical activity, activities of daily living, and occupational physical activity. Hamer and Chida (9) studied habitual walking only.

One pooled analysis (18) separately examined individuals meeting the 2008 physical activity guidelines—of 150 min of moderate, 75 $\text{min}\cdot\text{wk}^{-1}$ of vigorous or some equivalent combination—in one or two sessions in addition to the usual physical activity categories (inactive, insufficiently active, and regularly active). Merom et al. (19) examined dance versus walking.

Evidence on the overall relationship. All the included reviews addressed all-cause mortality as an outcome; five of them also examined CVD mortality. All studies reported an inverse relationship between MVPA and all-cause mortality in a dose–response fashion as described below. There were no null studies. The pooled analysis in which individuals meeting guidelines in one or two sessions per week (so-called weekend warrior) and individuals meeting guidelines with three or more sessions per week were compared to an inactive group, showed no differences in the effect sizes for all-cause mortality. Compared with the inactive participants, the hazard ratio (HR) for all-cause mortality was 0.66 (95% confidence interval [CI], 0.62–0.72) in insufficiently active participants who reported one to two sessions per week, 0.70 (95% CI, 0.60–0.82) in weekend warrior participants, and 0.65 (95% CI, 0.58–0.73) in regularly active participants. (18).

In the analysis by Kelly et al. (11), the effect sizes for cycling and walking were similar. For exercise of 11.25 $\text{MET}\cdot\text{h}\cdot\text{wk}^{-1}$ (675 $\text{MET}\cdot\text{min}\cdot\text{wk}^{-1}$), the reduction in relative risk for all-cause mortality was 11% (95% CI, 4%–17%) for walking and 10% (95% CI, 6%–13%) for cycling. The shape of the dose–response relationship was modeled through meta-analysis of pooled relative risks within three exposure intervals. Consistent with other studies, the dose–response analysis showed that for walking or cycling, the greatest relative risk for all-cause mortality reduction relative to the next lower physical activity amount occurred for those with the least amounts of physical activity.

Hamer and Chida (9) studied the association of walking only with both all-cause mortality and CVD mortality. The analysis included 18 prospective studies with 459,833 total participants. The forest plots, displayed in Figure 1, show a dose–response for amount (volume of walking) and walking pace. Hamer and Chida (9) found walking pace to be a stronger independent predictor of all-cause mortality than volume when both pace and volume were in the model: 48% versus 26% risk reductions, respectively. However, the studies had considerable heterogeneity within the exposure categories. The greatest walking exposure groups averaged more than 5.2 $\text{h}\cdot\text{wk}^{-1}$ or more than 10.7 $\text{miles}\cdot\text{wk}^{-1}$, and the groups ranged from more than 1 $\text{h}\cdot\text{wk}^{-1}$ to more than 2 $\text{h}\cdot\text{d}^{-1}$ and more than 6.0 $\text{miles}\cdot\text{wk}^{-1}$ to more than 12.4 $\text{miles}\cdot\text{wk}^{-1}$. Walking pace was generally assessed as a "relative" rather than an "absolute" measure (relative being defined in terms such as "brisk" which may be different in absolute terms—e.g., miles per hour—for those of different ages and fitness levels), although several studies defined "brisk" as more than 3.0 mph and "moderate" as 2.0 to 2.9 mph. Minimal walking categories averaged approximately 3 $\text{h}\cdot\text{wk}^{-1}$ (ranging from ~30 $\text{min}\cdot\text{wk}^{-1}$ to ~5 $\text{h}\cdot\text{wk}^{-1}$) or 6.1 $\text{miles}\cdot\text{wk}^{-1}$ (ranging from ~3.1 to ~9.3 $\text{miles}\cdot\text{wk}^{-1}$), equating to a casual or moderate walking pace of approximately 2 mph.

Dose–response. Every one of the 13 studies within our analysis demonstrated a significant inverse dose–response relationship with all-cause mortality across physical activity exposure groups. The uniformity and strength of these relationships led to the strength of evidence grade finding for this item. The uniformity of findings prompted us to highlight the two pooled analyses of Arem et al. (15) and Moore et al. (17). In these pooled analyses of six studies, combining data at the individual level allowed an examination of the strength of effects and confidence boundaries across large populations with great precision.

Authors (year)	Exposure	Sample size	Hazard ratio (95% CI)
Male			
1 Wannamethee *et al* (1998)[11]	Walking > 1 hour/day	4311	0.62 (0.37 to 1.05)
2 Hakim *et al* (1998)[12]	Walking > 3.2 km/day	707	0.55 (0.37 to 0.83)
3 Bijnen *et al* (1998)[13]	Walking > 1 hour/week	802	0.71 (0.58 to 0.88)
4 Davey Smith *et al* (2000)[19]	Brisk walking	6702	0.55 (0.48 to 0.63)
5 Fujita *et al* (2004)[24]	Walking > 1 hour/day	20 004	0.92 (0.80 to 1.06)
6a Schnohr *et al* (2007)[26]	Walking > 2 hours/day	3204	0.89 (0.69 to 1.14)
6b Schnohr *et al* (2007)[26]	Brisk walking	3204	0.43 (0.32 to 0.59)
Subtotal		38 934	0.66 (0.53 to 0.83)
Female			
1 Gregg *et al* (2003)[23]	Walking > 898 kcal/week	9518	0.71 (0.62 to 0.82)
2 Fujita *et al* (2004)[24]	Walking > 1 hour/day	21 159	0.72 (0.59 to 0.89)
3a Schnohr *et al* (2007)[26]	Walking > 2 hours/day	4104	0.81 (0.59 to 1.10)
3b Schnohr *et al* (2007)[26]	Brisk walking	4104	0.48 (0.35 to 0.66)
4 Matthew *et al* (2007)[27]	Walking > 10 MET-hours/day	67 143	0.86 (0.71 to 1.05)
Subtotal		106 028	0.72 (0.62 to 0.84)
Male and female			
1 LaCroix *et al* (1996)[10]	Walking > 4 hours/week	1645	0.73 (0.48 to 1.10)
2 Stessman *et al* (2000)[18]	Walking > 4 hours/week	456	0.14 (0.04 to 0.50)
Total		147 063	0.68 (0.59 to 0.78)
Test for heterogeneity			$\chi^2(13) = 31.35$, $p < 0.001$
Test for overall effect			$\chi^2(1) = 57.86$, $p < 0.001$

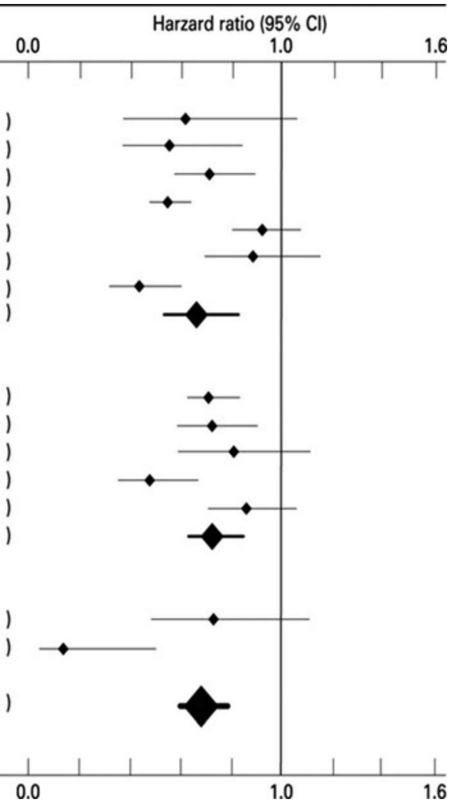

FIGURE 1—The association between walking and all-cause mortality in men and women. Forest plot showing point and 95% confidence interval estimates of the HR for all-cause mortality associated with different amounts of PA. Relative influence on the pooled results/effect sizes are represented by varying line weights of the symbols. Walking is favored, with a shift of the estimate to the left. These estimates are similar to the associations found for CVD mortality discussed later. Reprinted with permission from Hamer M, Chida Y. Walking and primary prevention: a meta-analysis of prospective cohort studies. *Br J Sports Med*. 2008;42(4):238–43. Copyright © 2008 BMJ Publishing Group Ltd.

Moore et al. (17) reported a pooled analysis of the association of leisure-time physical activity with mortality during follow-up in data from six prospective cohort studies in the National Cancer Institute Cohort Consortium. The pooled cohort included 654,827 individuals, ages 21 to 90 yr. Moderate-to-vigorous physical activity in MET-hours per week was used to generate adjusted survival curves (for participants ages 40 yr and older), with 95% confidence intervals derived by bootstrap. The study included a median follow-up of 10 yr and 82,465 deaths. Figure 2 shows the relation of leisure time physical activity and HR for mortality; it illustrates several characteristics of the relationship common among the studies reporting on dose–response on all-cause mortality. The survival curve from this analysis demonstrates several important points: 1) the beneficial effect has no lowest threshold; 2) effects are seen immediately upon moving from the least active category to the next category of MVPA; 3) the early part of the slope is the steepest. At least 70% of the population benefit on all-cause mortality is reached by achieving 8.25 MET-hours (150 min) per week of MVPA; 4) there is no obvious best amount; 5) there is no apparent upper threshold; 6) activity volumes (amounts) up to four times the 2008 Guidelines (150–300 min moderate-intensity physical activity), show no evidence of increased mortality risk.

Similarly, Arem et al. (15) reported a pooled analysis of six studies in the National Cancer Institute Cohort Consortium (baseline collection in 1992–2003; the same studies reported in Moore et al. (17)). These were population-based prospective cohorts in the United States and Europe, with self-reported physical activity analyzed in 2014. A total of 661,137 men and women (median age, 62 yr; range 21 to 98 yr) and 116,686 deaths were included. Cox proportional hazards regression with cohort stratification was used to generate multivariable-adjusted HR and 95% CI. Median follow-up time was 14.2 yr. The dose response-relationship from this report is shown in Figure 3. Several characteristics of this dose–response relationship are reminiscent of that of Moore et al. (17) (Fig. 2). However, several differences in results are described below.

Here the relationship is carried out to a category (>75 MET·h·wk^{-1}) representing approximately 10 times the exposure of the lower end of the 2008 guidelines (i.e., 150 min·wk^{-1}). At the greatest exposure category, an apparent uptick in mortality risk occurs. This possible uptick is not noted in the Moore et al., 2012 study that went only to about four times the guidelines exposure. In this pooled study of 661,137 individuals only 18,831 participants (2.8% of the total) were included in the 40 to 75 MET·h·wk^{-1} category, and only 4,077 (0.62%) in the more than 75 MET·h·wk^{-1} category. These accounted for only 1,390 (1.2%) and 212 (0.18%) of 116,686 deaths in the combined analysis, respectively; and the error bars are large. Figure 3 indicates that the point estimate of risk for the greatest exposure group is the same as the estimate

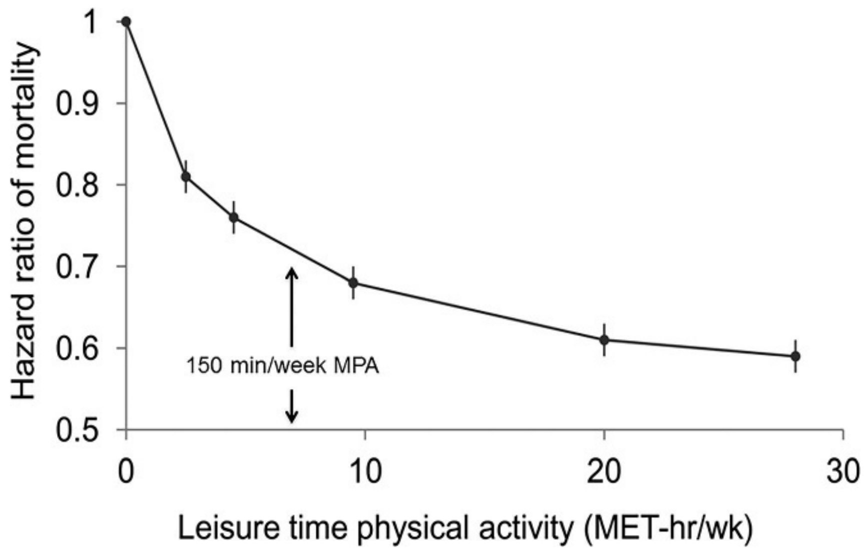

FIGURE 2—Relationships of MVPA to all-cause mortality, with highlighted characteristics common to studies of this type. Shown is the relation of leisure time physical activity amount and HR for mortality. The points shown represent the mortality HR for each of the physical activity categories; the vertical lines represent the 95% CI for that physical activity category. The reference category no leisure time physical activity. The lines connecting the points help to illustrate the dose–response relationship between physical activity and risk of mortality; the shape of the association shown here is similar to that obtained using spline modeling. As discussed in the text and displayed in this graphic, the characteristics of this curve seems to apply for most studies of the relationships of MVPA with all-cause and CVD mortality, as well as with incident coronary artery disease, ischemic stroke and all-cause heart failure: there is no lower threshold for effect; there is a steep, early slope; about 70% of the benefit obtained by physical activity alone is reached by 8.25 MET·h·wk^{-1} (150 min of "brisk walking" (3 mph); there is not apparent upper threshold for effect; there is no evidence for increased risk at the greatest amounts of physical activity; and there is not obvious "best amount." Source: adapted from Moore et al. (17).

for those meeting the 2008 guidelines (7.5 to 15 MET·h·wk^{-1}, or 150 to 300 min·wk^{-1}). This apparent uptick in risk at extreme volumes of exercise has been observed before. Paffenbarger (20,21) reported it in the Harvard Alumni Health Study for CVD (heart attack) risk, in 1978 and 1993. However, as in these previous reports, the apparent rise in risk at very high amounts of MVPA did not reach the level of statistical significance (15).

In a seminal paper in 2016, Ekelund et al. (8) examined the joint associations of sedentary behavior (sitting and television watching) and physical activity (MVPA) with all-cause mortality. (cf., *Sedentary Behavior* article in this issue.) Using 16 contributing studies, combining data across all studies to analyze the association of daily sitting time and physical activity with all-cause mortality, estimating summary HR using

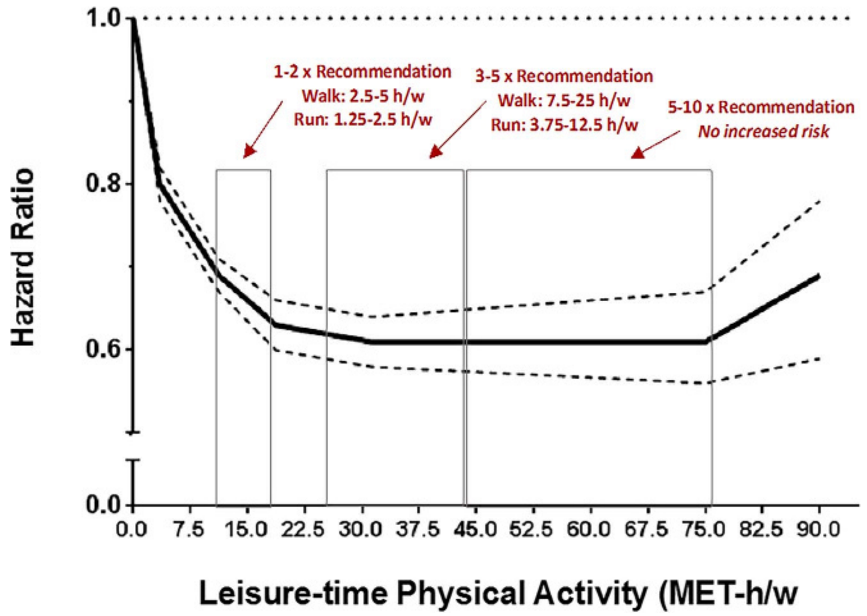

FIGURE 3—Relationships of MVPA to all-cause mortality, with highlighted characteristics common to studies of this type. The ranges of physical activity relative to 2008 US Physical Activity Guidelines for aerobic activity are shown as ranges. There is no increase in risk noted up to 10 times the current guidelines PA amounts. Source: adapted from Arem et al. (15).

Cox regression, and expressing physical activity in terms of MET-hours per week of MVPA, Ekelund et al. found the same curvilinear relationships among physical activity and all-cause mortality as observed in Arem et al. (15) and Moore et al. for four categories of sitting time (17).

Demographic factors and weight status. Most studies reported gross distributions of demographic factors (race, sex, weight status) across exposure groups within individual studies in their reviews and meta-analyses. Given the nature of meta-analyses—conducted at the study level versus the individual level—it is difficult to detect differential effects by demographic factors and weight status unless the specific component studies performed them within their analysis. Some studies examined subgroup effects directly in their review or meta-analysis; one focused on adults older than 60 yr (10). In such studies, no subgroup effects were detected. The O'Donovan analysis of "weekend warrior" physical activity behavior on all-cause mortality, showed no differential responses by sex (18).

However, the pooled analyses (15,17) permit a direct examination of the relative effects across demographic categories. In these studies effects were reported for strata across sex, race, and body mass index (BMI) and the aggregate event data reported according to strata. Although not directly tested in these reports, no differential effects across sex, race, or BMI strata were readily apparent. Strata for socioeconomic status and ethnicity were not reported.

Comparing 2018 findings with the 2008 scientific report. Our review of systematic reviews, meta-analyses, and pooled studies promoted the analysis of larger cohorts and provided more precision around the effect size estimates. Our review identified the same dose–effect estimates relating MVPA with all-cause mortality as was described in 2008. Given the large population sizes and heterogeneity studied, we have more confidence about the study effect sizes and dose response relationships (Fig. 2) and their generalizability to US adult men and women, and populations of all races, ages, and body sizes.

Physical Activity and CVD Mortality

A literature tree summarizing the selection of systematic reviews, meta-analyses, and pooled analyses for this outcome is contained in Supplemental Digital Content (see Figure, Supplemental Digital Content 2, literature search tree for CVD mortality, http://links.lww.com/MSS/B528). An initial search for systematic reviews, meta-analyses, pooled analyses, and reports identified sufficient literature to answer the research question as determined by the Committee. Additional searches for original research were not needed.

Articles collected from 2006 to 2017 typically included outcomes of all-cause mortality, CVD mortality, and incident CVD. Therefore, the systematic reviews and meta-analyses contributing to the understanding of the relation of physical activity to these three outcomes had significant overlap. Similarly, many of the same studies appeared in the systematic reviews and meta-analyses identified in our searches. In this section, we address only CVD mortality; however, the format and conclusions differ little from those made for all-cause mortality.

For this discussion, CVD mortality refers to mortality attributable to CVD in its broadest sense, referring to diseases beyond ischemic coronary artery disease, but not to include non-atheromatous or infectious valvular disease and others.

A total of six existing reviews were included: one systematic review (6), three meta-analyses (8,9,22), and two pooled analyses (18,19). The reviews were published from 2008 to 2017. The systematic review (6) included 121 studies and a timeframe from 1983 to 2013. The meta-analyses included a range of 16 to 36 studies and covered an extensive timeframe: from 1970s to 2014. The pooled analyses included data from 20 cohorts, each from different population surveys (18,19).

The majority of the included reviews examined self-reported leisure time MVPA. Most reviews also established specific physical activity dose categories in MET-minutes or MET-hours per week using quartiles or a variety of categories such as inactive and low, medium, and high levels of physical activity, or high versus low levels of physical activity.

One pooled analysis (18) examined a "weekend warrior" category (meeting the physical activity guidelines in one or two sessions per week) in addition to the usual physical activity categories (insufficiently active and regularly active) compared to an inactive group. Two reviews addressed specific types of physical activity: dancing (19) and habitual walking (9).

Evidence on the overall relationship. All of the included reviews addressed CVD mortality and four of them also assessed all-cause mortality in addition to other outcomes.

As it was for all-cause mortality, all reviews reported an inverse relationship between MVPA and CVD mortality in a dose–response fashion, as described below. The reviews included no null studies. The pooled analysis in which individuals meeting guidelines in one or two sessions per week and individuals meeting guidelines with three or more sessions per week were compared to an inactive group, showed no differences (overlapping HR) in the effect sizes for CVD mortality (HR, 0.59 to 0.60) (16).

As noted above, Hamer and Chida (9) studied walking only on both all-cause mortality and CVD mortality. The analysis included 18 prospective studies with 459,833 total participants. The effect sizes and confidence intervals for all categories of walking pace and amount are similar to reminiscent of those determined for all-cause mortality (Fig. 1). This is an example of how closely aligned the MVPA relationship is for both CVD mortality and all-cause mortality within and across studies.

Dose–response. Here also, the findings for the dose–response relationships between MVPA and CVD mortality are basically identical to those found for the relationships between MVPA and all-cause mortality. Every one of the 13 studies within our analysis demonstrated a significant inverse dose–response relationship with CVD mortality across physical activity exposure groups. The uniformity and strength of these relationships led to the strength of evidence determination for this item.

Wahid et al. (22) used 36 studies, 33 pertaining to CVD and 3 pertaining to type 2 diabetes mellitus to model the effects of three physical activity categories (low physical activity, 0.1–11.5 MET·h·wk^{-1}; medium physical activity, 11.5–29.5 MET·h·wk^{-1}; and high physical activity; ≥29.5 MET·h·wk^{-1}) in a dose–response fashion on CVD incidence and mortality, coronary heart disease incidence and mortality, myocardial infarction incidence, heart failure incidence, and stroke incidence (22). For those conditions for which all three categories had entries (CVD incidence, CVD mortality, stroke incidence, and coronary heart disease incidence), all but CVD mortality demonstrated a strong curvilinear dose–response relationship across categories, as observed for all-cause mortality (Fig. 2).

Demographic Factors and Weight Status

Similar to all-cause mortality, the studies providing the strongest evidence regarding subgroup moderation effects on CVD mortality were the pooled analyses of Merom et al. (19) and O'Donovan et al. (18). Again, as for all-cause mortality, although not directly tested in these reports, no differential effects across sex, race, or BMI strata were readily apparent. Strata for socioeconomic status and ethnicity were not reported.

Physical Activity and Incident CVD

Here CVD refers to diseases related to ischemic vascular events, such as diseases due to coronary heart disease secondary to coronary artery disease, to cerebrovascular disease secondary to a cerebrovascular accident or stroke; or to heart failure of ischemic (coronary) or non-ischemic etiology.

A literature tree summarizing the selection of systematic reviews, meta-analyses, and pooled analyses for this outcome is contained in Supplemental Digital Content (see Figure, Supplemental Digital Content 3, literature search tree for all-cause mortality, http://links.lww.com/MSS/B529). A total of 10 existing reviews were included: one systematic review (7) and nine meta-analyses (22–30). The reviews were published from 2008 to 2016. The systematic review (7) included 254 studies published between 1950 and 2008.

The meta-analyses included a range of 12 to 43 studies. Most meta-analyses covered an extensive timeframe: from database inception to 2013 (29), from 1954 and 1966 to 2007 (28,30), and from the 1980s and 1990s to 2005–2016 (22–27).

The majority of included reviews examined self-reported physical activity. Different domains of physical activity were also assessed. These included total (25); occupational and leisure (24); occupational, leisure, and transport (27); and leisure physical activity only (28). Some reviews also established specific dose categories in MET-minutes or MET-hours per week (22,25,26,30). Other reviews used minimal or low versus moderate or high physical activity levels as reported in individual studies (7,23,28). Two meta-analyses specifically examined tai chi chuan (29) and walking (30).

Included reviews addressed the incidence of CVD in a variety of ways. Several addressed incident coronary heart disease (25,27,28,30), incident stroke (23,25,29), and incident heart failure (24,26). Warburton et al. (7) reviewed incident stroke and coronary (ischemic) heart disease. Wahid et al. (22) used 33 studies to address CVD incidence and mortality, coronary heart disease incidence and mortality, myocardial infarction incidence, heart failure incidence, and stroke incidence. Thus, in all, six studies addressed incident coronary heart disease; five studies addressed incident stroke; and three studies addressed incident heart failure.

Evidence on the overall relationship. All of the six studies addressing incident coronary heart disease, the five studies addressing incident stroke, and the three studies addressing incident heart failure demonstrated significant dose–response inverse relationships with increased amounts of physical activity. There were no null studies. The shapes of the relationships are discussed below.

Physical Activity and Coronary Heart Disease

Sattelmair et al. (27) performed a pooled sample meta-analysis of epidemiologic studies to investigate the relationship of MVPA to incident coronary heart disease. Pooled dose–response estimates were derived from qualitative estimates describing low, moderate, and high amounts of physical activity. Of the 33 studies initially selected for analysis, nine permitted quantitative estimates of MET-hours per week of MVPA. Those participating in leisure-time physical activity at the lower limit of the 2008 guidelines had a 14% reduced risk of developing coronary heart disease (relative risk (RR), 0.86 ± 0.09) compared with those reporting no leisure-time physical activity. They reported an inverse dose–response relationship similar to the curves for all-cause mortality and CVD mortality. These curves are characterized by an early decrease in risk, continued benefit with greater exposure, no lower threshold, and no upper limit (Fig. 4). One MET-hour per week is approximately equal to 1.05 kcal·kg^{-1}·wk^{-1}. Therefore, for a 70-kg individual, the lower boundary of the 2008 guidelines for MVPA is achieved at 600 kcal·wk^{-1}.

This analysis points to an important aspect of understanding how the interpretation of dose–response relationships may depend on the modeling parameters. When the dose–response relationships of the pooled studies are modeled using the qualitative exposures of low, moderate, and high amounts of physical activity, the dose–response relationship appears linear. When, however, the physical activity exposures are modeled according to MET-hours per week (Fig. 4), the typical curvilinear relationship is unmasked.

Demographic factors and weight status. As it was for previously studied outcomes in this article, the studies providing the strongest evidence regarding subgroup moderation effects on ischemic heart disease incidence were the pooled analyses; particularly that of Sattelmair et al. (27). Of the six studies dealing with incident coronary heart disease in our analysis, to the best of our knowledge, only Sattelmair et al. explicitly tested for disease

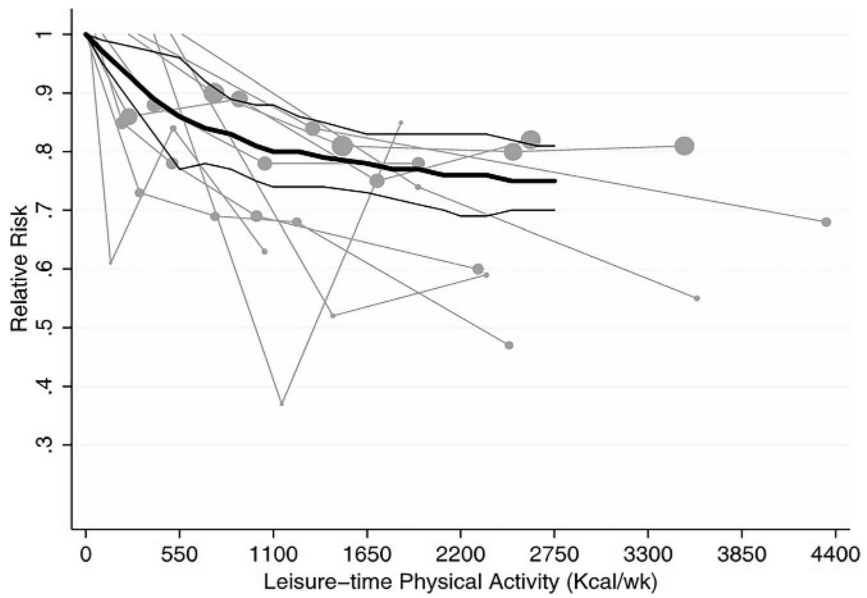

FIGURE 4—Plot with spline and 95% CI of relative risk of coronary heart disease by kcal per week of leisure-time physical activity. This summary of the synthesis of nine studies displays the characteristics of this dose–response relationship with all-cause mortality as shown and discussed in Figure 2. Source: Sattelmair et al. (27).

modification by specific factors. Although no interactions were reported for effect modification by race or BMI strata, they observed a significant interaction by sex ($P = 0.03$); the association was stronger among women than men.

Physical Activity and Stroke

Kyu et al. (25) studied the dose–response associations of total physical activity with risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events using 174 studies: 43 for ischemic heart disease, and 26 for ischemic stroke. Total physical activity—not just that within MVPA — in MET-minutes per week was estimated from all included studies. Continuous and categorical dose–response between physical activity and outcomes were assessed. Categorical dose–response compared insufficiently active (<10 MET·h·wk^{-1}), low active (10 to 66 MET·h) moderately active (67 to 133 MET·h) and highly active (≥134 MET·h). Compared with insufficiently active individuals, the relative risk reduction for those in the highly active category was 25% (RR, 0.754; 95% CI, 0.704–0.809) for ischemic heart disease; and 26% (RR, 0.736; 95% CI, 0.659–0.811) for ischemic stroke. Again, for ischemic stroke and ischemic heart disease (equivalent to coronary heart disease), the same typical curvilinear dose–response relationship is seen as for all-cause mortality and CVD mortality. However, the initial and maximal effect sizes are attenuated, so that achieving the lower bound of the 2008 Guidelines achieves only 36% reduction in initial risk for incident ischemic stroke and heart failure (Fig. 5).

Physical Activity and Heart Failure

Pandey et al. (26) studied the categorical dose–response relationships of physical activity to heart failure risk. As in the previously discussed analysis by Kyu et al. (25), these authors used generalized least-squares regression modeling to assess the quantitative relationship of physical activity (MET-minutes per week) to heart failure risk across studies reporting quantitative physical activity estimates. Twelve prospective cohort studies with 20,203 heart failure events among 370,460 participants (53.5% women; median follow-up, 13 yr) were included. As seen in Figure 6, take from the meta-analysis of Pandy et al. (26) the greatest levels of physical activity were associated with significantly reduced risk of heart failure (pooled HR for highest versus lowest PA, 0.70; 95% CI, 0.67–0.73). Compared with participants reporting no leisure-time physical activity, those who engaged in guideline-recommended minimum levels of physical activity (500 MET·min·wk^{-1}; 2008 guidelines) had modest reductions in heart failure risk (pooled HR, 0.90; 95% CI, 0.87–0.92). Only 33% of the maximal benefit was achieved at the 2008 guidelines amount. Thus, for heart failure, even though the data on this are still early, by inspection, it appears the dose–response relationship is more linear at lower physical activity amounts, and not the sharp, early curvilinear relationship observed for the other outcomes discussed in this chapter. Note, at this time, studies of the relationship between physical activity and heart failure incidence do not distinguish among the various types of heart failure: heart failure with preserved, reduced heart failure, or a combination of the two. This should be a point of emphasis for future research.

CONCLUSIONS AND PUBLIC HEALTH IMPACT

The effects of MVPA on ischemic CVD, including coronary heart disease, ischemic stroke, and heart failure are very similar to those of all-cause mortality and CVD mortality. The evidence for these conclusions was considered strong by

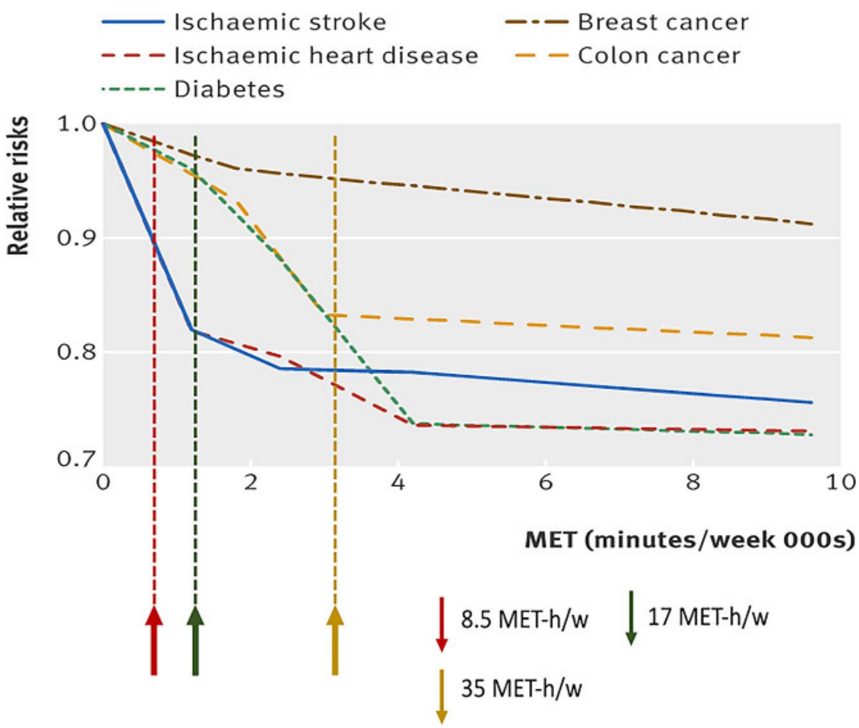

FIGURE 5—Dose–response relationships between total physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events using 174 studies (43 for ischemic heart disease, and 26 for ischemic stroke). For reference, shown are the lower end (*red arrows and dotted line*) and upper bounds (*green arrows and dotted line*) of the 2008 guidelines for MVPA. Also indicated is the MVPA amount associated with normalization of the risk from >8 h·d^{-1} of sedentary activity from Ekelund, 2016 (8) (*gold arrows and dotted line*). The latter would represent the amount of physical activity required to compensate for an entirely sedentary lifestyle. The risk for ischemic heart disease and ischemic stroke are reminiscent of the characteristic dose–response relationships established for all-cause and cardiovascular mortality noted previously and in Figure 2. The universality of the dose–response relationships described in the caption of Figure 2 to other outcomes—such as type 2 diabetes and some cancers—are shown in this figure. Reproduced with permission from Kyu HH, Bachman VF, Alexander LT, et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose–response meta-analysis for the global burden of disease study 2013. *BMJ*. 2016;354:i3857. Copyright © 2013 BMJ Publishing Group Ltd.

the Committee. The grading of the accumulated evidence is available in Supplemental Digital Content (see Table, Supplemental Digital Content 4, evidence statements for conclusions, http://links.lww.com/MSS/B530). The evidence continues to support the conclusion that increasing MVPA levels by modest amounts in the inactive US population has the potential to have an important and substantial impact on these outcomes in the adult population. With respect to reductions in risk for these endpoints, the following points are clear: 1) the associations of physical activity with beneficial health outcomes begin when adopting very modest amounts; 2) more MVPA is better than none; 3) meeting the 2008 MVPA guidelines reduces risk of all-cause mortality to about 75% of the maximal benefit; 4) more physical activity reduces risk even more, but more physical activity is required to obtain less benefit; and 5) there is no evidence of excess risk over the maximal effect observed at about three to five times the MVPA of the current guidelines; 6) when the activity is quantified by volume in terms of energy expenditure of task (MET-hours per week), these relationships seem to hold for several modes and intensities of physical activity, including walking, running, and biking.

Needs for Future Research

Several advances in our understanding of the relationships among physical activity and the outcomes described herein have occurred since the 2008 report. Most of the literature upon which the 2008 conclusions were based utilized survey data and questionnaire data; physical activity exposures were assessed using self-reported estimates of time spent in aerobic continuous MVPA accumulated in bouts of at least 10 min. Therefore, all other components across the physical activity spectrum—sedentary behavior, light-intensity physical activity, and any moderate- to vigorous-intensity physical activity in bouts less than 10 min—was considered "baseline" physical activity. The scientific community and public health researchers have begun to incorporate objective, device-based measures of physical activity—and sedentary behavior—into our measurement armamentarium. This has permitted assessments of the relationship of activity of less than moderate-to-vigorous intensity with health outcomes; it has permitted the assessment of the relations of episodes of MVPA of less than 10 min on health outcomes. Given this, more research is needed in these areas:

Conduct research on the role of light intensity physical activities and interaction with sedentary behavior in risk reduction for all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease (coronary heart disease, stroke and heart failure). This can most economically and efficiently be accomplished by incorporating devices (pedometers, wearables, watches) measuring physical activity into all

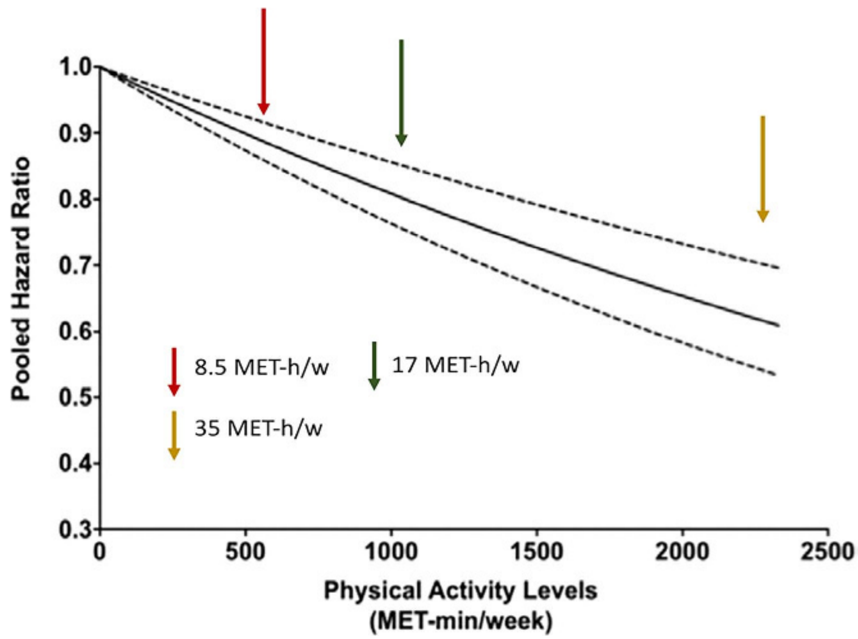

FIGURE 6—Dose–response relationships between MVPA and risk of incident heart failure. For reference, shown are the lower end (*red arrows and dotted line*) and upper bounds (*green arrows and dotted line*) of the 2008 guidelines for MVPA. Also indicated is the MVPA amount associated with normalization of the risk from >8 h·d^{-1} of sedentary activity from Ekelund et al., 2016 (8) (*gold arrows and dotted line*). The latter would represent the amount of physical activity required to compensate for a highly sedentary lifestyle. Note, the colors of the arrows are important, not the direction of the *arrow*. Source: Adapted from Pandey et al. 2015 (26).

clinical trials with all-cause mortality, CVD mortality, or incident CVD as outcomes.

Rationale. As reported in this chapter, the benefits of MVPA on all-cause mortality, CVD mortality, and incident CVD (coronary heart disease, stroke and heart failure) are well documented and strong. However, these studies ignore the effects of physical activity that are not characterized as moderate-to-vigorous intensity (light). The development of device-based measures of physical activity (pedometers, watches, accelerometers and other wearables) provide the scientific imperative to begin to explore the relations of all intensities and amounts of physical activity—light to vigorous; small to great total amounts. These studies are beginning to appear (31–35). Unfortunately, there are not enough studies on the relation of light physical activity, total physical activity, or step counts per day to provide sufficient information for meta-analyses to be performed in these areas for the outcomes of interest here. Further, the role of sedentary behavior on disease risk is an evolving concept. The ability to quantify this objectively is now available and will allow investigators to incorporate the interaction of sedentary behavior and physical activity on disease risk—a research area that until now has been relatively ignored or not possible.

This becomes a major future research need. This goal can most economically and efficiently be accomplished by incorporating devices (pedometers, wearables, watches) measuring physical activity and sedentary behavior into all clinical trials with all-cause mortality, CVD mortality, or incident CVD as outcomes.

Conduct research on the possibility of increased risk associated with great amounts of physical activity.

Rationale. Whether great amounts (volumes) of aerobic physical exercise lead to increased cardiac morbidity or mortality is an important, yet open question. As discussed in this chapter, there is a hint in some studies of an increase in cardiovascular risk in high volume aerobic athletes. Recent reports document increased coronary calcium scores in masters athletes (36,37); however, there seems to be a U-shaped relationship with lifelong volume of training (36). These findings may explain the hint of an increased cardiovascular risk in long-term athletes. Clearly, this issue demands more study in athletic populations.

Conduct research on the relative importance of the various characteristics of physical activity exposure (total volume, intensity, frequency and mode) and muscular strengthening physical activity on all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease (coronary heart disease, stroke and heart failure).

Rationale. Now into our second iteration of the Physical Activity Guidelines Scientific Report, we continue to rely on studies of aerobic ambulatory MVPA—primarily collected via survey—to understand the relationship of physical activity to all-cause mortality, CVD mortality, and incident CVD. Underexplored are the importance of frequency and intensity relative to volume of aerobic exercise; the importance of muscle strengthening to these clinical outcomes; whether swimming, biking, and rowing contribute to cardiovascular health equal to that of aerobic ambulatory exercise; and what the energy expenditures and programs are for these aerobic activities for equivalent clinical outcomes. If we are going to prescribe exercise of all modalities as options for adults wanting to exercise for health, we need better understanding of the relative contributions of a general range of options.

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PRONOUNCEMENT

Physical Activity and Health in Children Younger than 6 Years: A Systematic Review

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[1]Department of Exercise Science, Arnold School of Public Health, University of South Carolina, Columbia, SC; [2]Departments of Psychology and Physical Therapy, Movement and Rehabilitation Sciences, Northeastern University, Boston, MA; [3]Departments of Health and Human Physiology and Epidemiology, University of Iowa, Iowa City, IA; [4]Pennington Biomedical Research Center, Baton Rouge, LA; [5]Centers for Disease Control and Prevention, Atlanta, GA; [6]ICF, Atlanta, GA; and [7]Gramercy Research Group, Winston-Salem, NC

ABSTRACT

PATE, R. R., C. H. HILLMAN, K. F. JANZ, P. T. KATZMARZYK, K. E. POWELL, A. TORRES, and M. C. WHITT-GLOVER, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Physical Activity and Health in Children Younger than 6 Years: A Systematic Review. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1282–1291, 2019. **Purpose:** Physical activity is known to provide important health benefits in school-age youth. However, until recently, few studies have examined associations between physical activity and health in young children. The purpose of this study was to conduct a systematic review of the relationship between physical activity and selected health outcomes in children younger than 6 yr. **Methods:** A systematic search identified randomized controlled trials and prospective cohort studies examining the associations between physical activity and adiposity/weight status, bone health, cardiometabolic health, and cognition in children younger than 6 yr. **Results:** Twenty-seven studies met inclusion criteria and served as the basis for this systematic review. For weight status/adiposity, 12 of 15 studies found negative associations between physical activity and one or more measures of the outcome. For bone health, 10 articles based on four studies were identified, and nine studies showed stronger bone in more active children. For cardiometabolic health, three studies were identified and findings were limited and inconsistent. For cognition, two systematic reviews were identified and findings were limited. For all four health outcomes, evidence of dose–response relationships and effect modification by demographic factors was very limited. **Conclusions:** There is strong evidence indicating that higher amounts of physical activity are associated with better indicators of bone health and with reduced risk for excessive increases in weight and adiposity in children 3 to 6 yr. Evidence was too limited to support conclusions regarding the effects of physical activity on cardiometabolic health and cognition. **Key Words:** WEIGHT STATUS, ADIPOSITY, BONE HEALTH, CARDIOMETABOLIC HEALTH, DOSE–RESPONSE, EFFECT MODIFICATION

The body of knowledge on the relationship between physical activity and health in children and youth has been growing steadily since the 1950s, and the development of this research field has been particularly rapid over the last two decades (1). Much of the early research was focused on physical fitness and its relationship to growth and development

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in young persons (2). However, more recently, the emphasis has shifted to the effects of physical activity on risk factors for noncommunicable diseases that typically do not manifest until adulthood. These include cardiometabolic diseases, such as coronary heart disease and type 2 diabetes, and bone health outcomes, including osteoporosis and bone fractures (3). With the marked increase in the prevalence of overweight and obesity in US children, many recent studies have examined the impact of physical activity on adiposity and weight status in young persons (4).

The 2008 Physical Activity Guidelines Advisory Committee Report included an examination of the relationship between physical activity and health in children and adolescents. Key conclusions of that review were that, in school-age children and youth, higher levels of physical activity are associated with better status on indicators of cardiorespiratory and muscular fitness, body composition, cardiometabolic risk, and bone health (5). Those conclusions informed a physical activity guideline which indicated that children and adolescents should accumulate 60 min or more of at least moderate-intensity physical activity daily and that, within that hour of activity, vigorous-intensity physical activity and muscle-strengthening and bone-strengthening activities should be included at least 3 $d \cdot wk^{-1}$ (6). Notably, this guideline was applied only to youth in the 6- to 18-yr age range. No guideline was included for children younger than 6 yr, because the body of knowledge on physical activity and health in early childhood was very limited.

During the period between 2008 and 2018, a substantial volume of research was undertaken on the relationship between physical activity and health in children of preschool age (7). Further, during that period, physical activity guidelines for children younger than 6 yr were developed by public health agencies in some other countries, and physical activity guidelines for children attending childcare centers were released by the Institute of Medicine in the United States (8). Accordingly, the Youth Subcommittee of the 2018 Physical Activity Guidelines Advisory Committee opted to consider the evidence related to relationships between physical activity and selected health outcomes in children younger than 6 yr. The purpose of this article is to present the findings of a systematic review of the scientific literature addressing this issue. Specific health outcomes considered in the review were body weight and adiposity, bone health, cognition, and cardiometabolic risk factors.

METHODS

The methods used to conduct systematic reviews for the 2018 Physical Activity Guidelines Advisory Committee Scientific Report have been described in detail elsewhere (9). An initial search limited to systematic reviews, meta-analyses, pooled-analyses, and high-quality reports was conducted. That search yielded too few articles, so the search was repeated to identify relevant original research articles. Accordingly, for this review, a systematic search was conducted to identify randomized controlled trials and prospective cohort studies that assessed the association between any type of physical activity and health outcomes, including adiposity and weight status, bone health, and cardiometabolic health in children younger than 6 yr. The searches were conducted in electronic databases (PubMed®, CINAHL, and Cochrane) and were supplemented by asking subcommittee members, all experts in the area, to provide additional articles identified through their expertise/familiarity with the literature.

Articles published in English from data base inception until February 2017 were included in the Committee Report, and the search was extended to March 2018 for this article. Search terms included age-appropriate physical activity, active play and sedentary behavior terms combined with outcome-specific terms. The full search strategy is available at https://health.gov/paguidelines/second-edition/report/supplementary_material/pdf/Youth_Q1_Under6_Evidence_Portfolio.pdf. The identified articles were independently screened by two reviewers. The full-text of relevant articles was reviewed to include those that met the inclusion criteria. Inclusion/exclusion criteria are presented in Supplemental Material (see Table, Supplemental Digital Content 1, Inclusion/Exclusion Criteria, http://links.lww.com/MSS/B532). Two abstractors independently abstracted data and conducted a quality or risk of bias assessment using the USDA Nutrition Evidence Library Bias Assessment Tool for original research (9,10) and the AMSTAR ExBP for systematic reviews (11). Discrepancies in article selection or data abstractions were resolved by discussion or a third reviewer if needed. The protocol for this review was registered with the PROSPERO database (registration ID CRD42018092740). A summary of the bias assessment of the original research articles included in this review is available in the supplemental material [see Tables, Supplemental Digital Content 2, Nutrition Evidence Library Bias Assessment Tool: Original Research, http://links.lww.com/MSS/B533; and Supplemental Digital Content 3, AMSTAR ExBP: SR/MA, http://links.lww.com/MSS/B534].

RESULTS

Search results. A total of 1257 studies were identified through the systematic searches (Fig. 1). After screening titles and abstracts, 1166 studies were excluded and 91 reviewed in full. Of these, 19 studies met the full inclusion criteria. An additional eight studies were identified by the authors based on their knowledge in the area. Twenty-seven studies were included in this review until the release of the 2018 Physical Activity Guidelines Advisory Committee Scientific Report. One additional original research article and three systematic reviews were found when the search was updated for the purpose of this article.

Body weight and adiposity. In considering the evidence regarding the relationship between physical activity and body weight and/or adiposity in children younger than 6 yr, the committee identified and reviewed 15 studies (12–26). The study designs, methods, and findings of these studies are summarized in Table 1. All of the studies included in this review used prospective, longitudinal study designs. However, methods for measurement of physical activity were highly variable.

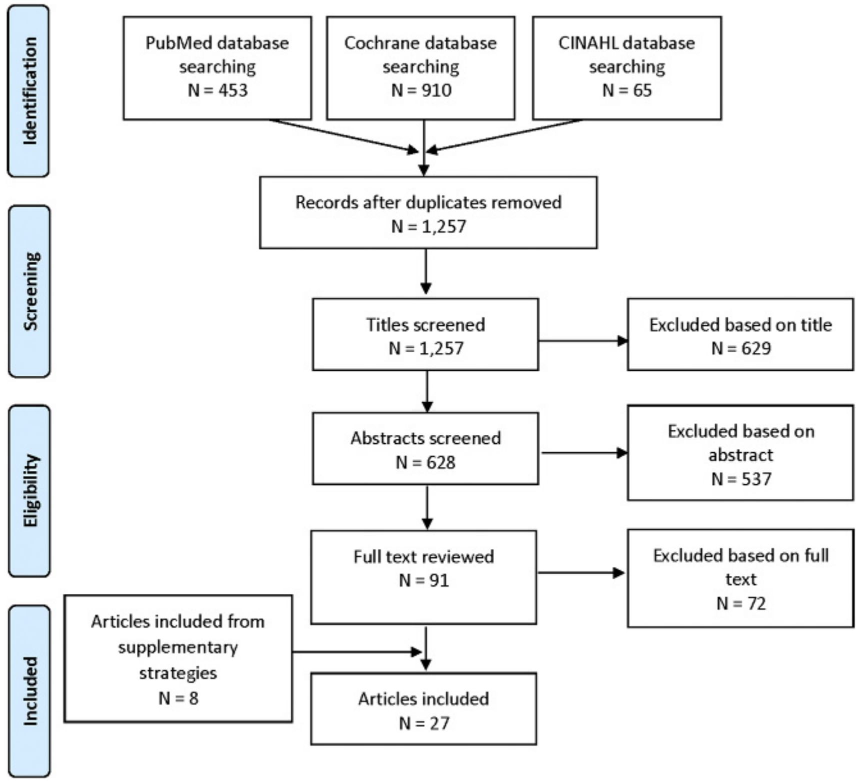

FIGURE 1—Summary of the search of primary research on physical activity and health outcomes in children younger than 6 yr.

Also, the studies were quite variable in terms of children's age range, years of follow-up, measurement of weight-related outcomes, and analytic procedures. Notwithstanding these differences, the studies were consistent in reporting that higher levels of physical activity were associated with lower levels of weight and/or adiposity in younger children. Twelve of the 15 studies found negative associations between physical activity and weight and/or adiposity (12–16,18,20–25). Although these studies were consistent in observing benefit with higher amounts of physical activity, limitations in study design and variability in methodologies across the studies precluded identifying a particular dose of physical activity that was needed to provide benefits.

Bone health. The literature search provided eight articles, with two additional articles added by committee members. These 10 articles represented four studies, two of which had prospective longitudinal study designs and two of which were randomized controlled trials (27–36). The study designs, methods, and findings of these studies are summarized in Table 2. Three of the four studies focused on preschool children (baseline ages, 3 to 5 yr) (27–35) and one study focused on infants (36). The dose of physical activity was defined and measured differently among the studies and included recreational gymnastics participation (months) (28–30), device-measured daily activity (min) (31–34), and bone-strengthening physical activity (sessions) (27,35,36). All studies used state-of-the-art imaging (dual-energy x-ray absorptiometry [DXA] and peripheral quantitative computed tomography) to measure bone outcomes and appropriate statistical modeling to control for growth. All studies examining children ages 3 to 5 yr showed statistically significant stronger bone in the more active children. The benefit differences were greater than expected via measurement error and large enough (almost always >3%) to indicate meaningful biological improvements. However, similar to the evidence for body weight and adiposity, the differences in physical activity measures prevented the assignment of a specific dose of physical activity needed for bone health benefits.

Cardiometabolic health. Very few studies have examined the association between physical activity and indicators of cardiometabolic health in children younger than 6 yr. The literature search resulted in the identification of three prospective cohort studies that included outcomes related to serum lipid and lipoprotein levels, respiratory symptoms, and blood pressure (13,37,38). One study reported that physical activity appeared to have an indirect association with blood lipids and lipoproteins in 3- to 4-yr-old children, through its relationship with lower levels of body fatness and higher levels of fitness (13), whereas another study reported an inverse association between physical activity and diastolic blood pressure in 5- to 7-yr-old children (38). A final study reported that physical activity at 2 yr of age was not related to respiratory symptoms, such as wheezing or shortness of breath at 3 to 4 yr of age (37). On the basis of the results from these available studies, the committee determined that there was insufficient evidence available to determine the effects of physical activity on cardiometabolic risk factors.

Cognition. The committee reviewed the scientific literature examining the relationship between physical activity and cognition in children younger than 6 yr. This review was

TABLE 1. Summaries of studies examining associations between physical activity and weight status on adiposity in children younger than 6 yr.

Study (Title, Citation)	Subjects	Sample Size	Study Design	Physical Activity Exposure	Adiposity Measures	Findings
Berkowitz et al., 1985 (12)	Infants at baseline (first 3 d of life); 4–8 yr old at follow up	52	Prospective Cohort	Neonatal physical activity measured by an electronic activity monitor inside a mattress	BMI and skinfolds	Neonatal PA was significantly correlated with measures of adiposity in childhood.
DuRant et al., 1993 (13)	3–4 yr olds at baseline, 4–5 yr old at follow up	123	Prospective Cohort	Physical activity assessed by heart rate monitoring	Waist-to-hip ratio, sum of skinfolds	Mean activity level was negatively correlated with waist/hip ratio. Temporal direction of the association is unclear.
Jago et al., 2005 (14)	3–4 yr old children at baseline; 6–7 yr old at follow up	133	Prospective Cohort	Physical activity assessed by heart rate monitoring and direct observation of sedentary behavior and TV viewing (CARS)	BMI	PA and TV viewing were significant predictors of BMI with both PA (– associated) and TV viewing (+ associated) becoming stronger predictors as the children age.
Janz et al., 2009 (15)	Ages 5, 8 and 11 yr	333	Prospective Cohort	Moderate-to-vigorous physical activity measured by accelerometry	Body fat measured by DXA	MVPA at age 5 yr was a predictor of adjusted fat mass at age 8 yr and age 11 yr, in both sexes.
Klesges et al., 1995 (16)	4 yr old at baseline	146	Prospective Cohort	Physical activity (Parent-reported structured, leisure, and aerobic activity)	BMI	Baseline aerobic activity predicted change in BMI over 2 yr.
Leppanen et al., 2017 (17)	4 yr old at baseline	138	Prospective Cohort	Light-intensity, moderate-intensity, vigorous intensity, and moderate-to-vigorous intensity physical activity & sedentary behavior measured by accelerometry	BMI and Fat Mass Index, Fat-free Mass Index, and %FM (from air-displacement plethysmography)	Higher VPA at the age of 4.5 yr was significantly associated with higher BMI and FFMI at 12-month follow-up. Higher baseline MVPA was also associated with higher FFMI at follow-up.
Li et al., 1995 (18)	Ages 6, 9, and 12 months	31	Prospective Cohort	Physical activity from 6-h direct observation (modified CARS)	Body fat measured by DXA	The percentage of body fat was inversely related to activity level. This association became stronger with increasing age and remained significant after adjustment for dietary energy intake.
Metcalf et al., 2008 (19)	5 yr old at baseline, 6–8 yr old at follow up	212	Prospective Cohort	Physical activity measured by accelerometry	BMI, skinfolds and waist circumference	PA above the government-recommended intensity of 3 METs was associated with a progressive improvement in metabolic health but not with a change in BMI or fatness.
Moore et al., 2003 (20)	4 yr old at baseline (males and females)	103	Prospective Cohort	Physical Activity by Caltrac accelerometer	BMI, Skinfolds	Higher levels of PA during childhood may lead to less body fat by the time of early adolescence. A protective effect of activity was evident in both sexes.
Moore et al., 1995 (21)	3–5 yr old	97	Prospective Cohort	Physical activity by Caltrac acclerometer	BMI, skinfolds	There was a protective effect of PA on body fat change in both sexes. Higher levels of PA during childhood lead to less body fat by the time of early adolescence.
Remmers et al., 2014 (22)	4–7 yr old at baseline, 6–9 yr at follow-up	470	Prospective Cohort	Light PA, MVPA and sedentary behavior measured by accelerometry	BMI z-scores	Increments of MVPA were associated with decreases in BMI z-score in heavier children, in both sexes.
Roberts et al., 1988 (23)	0–12 months old (6 infants from lean and 12 infants from overweight mothers)	18	Prospective Cohort	Total energy expenditure from doubly labeled water	Weight gain (1st year of life), triceps and subscapular skinfolds	Total energy expenditure at 3 months of age was 20.7% lower in infants who became overweight compared to other infants.
Saakslahti et al., 2004 (24)	4–7 yr old at baseline	155	Prospective Cohort	Physical activity measured by parental report (observation diary)	BMI	In girls, low-activity playing was positively correlated with BMI at age 4–5 yr and playing indoors was positively correlated with BMI at age 5–6 yr. There were no significant associations in boys.
Sugimori et al., 2004 (25)	3 yr old at baseline; 6 yr old at follow up	8170	Prospective Cohort	Physical activity measured by questionnaire (physical exercise/playing outdoor), physical club activities, duration of TV viewing)	BMI	Physical inactivity at age 6 yr was associated with temporal changes in overweight status between 3–6 yr in boys.
Wells et al., 1996 (26)	12 wk old at baseline; 2–3.5 yr old at follow up	30	Prospective Cohort	Physical activity energy expenditure measured from total energy expenditure (doubly labeled water) and minimal metabolism (Deltatrac Metabolic monitor); mother's diary of infant activity	Weight, BMI, skinfolds, and fat mass (from total body water)	PA energy expenditure at 12 wk was not associated with measures of adiposity at follow-up.

MVPA, moderate-to-vigorous physical activity; FFMI, fat free mass index.

TABLE 2. Summary of studies examining the association between physical activity and indicators of bone health in children younger than 6 yr.

Study (Title, Citation)	Subjects (Age, Sex, etc.)	Sample Size	Study Design	Physical Activity Exposure	Bone Outcomes	Findings
Binkley et al., 2004 (27)	3–5 yr old at baseline (males and females) mostly white	161	1 yr posttrial follow-up	Researcher delivered Intervention gross motor vs fine motor PA (5/d·wk^{-1}, 15–20 min·d^{-1}) and calcium supplementations	pQCT, DXA measured BMC and BA leg, periosteal and endosteal circumference tibia	Children in gross motor skill group maintained greater tibial periosteal circumference difference 1 yr postintervention compared to fine motor.
Erlandson et al., 2011 (28)	4–6 yr old at baseline (males and females) mostly white	163	Prospective Cohort Measured annually for 4 yr	Parent report (h·wk^{-1}) of recreational or precompetitive gymnastics	DXA measured total body, lumbar spine, and femoral neck BMC	Compared to nongymnasts in other recreational sports, gymnasts had 3% more total body BMC and 7% femoral neck BMC.
Gruodyte-Raciene et al., 2013 (29)	4–6 yr old at baseline (males and females) mostly white	165	Prospective cohort measured annually for 4 yr	Parent report (h·wk^{-1}) of recreational or precompetitive gymnastics	DXA and HSA program estimated CSA, Z, CT at NN, IT, S of hip	Compared to nongymnasts in other recreational sports, gymnasts had 6% greater NN CSA, 7% NN Z, 5% greater IT CSA, 6% greater IT Z and 3% greater S CSA.
Jackowski et al., 2015 (30)	4–6 yr old at baseline (males and females) mostly white	127	Prospective Cohort Measured over 3 yr	Parent report (h·wk^{-1}) of recreational or precompetitive gymnastics	pQCT measured distal and shaft measures of bone structure at radius and tibia	Compared to nongymnasts in other recreational sports, gymnasts had greater total bone area and total BMC at distal radius (8% to 21% difference).
Janz et al., 2006 (31)	4–6 yr old at baseline (males and females) mostly white	370	Prospective Cohort with a 3 yr follow-up	Device-measured MVPA 3000 ct/mn	DXA measured BMC hip, trochanter, spine, and total body	Compared to children maintaining low levels of PA, children maintaining high levels of PA throughout study accrued 14% more trochanteric BMC and 5% more total body BMC.
Janz et al., 2007 (32)	4–6 yr old at baseline (males and females) mostly white	468	Prospective Cohort Measured 3 times (baseline, approximately 8 yr and 11 yr)	Device-measured MVPA 3000 ct/mn	DXA and HSA estimated bone structure femoral neck Z and CSA	PA positive independent predictor of Z and CSA. 40 min·d^{-1} compared to 10 min·d^{-1} equated to 3%–5% greater CSA and Z
Janz et al., 2014 (33)	4–6 yr old at baseline (males and females) mostly white	530	Prospective cohort measured six times (baseline, approximately 8, 11, 13, 15, and 17 yr)	Device-measured MVPA (Evenson 2296 ct/min)	pQCT, DXA and HSA estimated BMC and bone structure of hip (CSA, Z) and tibia (bone stress index, polar moment of inertia)	Greater accumulation of MVPA resulted in great bone mass and structure at age 17 yr
Janz et al., 2010 (34)	4–6 yr old at baseline (males and females) mostly white	333	Prospective Cohort Measured three times baseline, approximately 8, and 11 yr)	Device-measured MVPA 3000 ct/min	DXA measured BMC total body, hip, spine	Children at highest quartile of MVPA at baseline had 4%–14% more BMC at age 8 and 11 yr when compared to peers in lowest quartile. Results attenuate when controlled for baseline BMC but remained significant in boys.
Specker and Binkley, 2003 (35)	3–5 yr at baseline (males and females) mostly white	239	1 yr randomized control trial	Researcher delivered Intervention gross motor vs fine motor PA (5/d·wk^{-1}, 15–20 min·d^{-1}) and calcium supplementations	pQCT, DXA measured BMC total body and leg, periosteal and endosteal circumference tibia	Children in gross motor skill group have greater tibial circumferences compared to fine motor.
Specker et al., 1999 (36)	6 months old at baseline (males and females) white	72	1 yr randomized control trial with outcome measures at baseline, 9, 12, 15 and 18 months.	Researcher delivered Intervention gross motor vs fine motor PA (5/d·wk^{-1}, 15–20 min·d^{-1}) and calcium supplementations	DXA measured BMC total body	No difference at follow-up between group.

pQCT, peripheral quantitative computed tomography; HSA, hip structural analysis; cross-sectional area; Z, section modulus; BMC, bone mineral content; CT, cortical thickness; NN, narrow neck; IT, intertrochanter; S, shaft.; MVPA, moderate-to-vigorous physical activity.

supported by a search of the literature that was independent of the search described above. That review process, and the committee's related conclusions, are described in detail in another article in this supplement (39). Two systematic reviews of the literature on physical activity and cognitive outcomes in preschool-age children met the criteria for inclusion (40,41). One of those systematic reviews considered seven observational and experimental studies, and the authors reported that six of the seven studies found that a higher amount of physical activity was associated with a beneficial effect on at least one cognitive outcome (40). The second systematic review reported that five of six randomized controlled trials found positive effects of selected indicators of cognitive development in 4- to 6-yr-old children (41). The existing studies and the cited systematic reviews point to possible beneficial effects of physical activity on cognitive outcomes in young children, but there is a clear need for more studies with rigorous research protocols.

Dose–response. Few studies of physical activity and health in children younger than 6 yr have been designed in a manner that allows examination of dose–response relationships. Given the absence of this information in the extant literature, there is a clear need to design experimental trials and prospective cohort studies to answer the question of whether a dose–response relationship exists for physical activity and health during this early period of the lifespan, and if so, what is the nature of that relationship. Such information is important toward not only understanding how physical activity influences health but also toward generating knowledge and support to best provide opportunities for intervention to support public health.

Effect modification. The studies on physical activity and health in children younger than 6 yr have rarely been designed in a manner that provided for examination of the potential modifying effects of demographic characteristics, such as sex, age, race/ethnicity, weight status, and socioeconomic status. Although studies included participants across a range of demographic characteristics, studies tended to control for potential confounders (e.g., sex, body size, lifestyle) but typically did not conduct stratified analyses to examine effect modification. Given the known differences in physical activity and health outcomes by demographic characteristics in older ages, it is important to understand the extent to which the health effects of physical activity may differ across demographic subgroups across the lifespan. Such information would provide additional understanding of whether the dose of physical activity needed to produce health benefits varies across population subgroups.

DISCUSSION

The overall conclusion of the systematic literature review presented in this article was that strong evidence demonstrates that higher amounts of physical activity are associated with more favorable indicators of bone health and with better weight status in children ages 3 to 6 yr. However, there was insufficient evidence to show a relationship between physical activity and indicators of cardiometabolic health in children younger than 6 yr. Further, for all health outcomes studied in this age group, evidence was insufficient to determine dose–response relationships and to determine whether the relationships between physical activity and health were moderated by factors, such as age, sex, race/ethnicity, or socioeconomic status. Relatively few studies have addressed the impact of physical activity on health in very young children, and there are a limited number of systematic reviews of this topic. Timmons et al. (7) reviewed the relevant literature for children in the 0- to 4-yr age range, and studies published up to May 2011 were included. Their conclusions were generally consistent with those of the present review. Although noting widely varying qualities of evidence, they concluded that, among preschoolers, higher levels of physical activity were associated with a number of positive health outcomes, including adiposity and indicators of cardiometabolic health.

More recently, systematic reviews have been undertaken to inform the development of the Canadian 24-Hour Movement Guidelines for the Early Years (42). The results of the review of the association between physical activity and health indicators indicated that intervention studies improved motor and cognitive development, and psychosocial and cardiometabolic health, whereas evidence from observational studies showed that physical activity was associated with favorable motor development, fitness, and bone and skeletal health (43). The Carson et al. review identified 96 studies in children 5 yr and younger compared with 25 studies we identified for the current review. However, we applied stricter inclusion criteria which, among other factors, excluded cross-sectional observational studies and studies which delivered parental or group-level interventions. These methodological differences may explain the somewhat different conclusions reached by the two reviews. Nonetheless, the conclusion of both reviews is that physical activity is positively associated with health indicators in preschool age children.

Weight status/adiposity. It is well documented that rates of overweight and obesity have increased dramatically in all segments of the US population, and this includes children younger than 6 yr (44). As a result of this trend, prevention of childhood obesity has become an important public health priority in the United States and other economically developed nations (45). In this context, the findings of the current systematic review are particularly important. It was concluded that there is strong evidence that higher amounts of physical activity are associated with better weight- and adiposity-related outcomes in 3- to 5-yr-old children. Several important factors were considered by the authors in arriving at that conclusion. First, rigorous standards were applied in selecting studies for inclusion in the review. Second, all studies included in this review applied prospective, observational research designs, which, in the view of the authors, is the best available method for studying the relationship between physical activity and weight/adiposity outcomes. In theory, experimental studies would be important, but there are concerns about the feasibility of treatments that would involve long-term, controlled exposures to modified physical activity in children younger than 6 yr. Third, most of the studies included in this review used objective, device-based measures of physical activity. Fourth, beneficial effects of higher amounts of physical activity were very consistently reported. Thirteen of the 15 studies included in this review found that more physically active children tended to gain less weight and/or fat mass than their less physically active counterparts. Other systematic reviews have drawn similar conclusions (4), although most have focused primarily on older children.

Although the authors found that the available evidence supports the conclusion that physical activity provides important benefits for weight-related outcomes in preschool age children, it is acknowledged that the existing research literature on this topic has important limitations. Because the number of currently available studies is modest, more studies with device-based measures of physical activity, well-validated measures of adiposity, and multiyear follow-up periods are needed. Further, future studies should carefully assess factors that might confound the relationship between physical activity and weight-related outcomes. These include diet and sleep behaviors. In addition, studies with large and diverse samples of children will be needed to determine whether or not the physical activity–weight/adiposity association is moderated by demographic factors and to describe dose–response relationships. Future studies will be needed to address these limitations. Nonetheless, it is the position of the authors that currently available evidence indicates that promotion of physical activity should be a major aim of public health efforts to prevent childhood obesity.

Bone health. Although few studies have focused on physical activity and bone health in preschool children, the results of the existing studies indicated that young children who engaged in bone-strengthening activities or in high levels of total physical activity have stronger bones. This conclusion is supported by observational evidence that the age of independent walking in toddlers is associated with greater lower-limb bone strength (46,47) and experiments that show mechanical loads create positive adaptations in the bones of young animals (48,49). The evidence related to relationships between physical activity and bone health in children younger than 6 yr when combined with the strong evidence that impact and muscle forces due to physical activity cause positive bone adaptations in older children and adolescents (50) indicate the important role of physical activity for ensuring strong and healthy bones throughout the growing years.

Cardiometabolic health. There is a paucity of information on the relationship between physical activity and cardiometabolic risk factors in children younger than 6 yr. In general, most preschool age children have a healthy cardiometabolic profile. Although the primordial prevention of cardiovascular disease is a lifelong endeavor, children do not typically begin to develop adverse cardiometabolic health outcomes until after being exposed to poor lifestyle behaviors for several years. With the exception of overweight and obesity, most available studies did not recruit children with elevated cardiometabolic risk factors. Therefore, there is a pressing need for studies among children with elevated levels of risk factors, in addition to the identification of novel cardiometabolic health markers that are sensitive to lifestyle changes, such as increased physical activity.

Cognition. The study of cognition sits within the broader field of brain health, which is a broad term conceptualized as the optimal or maximal functioning of behavioral and biological measures of the brain, including subjective experiences that arise from brain function (e.g., attention, mood). Brain health can be measured using biological markers of the brain (e.g., structural brain morphology) or via subjective manifestations of brain function, including mood and anxiety, perceptions of quality of life, cognitive function (e.g., attention and memory), and sleep. Relative to children younger than 6 yr, little is known regarding the relationship of physical activity to cognition and brain health. The available, preliminary evidence points to a beneficial association of physical activity to cognitive and academic outcomes, which should not be surprising given that findings in studies of older children and adults populations is much further along, and has evidenced benefits to brain structure and function, and a variety of cognitive outcomes. Regardless, further research is necessary to extend these effects to children younger than 6 yr, and to understand the nature of physical activity effects on cognition in this age group.

Children and youth—6 to 17 yr. The systematic review described above was focused on children younger than 6 yr. Though not described in detail in this article, the committee also reviewed systematic reviews and meta-analyses addressing the relationships between physical activity, sedentary behavior, and health outcomes in school-age children and youth (ages 6 to 17 yr; see detailed search description in the committee's report (50)). The findings for 6- to 17-yr-olds are consistent with, but go beyond, the findings for preschool-age children (3 to 6 yr). Similar to 3- to 6-yr-olds, higher amounts of physical activity were found to be associated with better indicators of bone health and with reduced risk for excessive increases in weight and adiposity among older children (50). Accordingly, for those two important health outcomes, the committee concluded that physical activity provides important benefits for young persons across the entire 3 to 17 yr age range. However, for several other health outcomes, beneficial effects of physical activity were found for older children but not documentable for children younger than 6 yr. These included indicators of cardiometabolic health, cardiorespiratory fitness, muscular fitness, cognition and risk of depression (39,50). The body of knowledge on physical activity and health is much more robust for school-age children than for children younger than 6 yr. Therefore, additional research will be needed to determine whether or not all the benefits of physical activity that have been documented for older children also accrue to those younger than 6 yr.

Strengths, limitations, and delimitations. The strengths of the review include a well-designed and transparent search and review process. In addition, most of the studies of adiposity or weight status used device-measured physical activity.

All the studies of bone health used state-of-the-art bone imaging procedures. The primary limitation is that relatively little research has been conducted on the relationship between physical activity and health in children younger than 6 yr. The existing volume and quality of research is sufficient to conclude that a beneficial relationship exists for bone health and weight status, but provides insufficient information about dose–response or any potential effect modification by age, sex, or race/ethnicity.

In the context of developing physical activity guidelines for dissemination to the public and professional groups, it is highly desirable to identify a specific amount of physical activity, or range of amounts of activity, that is known to be associated with important health outcomes. Hence, the authors' finding that the existing research is not sufficient to inform conclusions about dose–response relationships is particularly limiting. It was concluded that higher amounts of physical activity are associated with better outcomes for weight/adiposity and bone health than lower amounts of activity. However, the available research did not point to a specific dose of activity that was needed to produce these benefits. It is recognized that some authoritative groups have provided public health guidelines on physical activity for children younger than 6 yr (51–53). These guidelines have recommended that young children engage in three or more hours of total physical activity (light, moderate, and vigorous intensity), a level that corresponds approximately to the median for device-based measurement of physical activity in 3- to 5-yr-old children (8).

Further, it is important to acknowledge that the authors conducted this systematic review within certain delimitations. The charge to the 2018 Physical Activity Guidelines Advisory Committee was to consider new evidence that might inform revision of the 2008 Physical Activity Guidelines for Americans. Children younger than 6 yr were not included in the 2008 guidelines because, at that time, very limited research had been conducted on the health effects of physical activity in that age group. Accordingly, an important goal of the 2018 committee was to determine whether or not the available scientific evidence supported a conclusion that physical activity is related to important health outcomes in children younger than 6 yr. Hence the focus of the review was on studies in which amount of physical activity, of various types, was examined in relationship to one or more physiologic risk factors for development of noncommunicable diseases, such as cardiovascular disease, type 2 diabetes, and osteoporosis. The committee did not consider exposures, such as the behavioral quality of the physical activity exposure (e.g., enjoyment) or outcomes, such as fundamental motor skills. Nonetheless, it is noted that these are important constructs and are worthy of consideration in future comprehensive reviews of physical activity and health in young children.

Recommendations for future research. In reviewing the research evidence on the relationships between physical activity and health outcomes in children younger than 6 yr the committee found many areas in which existing evidence is limited and new studies are needed. Table 3 lists seven research recommendations that, if addressed in future investigations, would address current limitations and markedly expand the body of knowledge on physical activity and health in young people. The rationale for each of these recommendations is provided in the full 2018 Physical Activity Guidelines Advisory Committee Scientific Report (50). In particular, there is a need for studies in large samples using rigorous designs and methodologies. Because the committee's charge was to address questions and draw conclusions that inform public health guidelines on physical activity, the research recommendations identified by the committee were selected on the basis of their relevance to the guidelines development process. It is acknowledged that much remains to be learned about the effects of physical activity on health-related factors in children and youth in many areas that are not directly relevant to public health guidance.

TABLE 3. Recommendations for further research on physical activity and health in children and youth younger than 6 yr.

Conduct randomized controlled trials and prospective observational studies to elucidate the dose–response relationships for physical activity and health outcomes, including adiposity, cardiometabolic health, and bone health.
Undertake randomized controlled trials and prospective observational studies to determine whether the health effects of physical activity during early childhood differ across groups based on sex, age, maturational status, race/ethnicity, and socioeconomic status.
Conduct randomized controlled and prospective observational studies to examine the health effects of physical activity in young children with elevated risk status based on adiposity, cardiometabolic health, and bone health.
Develop valid methods for measuring physical activity and examine the health effects of physical activity in very young children between birth and 2 yr.
Examine the interactive effects of sedentary behavior and physical activity on health outcomes in young children.
Undertake prospective observational studies to examine the effects of physical activity during early childhood on health outcomes later in life.
Determine in young children the impact of genetic profiles on behavioral and physiological responses to physical activity and on the health effects of physical activity.

For children younger than 6 yr, the evidence linking physical activity to health was rated as strong only for two outcomes, weight/adiposity and bone health. Accordingly, there is a great need for research that will bolster our knowledge of other health outcomes, particularly including indicators of cardiometabolic health and cognition. Further, existing research is not adequate to identify clear dose–response relationships or to determine whether or not the health effects of physical activity are influenced by demographic factors such as sex, age, maturational status, race/ethnicity, or socioeconomic status. In addition, the research evidence on physical activity and health is very limited in children younger than 3 yr, and for this age group, methodological studies are needed to identify appropriate measures of physical activity for use in future investigations.

SUMMARY AND CONCLUSIONS

The 2018 Physical Activity Guidelines Advisory Committee reviewed the primary research literature addressing the relationship between physical activity and health outcomes in children younger than 6 yr. It was concluded that there is strong evidence indicating that higher amounts of physical activity are associated with better bone health and with better weight status/reduced risk for increases in weight and adiposity in children age 3 to 6 yr. The evidence was too limited to support conclusions regarding the effects of physical activity on cardiometabolic health and cognition, to delineate dose–response relationships, or to determine the influence of demographic effect modifiers. The evidence is particularly limited for children younger than 3 yr.

The committee also considered the relationships between physical activity and multiple health outcomes in children and youth across developmental stages from birth to adolescence. Most of the available evidence addressed these relationships in school-age youth (ages, 6–17 yr). The conclusions for the older age group were consistent with the findings for children younger than 6 yr in that higher amounts of physical activity were found to be associated with beneficial effects on adiposity and bone health.

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PRONOUNCEMENT

Benefits of Physical Activity during Pregnancy and Postpartum: An Umbrella Review

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ABSTRACT

DIPIETRO, L., K. R. EVENSON, B. BLOODGOOD, K. SPROW, R. P. TROIANO, K. L. PIERCY, A. VAUX-BJERKE, and K. E. POWELL, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Benefits of Physical Activity during Pregnancy and Postpartum: An Umbrella Review. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1292–1302, 2019. **Purpose:** This study aimed to summarize the evidence from the *2018 Physical Activity Guidelines Advisory Committee Scientific Report*, including new evidence from an updated search of the effects of physical activity on maternal health during pregnancy and postpartum. **Methods:** An initial search was undertaken to identify systematic reviews and meta-analyses published between 2006 and 2016. An updated search then identified additional systematic reviews and meta-analyses published between January 2017 and February 2018. The searches were conducted in PubMed®, CINAHL, and Cochrane Library and supplemented through hand searches of reference lists of included articles and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. **Results:** The original and updated searches yielded a total of 76 systematic reviews and meta-analyses. Strong evidence demonstrated that moderate-intensity physical activity reduced the risk of excessive gestational weight gain, gestational diabetes, and symptoms of postpartum depression. Limited evidence suggested an inverse relationship between physical activity and risk of preeclampsia, gestational hypertension, and antenatal anxiety and depressive symptomology. Insufficient evidence was available to determine the effect of physical activity on postpartum weight loss, postpartum anxiety, and affect during both pregnancy and postpartum. For all health outcomes, there was insufficient evidence to determine whether the relationships varied by age, race/ethnicity, socioeconomic status, or prepregnancy weight status. **Conclusions:** The gestational period is an opportunity to promote positive health behaviors that can have both short- and long-term benefits for the mother. Given the low prevalence of physical activity in young women in general, and the high prevalence of obesity and cardiometabolic diseases among the U.S. population, the public health importance of increasing physical activity in women of childbearing age before, during, and after pregnancy is substantial. **Key Words:** ANXIETY, EXERCISE, GESTATIONAL DIABETES, DEPRESSION, PREECLAMPSIA, WEIGHT GAIN

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Pregnancy is a unique period of life for most women. The multiple hormonal, physiologic, and biomechanical changes that occur, such as increased blood volume and heart rate, weight gain, and shift in the center of mass, almost always proceed normally. For women experiencing a healthy pregnancy, regular engagement in moderate-intensity physical activity for at least 20 to 30 $min \cdot d^{-1}$ on most or all days of the week has been recommended during pregnancy and postpartum period by the American College of Obstetricians and Gynecologists (ACOG) in 2015 (1) and reaffirmed in 2017 (2). Similarly, the *2008 Physical Activity Guidelines for Americans* recommended 150 to 300 $min \cdot wk^{-1}$ of moderate-intensity aerobic activity during pregnancy and postpartum spread throughout the week (3). These recommendations were made in an effort to prevent several complications that may occur during the gestational period. Such complications include the development of diabetes, gestational hypertensive disorders, and fetal growth impairments that are associated with increased risk of adult cardiovascular disease and early mortality in the mother (4) and possibly in their offspring (5).

Despite substantial advances in scientific knowledge and development of guidelines to promote physical activity in pregnancy, most pregnant women do not achieve the current physical activity recommendations, and many continue to be inactive during and after pregnancy (6,7). In fact, only 23% to 29% of pregnant women at any gestational stage in the United States met the minimum physical activity guidelines, based on the National Health and Nutrition Examination Survey data collected between 2007 and 2014 (8). Moreover, women who were active before pregnancy report that their physical activity level decreased once they became pregnant (9). There is also evidence that during postpartum, women may not return to their earlier physical activity levels for reasons such as lack of time, fatigue, or depressive symptoms (10).

The 2018 Physical Activity Guidelines Advisory Committee (PAGAC) Pregnancy and Postpartum Work Group recently conducted a systematic review of the evidence concerning the relationship between physical activity and various health outcomes during pregnancy and postpartum period (defined up to 12 months after delivery). Results of this review were published in the 2018 PAGAC Scientific Report (11). This current article summarizes the evidence from the 2018 PAGAC Scientific Report, including new evidence from an updated search of the effects of physical activity on maternal health during pregnancy and postpartum.

METHODS

The PAGAC Pregnancy Work Group addressed four major questions (11):

1. What is the relationship between physical activity and weight gain during pregnancy and weight loss during postpartum?
2. What is the relationship between physical activity and the incidence of gestational diabetes mellitus (GDM)?
3. What is the relationship between physical activity and the incidence of preeclampsia and hypertensive disorders during pregnancy?
4. What is the relationship between physical activity and affect, anxiety, and depression during pregnancy and postpartum?

Questions 1 through 4 had the following subquestions: (a) What dose of physical activity is associated with the reported quantitative benefit or risk? (b) Is there a dose–response relationship? If yes, what is the shape of the relationship? (c) Does the relationship vary by age, race/ethnicity, socioeconomic status, or prepregnancy weight status?

Literature search strategy and study selection. The work group first identified two high-quality existing reports: 1) the *2008 Physical Activity Guidelines Advisory Committee Report* (12) and 2) the 2015 ACOG Committee Opinion on Physical Activity and Exercise during Pregnancy and the Postpartum Period (1). After reviewing these documents, the work group decided that they could serve as a foundation for describing the relationship between physical activity and maternal heath during pregnancy and postpartum (refer to Table F8-3 in the 2018 PAGAC Scientific Report).

To identify the most recent pertinent literature, the work group used the literature searches conducted by three of the 2018 PAGAC subcommittees that had outcomes of interest related to the pregnancy and postpartum questions. Seven searches for systematic reviews, meta-analyses, pooled analyses, and high-quality reports conducted by other PAGAC subcommittees were considered to provide potentially pertinent information (Table 1). An initial search was undertaken in October 2016 to include publications from 2006 to 2016. The searches were conducted in PubMed®, CINAHL, and Cochrane Library and supplemented through hand searches of reference lists of included articles. Findings were reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines (13).

TABLE 1. Research questions from other subcommittees that provided evidence to answer questions related to pregnancy and postpartum (2018 PAGAC Scientific Report).

Subcommittee, Question No.	Question
Cardiometabolic Health and Weight Management, Q1	What is the relationship between physical activity and prevention of weight gain?
Cardiometabolic Health and Weight Management, Q2	In people with normal blood pressure or prehypertension, what is the relationship between physical activity and blood pressure?
Cardiometabolic Health and Weight Management, Q3	In adults without diabetes, what is the relationship between physical activity and incident type 2 diabetes?
Brain Health, Q2	What is the relationship between physical activity and quality of life?
Brain Health, Q3	What is the relationship between physical activity and 1) affect, 2) anxiety, and 3) depressed mood and depression?
Brain Health, Q4	What is the relationship between physical activity and sleep?
Aging, Q2	What is the relationship between physical activity and physical function? (The search for this question was not restricted to older age-groups).

All search results that included "gestation," "postp," "pregn," "natal," or "maternal" in the title or abstract were provided to the work group. The title, abstract, and full-text triage review process was the same as that used for other 2018 PAGAC topics (11,14). The work group relied on these publications as the sources of potential evidence regarding quantifiable benefits or risks of physical activity, as well as the dose associated with specific health outcomes. The work group also completed one supplementary search by adding "eclampsia" and "preeclampsia" to the Cardiometabolic Health and Weight Management Subcommittee search on hypertension. In March 2018, an updated systematic review was undertaken to identify additional systematic reviews and meta-analyses published between January 2017 and February 2018.

Quality assessment. The evidence to inform each of the work group's four questions and subquestions was graded as strong, moderate, limited, or "grade not assignable" based on several criteria, including applicability, generalizability, risk of bias/study limitations, quantity and consistency of results across studies, and magnitude and precision of effect. These criteria are described in Supplemental Table 1 (see Table, Supplemental Digital Content 1, 2018 Physical Activity Guidelines Advisory Committee Grading Criteria, http://links.lww.com/MSS/B531).

RESULTS

After duplicates were removed, a total of 254 articles were identified through the initial search process, and the titles were reviewed by two of the three members of the work group. A total of 122 articles were deemed potentially relevant based on the title search (Fig. 1). The abstracts of these articles were then reviewed by at least two members of the work group. The quality for each systematic review, meta-analysis, or pooled analysis was assessed using AMSTARExBP (15). Risk of bias was assessed for each study using an adapted version of the Nutrition Evidence Library Bias Assessment Tool by the U.S. Department of Agriculture (16). Two original review articles were added to the group of articles being reviewed at full text, and thus, a total of 73 articles were determined to be potentially relevant, and the full articles were retrieved and reviewed.

The updated search (conducted in March 2018) identified 47 articles, of which 7 were deemed relevant for full-text

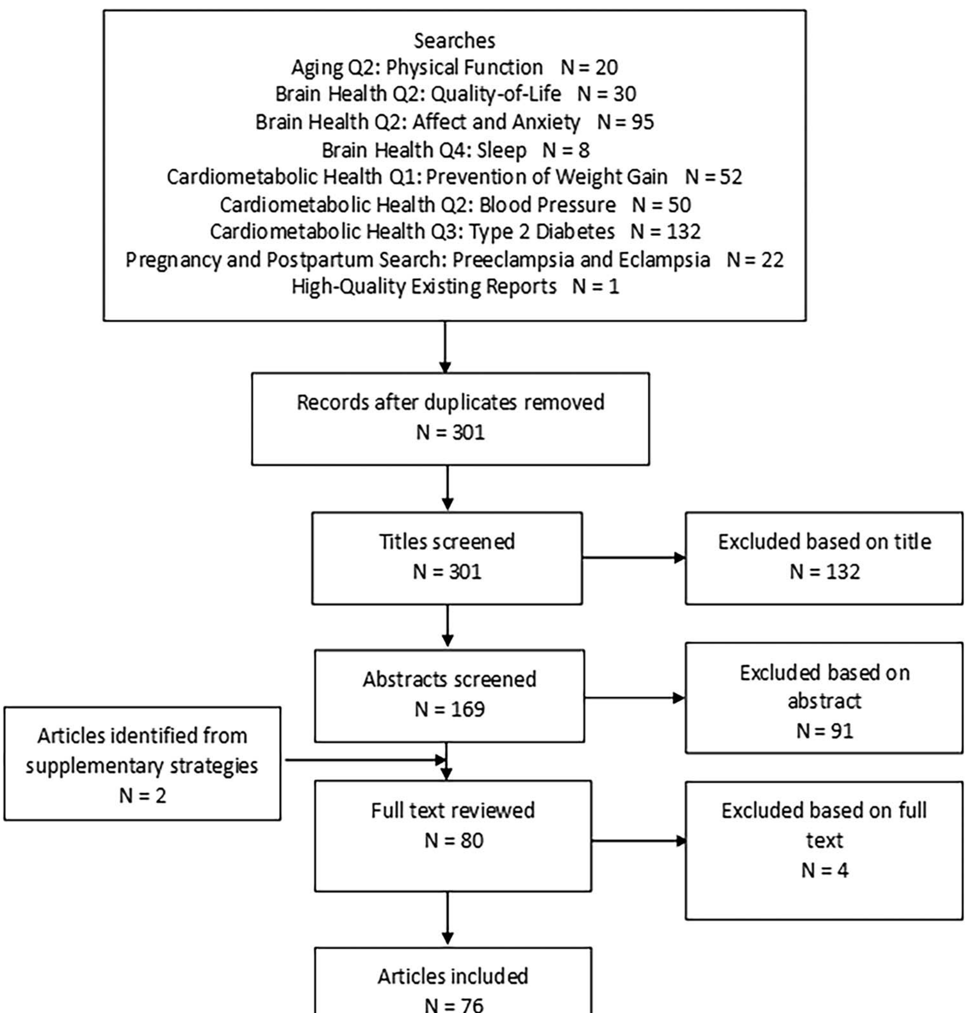

FIGURE 1—Flow diagram of search strategy and study selection for both the initial 2018 PAGAC Scientific Report and the updated search. *Articles from the updated search.

review. After full-text review by three members of the work group, four articles were excluded because they failed to meet the inclusion criteria. Of the remaining three reviews from the updated search, one provided information about gestational weight gain, GDM, and hypertensive disorders (17); one about gestational hypertensive disorders (18); and one about postpartum depression (19). Therefore, the initial and updated searches yielded a total of 76 articles, 38 of which are reported on in this current review (Fig. 1).

Table 2 summarizes the level of evidence for the relationship between physical activity and each health outcome during pregnancy and postpartum. Overall, there was strong evidence demonstrating an inverse relationship between physical activity during pregnancy and gestational weight gain, GDM, and postpartum depression.

Gestational Weight Gain

In the 2018 PAGAC Scientific Report, 11 systematic reviews provided strong evidence that women assigned to physical activity interventions gain about 1 kg less weight during pregnancy than women in comparison groups. Of the nine reviews that included meta-analyses (20–28), all but one reported significantly less weight gained in the physical activity group. The other meta-analysis included only pregnant women who were overweight or obese and reported significantly attenuated weight gain among active versus inactive women who were obese but not among those who were overweight (26).

One meta-analysis (20) reviewed 30 randomized controlled trials (RCT). On the basis of a meta-analysis of 18 of those RCT, which included 1598 women performing a structured exercise program and 1605 receiving standard care, the standardized mean difference (SMD) in gestational weight gain was −1.11 kg (95% confidence interval [CI] = −1.59 to −0.69), with women in the exercise group gaining less weight than women receiving standard care. The other meta-analyses of RCT (21–28) reported similar SMD in gestational weight gain between exercising and control women, ranging from −0.36 kg (95% CI = −0.64 to −0.09; 5 studies) (24) to −2.22 kg (95% CI = −3.14 to −1.30; 3 studies) (21). The updated search identified a meta-analysis that analyzed participant-level data by the International Weight Management in Pregnancy (i-WIP) Collaborative Group (17), which further corroborated the finding that women who were physically active during pregnancy experience attenuated weight gain compared with women who are not (SMD = −0.73 kg, 95% CI = −1.11 to −0.34 kg; 15 studies).

Several of the systematic reviews and meta-analyses (20,22,23) examined the relationship between physical activity and "excess" weight gain, as defined by the Institute of Medicine Guidelines (29). In general, women who reported physical activity during pregnancy experienced a significantly lower risk of excess weight gain compared with women who did not, with pooled effect sizes (ES) ranging from 18% (20) to 23% (23). On the basis of this literature review, the overall evidence was strong for an inverse association between physical activity and excess gestational weight gain. Muktabhant et al. (23) also examined the relationship between exercise during pregnancy and "low" or insufficient gestational weight gain. Women from the general population having a normal (18.5–24.9 $kg \cdot m^{-2}$) body mass index (BMI; "low risk") or any BMI ("mixed risk") experienced a marginally greater chance of "low" weight gain compared with the nonexercising control group (average relative risk [RR] = 1.20, 95% CI = 1.00 to 1.43; 3 studies). There was no relationship between exercise and insufficient weight gain among women whose pregnancies were considered high risk and who also were overweight or obese ("high risk") (average RR = 1.03, 95% CI = 0.66–1.60; 3 studies).

Dose and dose–response. The dose of physical activity prescribed in the RCT varied among the studies. Similarly, the assessment and categorization of the reported leisure time physical activity was not consistent. It appears, however, that most RCT interventions used an exercise regimen involving primarily aerobic activity of moderate-intensity (walking, swimming, and aerobic exercise), occurring at least three times per week for a duration of 30 to 60 min per session. This dose of physical activity is similar to the recommendations of both the ACOG Guidelines and the 2008 Physical Activity Guidelines (1,3).

Most of the reviews did not assess whether maternal physical activity and gestational weight gain had a dose–response relationship. Indirect evidence of a dose–response relationship was suggested, however, by the observation that adherence to the prescribed exercise program was significantly higher in the "successful" interventions (22), and the observation in a meta-analysis of 28 RCT in which the mean difference in gestational weight gain between the exercise and the control groups was

TABLE 2. Summary of the level of evidence for the relationship between physical activity and each health outcome during pregnancy and postpartum.

	Overall Evidence	Dose	Dose–response	Effect Modification by Sociodemographic Factors or Weight
Gestational weight gain	Strong	Limited	Limited	Not assignable
Weight loss during postpartum	Not assignable	Not assignable	Not assignable	Not assignable
Gestational diabetes	Strong	Limited	Limited	Not assignable
Preeclampsia/gestational hypertension	Limited	Limited	Limited	Not assignable
Antenatal affect, anxiety, and depression	Not assignable	Not assignable	Not assignable	Not assignable
	Limited	Not assignable	Not assignable	Not assignable
	Limited	Not assignable	Not assignable	Not assignable
Postpartum affect, anxiety, and depression	Not assignable	Not assignable	Not assignable	Not assignable
	Not assignable	Not assignable	Not assignable	Not assignable
	Strong	Not assignable	Not assignable	Not assignable

inversely correlated with both the duration (wk) of the intervention (Pearson product moment correlation coefficient [r] = −0.51, P = 0.023) and the volume (h·wk^{-1}) of exercise prescribed (r = −0.45, P = 0.05) (28). The evidence grade for the dose and dose–response relationship between physical activity and gestational weight gain was limited.

Sociodemographic factors and weight status. None of the systematic reviews or meta-analyses from the 2018 PAGAC Scientific Report assessed whether the purported relationship between physical activity and gestational weight gain varied by age, race/ethnicity, socioeconomic status, or prepregnancy weight status. The i-WIP Collaborative Group meta-analysis (17), which analyzed participant-level data from 15 RCT (N = 2915), reported that the inverse relationship between physical activity and gestational weight gain did not vary by age, race/ethnicity, or prepregnancy weight status.

With regard to weight status, most of the findings were reported among women of normal weight (i.e., BMI = 18.5–24.9 kg·m^{-2}). However, four systematic reviews (22,23,26,28) stratified their data by prepregnancy weight status (i.e., normal weight, overweight [BMI = 25–29.9 kg·m^{-2}], or obese [BMI ≥30 kg·m^{-2}]). Three of these studies observed stronger effects among pregnant women of normal weight, compared with those who were overweight or obese (22,23,28). One meta-analysis of women who were overweight or obese (26) reported a greater difference in gestational weight gain between the exercise and the control groups among women with obesity (SMD = −0.91 kg, 95% CI = −1.66 to −0.16; 3 studies), but not in women who were overweight (SMD = −0.12, 95% CI = −0.52 to 0.26; 3 studies). By contrast, the meta-analysis from the i-WIP Collaborative Group (17) reported that the inverse relation between physical activity and gestational weight gain did not vary across different subgroups of women categorized by BMI (normal weight, overweight, and obese). Thus, the evidence grade for effect modification on the relationship between physical activity and gestational weight gain was not assignable.

Weight loss during the postpartum period. A total of five systematic reviews and meta-analyses (21,30–33) that included only six original research articles and a total of 287 participants addressed the relationship between physical activity and weight loss during the postpartum period. Most of these reviews reported no significant difference in weight loss between women who performed physical activity during postpartum (alone, without dietary restriction) and the control group. Because of the insufficient number of studies linking physical activity to postpartum weight loss, an evidence grade for this relationship was not assignable.

GDM

Of the 13 meta-analyses from the 2018 PAGAC Scientific Report, 8 described higher levels of physical activity to be associated with statistically significant reductions in the risk of GDM (Table 3) (20,24,34–39), 4 reported nonsignificant reductions (40–43), and 1 reported a nonsignificant increase (44). The reduced RR of GDM (regardless of statistical significance) ranged from 0.45 to 1.01, with a median value of RR = 0.73. The updated search identified one additional meta-analysis of 10 RCT (N = 2700 women) that also reported a significantly lower risk of GDM among women participating in physical activity interventions compared with those in a control condition (odds ratio [OR] = 0.67, 95% CI = 0.46 to 0.99) (17). Notably, this risk reduction in the incidence of GDM reported in many of these meta-analyses is similar to the 25%–30% reduction in the risk of type 2 diabetes among the general population that is associated with 150 to 300 min·wk^{-1} of moderate-intensity physical activity (for more details, refer to the 2018 PAGAC Scientific Report, Part F, Chapter 5).

TABLE 3. Summary of findings from 14 meta-analyses of the relationship between prepregnancy and early pregnancy physical activity and risk of GDM.

Author, yr	Study Design	Effect (95% CI)
Prepregnancy physical activity		
Aune et al. (2016)	**Cohort (N = 8)**	**sRR = 0.78 (0.61–1.00)**
Tobias et al. (2011)	**RCT (N = 7)**	**pOR = 0.45 (0.28–0.75)**
Early pregnancy physical activity		
i-WIP Collaborative Group (2017)[a]	**RCT (N = 10)**	**OR = 0.67 (0.46–0.99)**
Aune et al. (2016)	Cohort (N = 5)	sRR = 0.97 (0.73–1.28)
	RCT (N = 12)	**sRR = 0.69 (0.50–0.96)**
	Combined (N = 17)	**sRR = 0.80 (0.64–1.00)**
da Silva et al. (2017)	Cohort (N = 6)	sOR = 0.75 (0.55–1.01)
	RCT (N = 10)	**sOR = 0.67 (0.49–0.92)**
Di Mascio et al. (2016)	**RCT (N = 4)**	**sRR = 0.51 (0.31–0.82)**
Han et al. (2011)	RCT (N = 3)	sRR = 1.10 (0.66–1.84)
Madhuvrata et al. (2015)	RCT (N = 3)	pOR = 0.77 (0.33–1.79)
Oostdam et al. (2011)	RCT (N = 3)	Risk difference = −0.05 (−0.20 to 0.10)
Russo et al. (2015)	**RCT (N = 10)**	**sRR = 0.72 (0.58–0.91)**
Sanabria-Martinez et al. (2015)	**RCT (N = 8)**	**sRR = 0.69 (0.52–0.91)**
Song et al. (2016)	RCT (N = 10)	sRR = 0.77 (0.54–1.09)
Tobias et al. (2011)	**RCT (N = 5)**	**pOR = 0.76 (0.70–0.83)**
Yin et al. (2014)	RCT (N = 6)	sRR = 0.91 (0.57–1.44)
Yu et al. (2017)	**RCT (N = 5)**	**SMD = 0.59 (0.39–0.88)**
Zheng et al. (2017)	**RCT (N = 4)**	**SMD = 0.62 (0.43–0.89)**

Studies with statistically significant findings are in bold type.
[a]Identified in the updated search.
sRR, standardized relative risk; sOR, standardized odds ratio; pOR, pooled odds ratio.

Aune et al. (34) reviewed 23 studies of total physical activity (leisure time, occupational, and household activity combined) and of leisure time physical activity performed before or during early pregnancy and the incidence of GDM. Those women who reported performing highest levels of total physical activity before pregnancy experienced a significantly lower risk of GDM compared with women reporting lowest levels of total activity (RR = 0.62, 95% CI = 0.41 to 0.94; 4 studies), whereas high versus low levels of total activity performed during early pregnancy did not significantly lower the risk of GDM (RR = 0.66, 95% CI = 0.36 to 1.21; 3 studies). On the other hand, women performing the highest levels of moderate-intensity leisure time physical activity either before (RR = 0.78, 95% CI = 0.61 to 1.00; 8 studies) or during pregnancy (RR = 0.80, 95% CI = 0.64 to 1.00; 12 studies) significantly lowered their risk of GDM by about 20% (34). Women who performed such physical activity both before and during pregnancy lowered their risk by 59% (RR = 0.41, 95% CI = 0.23 to 0.73; 2 studies) compared with those reporting no physical activity during both time periods. High versus low levels of vigorous activity performed before pregnancy significantly lowered the risk of GDM by nearly 25% (summary RR = 0.76, 95% CI = 0.66 to 0.88; 3 studies), but this was not the case for vigorous activity performed during pregnancy (RR = 0.95, 95% CI = 0.55 to 1.63; 2 studies). On the basis of this review of literature, the overall evidence was strong for an inverse association between physical activity and GDM.

Dose and dose–response. The dose of physical activity prescribed in the RCT varied among the studies. Similarly, the assessment and categorization of reported leisure time physical activity from observational studies was not detailed nor consistent. Most RCT interventions used a physical activity regimen involving primarily aerobic activity of at least moderate intensity (walking, cycling, swimming, and aerobic dance), occurring at least three times per week for a duration of 30 to 60 min per session, which is similar to both ACOG Guidelines and the 2008 Physical Activity Guidelines (1,3).

Aune et al. (34) performed a dose–response analysis and reported that each 5 $h \cdot wk^{-1}$ increment in prepregnancy physical activity lowered the risk of GDM by about 30% (RR = 0.70, 95% CI = 0.49–1.01; 3 studies), with significant evidence of nonlinearity ($P < 0.005$). A similar relationship was not observed for physical activity performed during early pregnancy (RR = 0.98, 95% CI = 0.87–1.09; 3 studies). Evidence from two observational studies in the meta-analysis by Tobias et al. (37) suggests that women who walked at a brisk pace before pregnancy and for a longer duration significantly lowered their risk of GDM compared with women who walked at a casual pace for shorter durations (pooled OR = 0.59, 95% CI = 0.30 to 0.87). The evidence grade for the dose and dose–response relationship between physical activity and GDM was limited.

Sociodemographic factors and weight status. Almost none of the systematic reviews or meta-analyses assessed whether the relationship between physical activity and GDM varied by age, race/ethnicity, or socioeconomic status. The review by Song et al. (42) reported that physical activity during pregnancy had a significant effect on GDM risk in women ages 30 yr and older, but not in women younger than age 30 yr. The i-WIP Collaborative Group reported that the benefits of physical activity to the reduction in risk of GDM were similar across the different subgroups of women categorized by age, race/ethnicity, or BMI (17).

Preeclampsia and Gestational Hypertension

Hypertensive disorders during pregnancy include preeclampsia and gestational hypertension. Preeclampsia is characterized by high blood pressure, high levels of protein in the urine (proteinuria), and swelling in the hands and feet. Gestational hypertension is elevated blood pressure without concomitant signs of preeclampsia such as proteinuria. Its relationship, if any, with preeclampsia is unclear.

Nine reviews from the 2018 PAGAC Scientific Report provided only limited evidence of an inverse relationship between total volume of physical activity and risk of preeclampsia or incident gestational hypertension (20,23,35,39,45–49). One meta-analysis that included cohort and case–control studies reported a beneficial association between higher levels of physical activity and reduced risk of preeclampsia from both prepregnancy (RR = 0.65, 95% CI = 0.47 to 0.89; 5 studies) and early pregnancy physical activity (RR = 0.79, 95% CI = 0.70 to 0.91; 11 studies) (45). The meta-analysis of 10 cohort studies by Kasawara et al. (46) reported no association between leisure time physical activity and preeclampsia (OR = 0.99, 95% CI = 0.93 to 1.05). By contrast, their meta-analysis of six case–control studies reported a significantly lower odds of preeclampsia (OR = 0.77, 95% CI = 0.64 to 0.91) with physical activity performed in prepregnancy (summarized from only two studies) being more effective (OR = 0.56, 95% CI = 0.41–0.76) than physical activity performed during pregnancy (OR = 0.77, 95% CI:0.64 to 0.91). Three meta-analyses comprising RCT and cohort studies found no association between physical activity and preeclampsia; one of the studies examined prepregnancy physical activity (20), whereas the other two studies examined early pregnancy physical activity (23,39).

One systematic review (47) and one meta-analysis (35) examined the relationship between physical activity and hypertensive disorders during pregnancy. Di Mascio et al. (35) reported an RR of 0.21 (95% CI = 0.09–0.45; 3 studies) for hypertensive disorders among women performing moderate-intensity leisure activities (aerobic dance, cycling, hydrotherapy, and resistance exercises) during pregnancy, compared with women performing no activity. The updated search identified two additional meta-analyses (17,18) about physical activity and hypertensive disorders during pregnancy. The i-WIP Collaborative Group (17) reported null findings (OR = 0.74, 95% CI = 0.42 to 1.33); however, Magro-Malosso et al. (18) reported a significantly lower incidence of gestational hypertensive disorders (RR = 0.39, 95% CI = 0.20 to 0.73; 7 studies) and gestational hypertension (RR = 0.54, 95% CI = 0.32 to 0.91; 16 studies) and a similar incidence of preeclampsia (RR = 0.37, 95% CI = 0.12 to 1.15; 6 studies) in pregnant women assigned to aerobic exercise (without dietary counseling) groups compared with women assigned to standard care control groups. On the basis of this review of literature, the overall evidence was limited for an inverse association between physical activity and both preeclampsia and gestational hypertension.

Dose and dose–response. The meta-analysis by Aune et al. (45) was the only review to report on the dose–response relation between physical activity and risk of preeclampsia. In their analysis of prepregnancy physical activity, the results indicated a 28% lower risk of preeclampsia for each 1 $h \cdot d^{-1}$ increment in physical activity (OR = 0.72, 95% CI = 0.53 to 0.99; 3 studies) and a 22% lower risk for each 20-$MET \cdot h \cdot wk^{-1}$ increment (OR = 0.78, 95% CI = 0.63 to 0.96; 2 studies). This relationship appeared nonlinear, with a flattening of the curve at higher levels of physical activity. Indeed, there was a 40% reduction in risk up to 5–6 $h \cdot wk^{-1}$ but no further reductions at higher physical activity levels (Fig. 2). With regard to physical activity performed

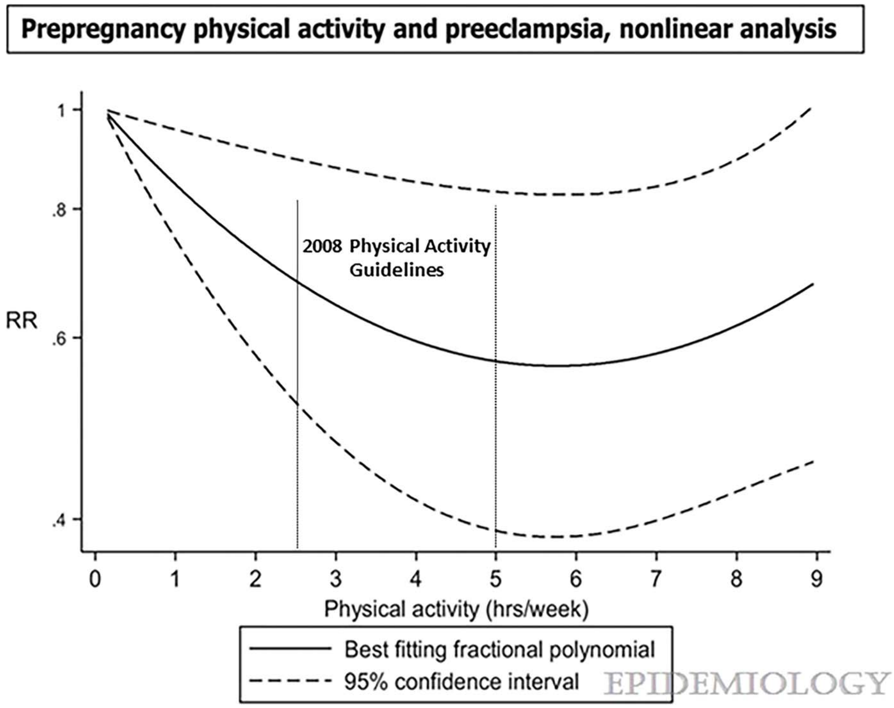

FIGURE 2—The dose–response relationship between prepregnancy physical activity and risk of preeclampsia. The results indicate a 28% lower risk of preeclampsia for each 1 h·d^{-1} increment in activity, compared with no activity (OR = 0.72, 95% CI = 0.53 to 0.99). Adapted with permission from Aune D, Saugstad OD, Henriksen T, Tonstad S. Physical activity and the risk of preeclampsia: a systematic review and meta-analysis. *Epidemiology*. 2014;25(3):331–343. Copyright © 2014 Wolters Kluwer Health, Inc.

during early pregnancy, the risk of preeclampsia was reduced in a linear manner by 17% for each 1 h·d^{-1} increment in physical activity (OR = 0.83, 95% CI = 0.72 to 0.95; 7 studies) and by 15% for every 20 MET·h·wk^{-1} increment (OR = 0.85, 95% CI = 0.68 to 1.07; 3 studies). The evidence grade for the dose and dose–response relationship between physical activity and both preeclampsia and gestational hypertension was limited.

Sociodemographic factors and weight status. There was no available evidence that evaluated whether the relationship between physical activity and preeclampsia varied by age, race/ethnicity, socioeconomic status, or weight status. Mutkabhant et al. (23) analyzed their data according to prepregnancy weight status (normal weight, overweight, or obese) and observed that even among pregnant women with overweight or obesity, there was no difference in risk of preeclampsia (based on two studies) between women in the exercise groups and those in the control groups (RR = 1.60, 95% CI = 0.38 to 6.73). The i-WIP Collaborative Group reported that the relationship between physical activity and hypertensive disorders during pregnancy were similar across the different age, race/ethnicity, and BMI subgroups of women (17). The evidence grade for effect modification on the relationship between physical activity and both preeclampsia and gestational hypertension was not assignable.

Physical activity, affect, anxiety, and depression during pregnancy and postpartum. We identified no systematic reviews or meta-analyses that examined the relationship between physical activity and affect, either during pregnancy or during the postpartum period. We found limited evidence that yoga performed during pregnancy significantly reduced anxiety symptomology (50,51); however, no systematic reviews or meta-analyses were found that examined this relationship during the postpartum period. There was also limited evidence to suggest that higher levels of physical activity were associated with reduced symptoms of depression during pregnancy (50,51). On the other hand, strong evidence demonstrated that there was an inverse relationship between physical activity and reduced symptoms of depression during postpartum.

With regard to antenatal anxiety and depressive symptoms, Sheffield et al. (50) provided a systematic review of 13 studies (7 of which were RCT) that examined the effects of practicing yoga during pregnancy on symptoms of anxiety and depression during that same period. Of the five studies that evaluated anxiety symptomology, all of them reported statistically significant improvements in the State/Trait Anxiety Inventory scores after a yoga intervention, and six of seven studies observed a statistically significant improvement in the Center for Epidemiologic Studies Depression scale score. Shivakumar et al. (51) reported that women who were more physically active during pregnancy reported reduced symptoms of anxiety in one of three studies that examined symptoms of anxiety, whereas two other studies in the same review both reported reduced symptoms of depression in pregnant adolescent girls who performed physical activity compared with their sedentary counterparts.

Two meta-analyses (52,53) and one systematic review (54) examined the relationship between physical activity and symptoms of depression during the postpartum period. The updated search identified an additional meta-analysis of 13 RCT (19). McCurdy et al. (52) examined 16 RCT comparing light- to moderate-intensity aerobic exercise (initiated in the first year postpartum) to standard care in postpartum women (N = 1327) with (10 RCT) and without (6 RCT) mild to moderate depression. In general, depressive symptom scores (based on the Edinburgh Postnatal Depression Scale [EPDS]) were lower among those in postpartum exercise intervention groups compared with those in control groups (pooled SMD = −0.34, 95% CI = −0.50 to −0.19). Among the 10 treatment RCT in women with postpartum depression, a moderate beneficial effect of exercise on depressive symptoms also was observed (SMD = −0.48, 95% CI = −0.73 to −0.22) relative to the control group. Moreover, in women classified with depression preintervention (defined as an EPDS score greater than 12), exercise increased the odds of resolving depression postintervention by 54% (OR = 0.46, 95% CI = 0.25 to 0.84; 3 trials; N = 173) compared with the control group. It is not clear, however, whether these benefits were independent of medication or social support. In the six prevention trials (i.e., women without depression), a beneficial effect of postpartum exercise was observed based on the EPDS score (SMD = −0.22, 95% CI = −0.36 to −0.08) compared with standard care.

These findings are consistent with those from a smaller review and meta-analysis by Poyatos-Leon and colleagues (53), which reported improved postpartum depressive symptomology (measured by EPDS or by the Beck Depression Inventory [BDI]) among women performing physical activity during pregnancy and the postpartum period, compared with those who were not (ES = 0.41, 95% CI = 0.28 to 0.54; 12 studies). Of note, the benefits of physical activity were more pronounced in women who met criteria for postpartum depression (ES = 0.67, 95% CI = 0.44–0.90; 6 studies) compared with those who did not (ES = 0.29, 95% CI = 0.14 to 0.45). Most (10 of 12) of the interventions started during the postpartum period and involved a variety of activities, such as walking, aerobics, Pilates, yoga, and stretching. Similarly, Pritchett et al. (19) performed a meta-analysis of 13 RCT (7 trials recruited postpartum women with depression; 6 trials recruited postpartum women from the general population). In general, postpartum aerobic exercise interventions significantly reduced depressive symptoms (assessed by EPDS, BDI, or *Diagnostic and Statistical Manual of Mental Disorders IV*) in women with postpartum depression (SMD = −0.32, 95% CI = −0.63 to −0.00) as well as in postpartum women without it (SMD = −0.57, 95% CI = −1.12 to −0.02). In the exercise-only interventions (i.e., no cointerventions of social support or dietary counseling; N = 8 RCT), exercise had a marginal effect in reducing postpartum depressive symptoms (SMD = −0.56, 95% CI = −1.13 to 0.01).

Dose and dose–response. Insufficient information was available to determine the dose of physical activity associated with improved affect and reduced anxiety and depressive symptomology. Most of the RCT reviewed in the recently added meta-analysis by Pritchett et al. (19) observed improvements in postpartum depressive symptoms from about 30 min of moderate-intensity activity, performed 3 to 5 times weekly, for 4 wk to 6 months duration. The evidence grade for the dose and dose–response relationship between physical activity and affect, anxiety, and depression was not assignable.

Sociodemographic factors and weight status. There was no available evidence that tested whether the relationship between physical activity and affect, anxiety, or depression during pregnancy or postpartum varied by age, race/ethnicity, socioeconomic status, or prepregnancy weight status. The evidence grade for effect modification on the relationship between physical activity and both antenatal and postpartum affect, anxiety, and depression was not assignable.

DISCUSSION

The gestational period is an opportunity to promote positive health behaviors that can have both short- and long-term benefits for the mother. Given the low prevalence of physical activity in young women in general (55) and the high prevalence of obesity and cardiometabolic diseases among the U.S. population (56), the importance of increasing physical activity levels in women of childbearing age, before, during, and after pregnancy is substantial. The 2018 PAGAC Scientific Report concluded that for women with a healthy pregnancy, regular physical activity *probably* reduces the risk of gestational diabetes, *possibly* reduces the risk of preeclampsia, and *appears* to improve mood both during and after pregnancy (12). Our findings in 2018 support those from 2008 and extend them in several ways. Strong evidence now shows that moderate-intensity physical activity commensurate with the current recommendations (150–300 min·wk^{-1}) reduces the risk of excessive gestational weight gain, GDM, and symptoms of postpartum depression. Unfortunately, only about 23% to 29% of pregnant women living in the U.S. meet even the minimum physical activity recommendations (8), and therefore, the majority of pregnant women receive few or none of the physical and emotional health benefits of being physically active.

We found strong evidence that physically active pregnant women (i.e., those meeting at least the minimum ACOG or 2008 Physical Activity Guidelines of 150 min·wk^{-1} of moderate-intensity activity) gain less weight than their nonactive counterparts and are about 18% to 23% less likely to exceed the Institute of Medicine recommendations for healthy weight gain (29). Because gestational weight gain is attenuated in women who are active during pregnancy, they are also at lower risk of excessive postpartum weight retention, future obesity, and birth of an infant with macrosomia (57). Although not systematically examined by the 2018 PAGAC, active pregnant women also appear to be at lower risk of undergoing a cesarean section (23,27,28,35,44) and appear at no greater risk of preterm delivery (23,27,35,38,39) than are inactive women. Additional information on weight gain patterns in physically active

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pregnant women, according to IOM recommendations and their prepregnancy weight status, would increase the clinical value of these findings substantially.

There was also strong evidence demonstrating that women who meet ACOG Physical Activity Guidelines during prepregnancy or during pregnancy are about 25% to 30% less likely to develop GDM than their inactive peers. This is significant because GDM occurs in approximately 5% to 9% of women, and those with GDM are also at increased risk of delivery by cesarean section and having an infant with macrosomia and/or neonatal hypoglycemia (58). Gestational diabetes also is associated with a 7-fold increase in the risk of developing type 2 diabetes after pregnancy (58).

Finally, about 10% of women experience postpartum depression, with nearly 25% of them still in treatment after 1 yr (59). This review provides strong evidence that physically active women experience significantly fewer symptoms of depression during the postpartum period compared with their inactive counterparts. In fact, the benefits of physical activity to postpartum depression are consistent with those for depressive symptoms among the general population as indicated in the 2018 PAGAC Scientific Report (see Part F, Chapter 3; Brain Health; Question 3).

The need for future research. In sum, the health benefits documented in this review confirm the substantial public health importance of regular participation in moderate-intensity physical activity before, during, and after pregnancy. However, both the 2018 Scientific Report (11) and this umbrella review underscore the need for future research in several areas. For example, there is a need to investigate longitudinally the timing of the physical activity exposure (e.g., prepregnancy, early pregnancy, and throughout pregnancy postpartum) relative to specific maternal outcomes of interest. For some pregnancy outcomes like excessive weight gain, GDM, or preeclampsia, prepregnancy or early pregnancy physical activity may be sufficient for reducing risk during the entire gestational period. For other issues such as postpartum weight loss or depression, however, postpartum physical activity may be more important than activity at other stages of pregnancy for promoting weight loss, mitigating depressive symptoms, and improving quality of life. The determinants and barriers to postpartum exercise also need further study.

Second, the safety and benefits of vigorous-intensity physical activity to maternal health are less well-documented than those for light- to moderate-intensity activity, and this type of activity may be discouraged by some health care providers. There are substantial numbers of women who participate regularly in vigorous-intensity physical activity (e.g., running, cycling, and rowing) before pregnancy, who may want to continue such activity for as long as possible throughout pregnancy. Information from such studies would provide valuable information on minimal effective levels of vigorous activity, as well as on maximal threshold levels for safety concerns (e.g., insufficient gestational weight gain, hyperthermia, musculoskeletal injuries, or low birth weight) that may affect the health of mothers and their offspring.

Finally, most of the experimental research on physical activity during pregnancy relies on the 2008 Physical Activity Guidelines or the 2015 ACOG recommendations of 150 $\min \cdot wk^{-1}$ of moderate-intensity activity. Limited evidence suggests that certain types of physical activity, such as prolonged standing or lifting heavy loads performed in an occupational setting, may have different health effects for pregnant women than when performed during leisure time (48). The validity of this claim needs to be determined, as well as whether these differential findings are caused by the nature of the activities and the setting itself, or perhaps by confounding factors such as socioeconomic status, educational attainment, or age. Also, there are limited data concerning the dose–response relationships between any type of physical activity (performed before, during, or after pregnancy) and important pregnancy outcomes such as GDM and preeclampsia. Some data suggest a nonlinear relation between prepregnancy activity and these outcomes (34,45), whereas data on early pregnancy physical activity show a more linear dose–response curve (45). Examining the effect of different types, intensities, doses, and timing of physical activity across various domains (leisure time, occupational, household, and transportation) on a range of maternal outcomes would significantly advance current knowledge and inform both clinical and public health practice.

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HHS staff provided general administrative support to the committee and assured that the committee adhered to the requirements for Federal Advisory Committees. HHS also contracted with ICF, a global consulting services company, to provide technical support for the literature searches conducted by the committee. HHS and ICF staff collaborated with the committee in the design and conduct of the searches by assisting with the development of the analytical frameworks, inclusion/exclusion criteria, and search terms for each primary question; using those parameters, ICF performed the literature searches.

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AMERICAN COLLEGE of SPORTS MEDICINE.
PRONOUNCEMENT

Physical Activity, Injurious Falls, and Physical Function in Aging: An Umbrella Review

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ABSTRACT

DIPIETRO, L., W. W. CAMPBELL, D. M. BUCHNER, K. I. ERICKSON, K. E. POWELL, B. BLOODGOOD, T. HUGHES, K. R. DAY, K. L. PIERCY, A. VAUX-BJERKE, and R. D. OLSON, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Physical Activity, Injurious Falls, and Physical Function in Aging: An Umbrella Review. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1303–1313, 2019. **Purpose:** To review and update the evidence of the relationship between physical activity, risk of fall-related injury, and physical function in community-dwelling older people that was presented in the *2018 Physical Activity Guidelines Advisory Committee Scientific Report* (PAGAC Report). **Methods:** Duplicate independent screenings of 1415 systematic reviews and meta-analyses published between 2006 and 2016 identified from PubMed®, Cochrane Library, and CINAHL databases yielded 111 articles used for the PAGAC Report. The PAGAC Aging Subcommittee members graded scientific evidence strength based upon a five-criteria rubric and assigned one of four grades: strong, moderate, limited, or not assignable. An updated search of 368 articles published between January 2017 and March 2018 yielded 35 additional pertinent articles. **Results:** Strong evidence demonstrated that physical activity reduced the risk of fall-related injuries by 32% to 40%, including severe falls requiring medical care or hospitalization. Strong evidence also supported that physical activity improved physical function and reduced the risk of age-related loss of physical function in an inverse graded manner among the general aging population, and improved physical function in older people with frailty and with Parkinson's disease. Aerobic, muscle-strengthening, and/or multicomponent physical activity programs elicited the largest improvements in physical function in these same populations. Moderate evidence indicated that for older adults who sustained a hip fracture or stroke, extended exercise programs and mobility-oriented physical activity improved physical function. **Conclusions:** Regular physical activity effectively helps older adults improve or delay the loss of physical function and mobility while reducing the risk of fall-related injuries. These important public health benefits underscore the importance of physical activity among older adults, especially those living with declining physical function and chronic health conditions. **Key Words:** EXERCISE, FUNCTIONAL PERFORMANCE, GERIATRICS, MOBILITY

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MEDICINE & SCIENCE IN SPORTS & EXERCISE®

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Advances in public health and in health care are keeping people alive longer, and consequently, the proportion of older people in the global population is increasing rapidly. As of 2016, individuals ages 65 yr and older comprise about 13% of the United States population, and their numbers are projected to reach 72.1 million (19% of the total population) by the year 2030 (1). This represents a twofold increase compared with the older adult population in 2000. Moreover, the number of people 85 yr and older is projected to rise to 14.6 million by 2040 (1). Due to these growing demographic trends, the prevention of chronic disease, the maintenance of functional status, and the preservation of physical independence in aging present major challenges that have substantial personal and public health implications.

Physical activity is any bodily movement that results in increased energy expenditure and can be achieved by a variety of leisure-time, work or transportation-related activities (2). Exercise refers to physical activities that are planned, structured, repetitive, and intended to improve or maintain fitness, function, and health (2). Ample evidence now exists that regular physical activity is key to preventing and managing major chronic diseases common to older people (3). Physical activity is also important for preserving physical function and mobility, which can then delay the onset of major disability (4). Current physical activity guidelines for older people recommend at least 150 $\text{min}\cdot\text{wk}^{-1}$ of moderate-intensity aerobic activity, with muscle-strengthening activity performed on two or more days per week (5). Despite the known benefits of physical activity to health and physical function in aging, however, the proportion of older adults meeting recommended physical activity guidelines for aerobic activity remains low (27%), based on data from the 2011–2012 National Health and Nutrition Examination Survey (6). This low prevalence of physical activity has important implications because it is a modifiable behavior that contributes substantially to the burden of chronic disease mortality in the United States (7).

Since the *2008 Physical Activity Guidelines Advisory Committee (PAGAC) Scientific Report* (3), considerable evidence has emerged regarding the relative benefits of additional modes or combinations of physical activity to specific physical function outcomes (e.g., strength, gait speed, balance, activities of daily living [ADL] function). These additional physical activity interventions include progressive resistance training, multicomponent exercise, dual-task training, active video gaming, tai chi, yoga, and dance. In addition, the current research has begun to address the issues of the dose–response relationship between physical activity and physical function in aging. Similar to studies of pharmacologic agents, it is not only important to determine if a graded relationship exists but also to determine the shape of the relationship for specific health outcomes to establish a minimal effective dose and a maximal threshold dose for safety.

The 2018 PAGAC Scientific Report (8) expanded on the 2008 report by examining the relationship between physical activity and the risk of fall-related injuries, as well as the relationship between physical activity and physical function, in both the general aging population and in people living with specific chronic diseases (cardiovascular disease [CVD], chronic obstructive pulmonary disease (COPD), cognitive impairment, frailty, hip fracture, osteoporosis, Parkinson's Disease, stroke, and visual impairments). The 2018 PAGAC Scientific Report further leveraged current research in examining: 1) the dose–response relationship between exposure and outcome; 2) the mode of activity most beneficial to a specific functional outcome; and 3) whether the relationship between physical activity and physical function varied by age, race, sex, sociodemographic characteristics, or by body weight. This current article summarizes the evidence from the 2018 PAGAC Scientific Report and includes new evidence from an updated search of the effects of physical activity on fall-related injuries, and physical function in older people.

METHODS

Search strategy, study selection, and quality assessment. Table 1 provides the specific questions and subquestions addressed by the Aging Subcommittee of the 2018 PAGAC in their report. A first search was undertaken to include publications from 2006 to 2016. The searches were conducted in PubMed®, CINAHL, and Cochrane Library and supplemented through hand-searches of reference lists of included articles and are reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (9). The Subcommittee determined that systematic reviews (SR), meta-analyses (MA), pooled analyses, and reports provided a wealth of quality information to answer two of its three research questions. Thus, to increase work efficiency, the searches were limited to these types of reviews. For

TABLE 1. List of questions addressed by the aging subcommittee of the 2018 Physical Activity Guidelines Advisory Committee.

1. What is the relationship between physical activity and risk of injury due to a fall?
   a. Is there a dose–response relationship? If yes, what is the shape of the relationship?
   b. Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
   c. What type(s) of physical activity are effective for preventing injuries due to a fall?
   d. What factors (e.g., level of physical function, existing gait disability) modify the relationship between physical activity and risk of injury due to a fall?
2. What is the relationship between physical activity and physical function among the general aging population?
   a. Is there a dose–response relationship? If yes, what is the shape of the relationship?
   b. Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
   c. What type(s) of physical activity (single component, dual task, multicomponent) are effective for improving or maintaining physical function among the general aging population?
   d. What impairment(s) (e.g., visual impairment, cognitive impairment, physical impairment) modify the relationship between physical activity and physical function among the general aging population?
3. What is the relationship between physical activity and physical function in older adults with selected chronic conditions? These conditions are: 1) cardiovascular disease; 2) chronic obstructive pulmonary disease (COPD); 3) cognitive impairment; 4) frailty; 5) hip fracture; 6) osteoporosis and osteopenia; 7) Parkinson's disease; 8) stroke; and 9) visual impairment.

Question 1 (What is the relationship between physical activity and risk of injury due to a fall?*),* the Subcommittee found that existing reviews (SR, MA, pooled analyses, and reports) covered only evidence from randomized controlled trials (RCT), and therefore a supplementary search for cohort and case–control studies was conducted to capture the most complete literature. Search terms included physical activity and sedentary time terms combined with physical function or falls and injuries terms. The full search strategies are available at https://health.gov/paguidelines/second-edition/report/supplementary_material/pdf/Aging_Q1_Risk_of_Injuries_Evidence_Portfolio.pdf and https://health.gov/paguidelines/second-edition/report/supplementarymaterial/pdf/Aging_Q2_Physical_Function_Evidence_Portfolio.pdf.

The inclusion criteria were predefined, and studies were considered potentially eligible if they were SR, MA, pooled analyses, or reports published in English from 2006 until February 2016 (also cohort studies published in English from 2006 until 2016 for risk of fall-related injuries) and investigated the association between all types and intensities of physical activity and physical function and/or risk of injuries from falls in the aging population. Studies of nonambulatory adults, hospitalized patients, or animals were excluded. Two reviewers independently screened titles, abstracts, and full-text of the identified articles. A third reviewer helped resolve disagreement between reviewers.

In March, 2018, two updated SR were undertaken to identify additional SR and MA published between January 2017 through February 2018 that assessed the relationship between 1) any type of physical activity and fall-related injury or 2) physical function in the aging population. The searches were also conducted in PubMed®, CINAHL, and Cochrane Library and supplemented through hand-searches of reference lists of included articles. The updated review followed an established protocol that was registered as two reviews with PROSPERO [CRD42018096687 (fall-related injuries) and CRD42018095776 (physical function)].

Evidence to inform each question was graded as strong, moderate, limited, or "not assignable" based on several grading criteria, including applicability, generalizability, risk of bias/study limitations, quantity and consistency of results across studies, and magnitude and precision of effect (8) (see Table, Supplemental Digital Content 1, 2018 Physical Activity Guidelines Advisory Committee Grading Criteria, http://links.lww.com/MSS/B523). Table 2 provides a summary of the relationships and level of evidence for each health outcome examined by the 2018 PAGAC Aging Subcommittee.

RESULTS

After duplicates were removed, a total of 1415 articles were identified from the original search process. Following full-text review, a total of four articles were deemed relevant to the question about fall-related injuries (question 1); 38 were relevant to physical function in the general aging population (question 2); and 63 were relevant to physical function in older people with specific chronic diseases (question 3). Quality for each SR, MA, or article was assessed using AMSTARExBP (10). Risk of bias, or internal validity, was assessed for each original study using an adapted version of the USDA Nutrition Evidence Library Bias Assessment Tool (11).

The updated systematic search for fall-related injury risk identified 38 unique SR and MA after duplicates were removed. Of these, 32 were excluded after a review of the titles and abstracts and five more were excluded after full-text review leaving one new review (Fig. 1). The updated search for physical function in the general aging population and in those with selected chronic conditions identified 330 SR and MA, of which 288 were excluded after review of titles, six were excluded after review of the abstracts, and two more excluded after full-text review leaving 34 new reviews (Fig. 2).

TABLE 2. Summary of the level of evidence for the relationship between physical activity, fall-related injuries, and physical function in older people: 2018 PAGAC Scientific Report.

	Overall Evidence	Dose–Response	Type of Activity Reported	Effect Modification by Demographic Factors, Weight, or Other Functional Factors
Fall-related injury	Strong	Limited (MVPA)	Moderate (multicomponent)	NOT ASSIGNABLE
Physical function in the general aging population	Strong	Strong (aerobic) Limited (strength and balance)	Strong (aerobic, strength, multicomponent) Moderate (balance) Limited (tai chi, dance, AVG, dual-task, functional) Not assignable (flexibility, yoga, qigong)	LIMITED/NOT ASSIGNABLE
Physical function in older people with specific chronic conditions*				
• Cardiovascular disease	Limited		Muscle-strengthening, tai chi, qigong, aerobic	
• COPD	Limited		Tia chi, qigong, walking, cycling, leg exercises	
• Cognitive impairment	Limited		Supervised multicomponent	
• Frailty	Strong		Multicomponent	
• Hip fracture	Moderate		Weight-bearing multicomponent	
• Osteoporosis	Limited		Muscle-strengthening, multicomponent	
• Parkinson's disease	Strong		Aerobic, resistance, dance, VRT, yoga, tai chi	
• Stroke	Moderate		Mobility-oriented, treadmill walking	
• Visual impairment	Insufficient			

The activities in parentheses refer to the level of evidence. For example among the general aging population, we found strong evidence linking aerobic, strength, and multicomponent activities to improvements in physical function.

*Question 3 did not examine dose–response or effect modification.

MVPA, moderate-to-vigorous intensity physical activity; AVG, active video gaming; VRT, virtual reality training.

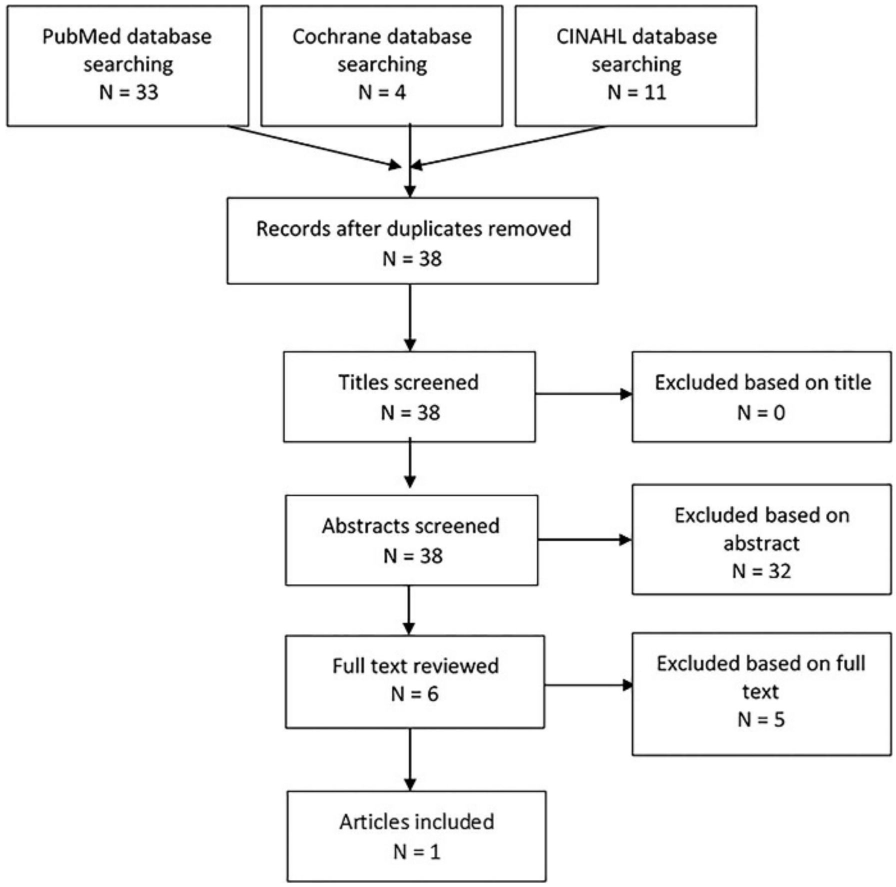

FIGURE 1—Risk of injuries from falls: SR, MA, pooled analyses, and report flow diagram of search strategy and study selection from the updated search, March 2018.

Physical Activity and Risk of Fall-Related Injury

The 2018 PAGAC Scientific Report cited strong and consistent evidence from RCT demonstrating that multicomponent physical activity (i.e., combinations of aerobic, muscle-strengthening, balance, and flexibility) significantly reduced the risk of fall-related injuries by about 32%–40%, including severe falls that result in bone fracture, head trauma, open wound soft tissue injury, or any other injury requiring medical care or admission to hospital (12–15). Moreover, the benefits of physical activity programs to reduce the risk of these four categories of fall-related injuries were similar between older adults identified as being at high risk of falling versus those who were at an unspecified risk (12). Also, fall prevention programs using multicomponent activity reduced the risk of fall-related bone fractures by 40% to 66% among older adults in community and home settings (12–15). These RCT findings were supported by data from three prospective cohort studies (16–18) and one case–control study (19).

The updated search identified one review that supported the evidence from the 2018 PAGAC Report (20). A MA of five RCT conducted in Asian countries reported that participation in physical activity programs (primarily tai chi) by community-dwelling older adults reduced the risk of fall-related injuries by 50% (relative risk [RR]. 0.50; 95% confidence interval [CI], 0.35–0.71).

Dose–response. There was some evidence in the 2018 PAGAC Scientific Report to suggest that a dose–response relationship exists between the amount of moderate-to-vigorous physical activity or home and group exercise and risk of fall-related injury and bone fracture; however, the small number of studies available and the diverse array of physical activities studied made it difficult to describe the shape of the relationship. Consistent results from four high-quality epidemiologic studies (three cohort and one case–control) suggested that adults age 65 yr and older who participated in physical activity of at least moderate-intensity for $\geq$30 min$\cdot$d^{-1} (16) or engaging in high/very high levels of activity (i.e. a weekly physical activity index score $\geq$25) (17), reduced the risk of fall-related injury and bone fracture. Evidence also exists that even adults ages 85 yr and older obtained similar benefits from $\geq$60 min$\cdot$wk^{-1} of home- or group-based physical activity (18). However, it is important to note that lower amounts of moderate-intensity physical activity (16,17) and walking (18) may not be sufficient to reduce the risk of fall-related injury and bone fracture in older age.

Physical activity type. The physical activity programs that effectively reduced the risk of fall-related injuries and bone fractures contained a variety of group- and home-based activities (12,14,15,18,19). Most programs were multicomponent and included various combinations of moderate-intensity

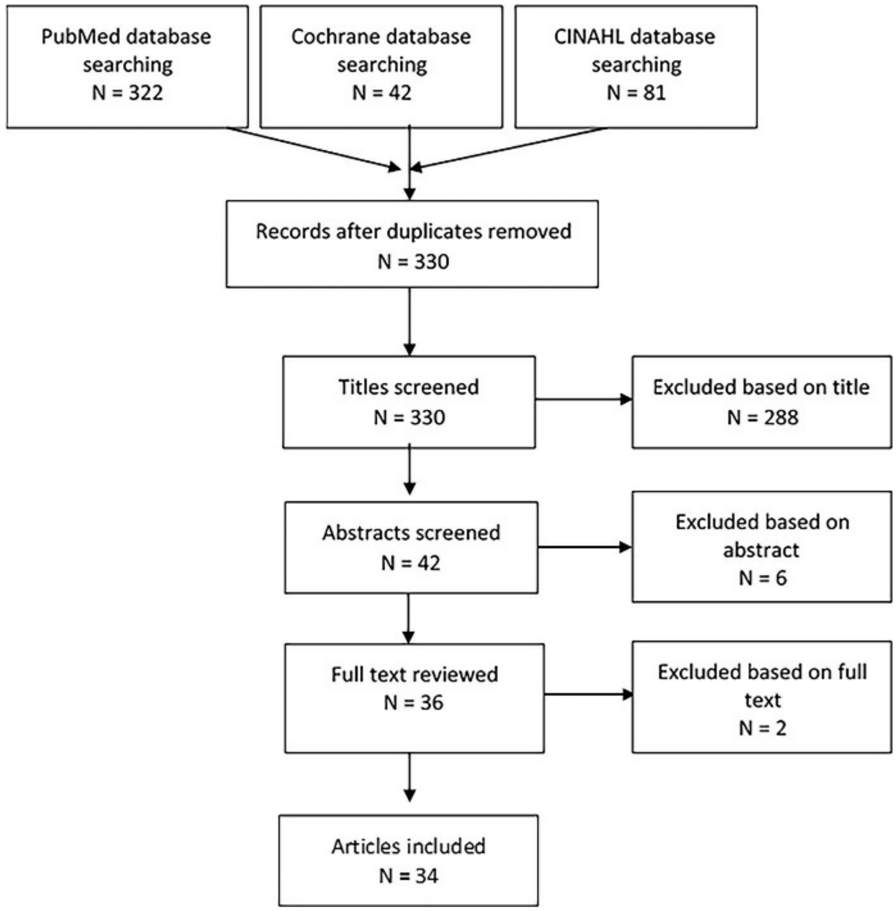

FIGURE 2—Physical function SR, MA, pooled analysis, and report flow diagram of search strategy and study selection from the updated search, March 2018.

balance, strength, endurance, gait, flexibility, and "physical function" training, as well as recreational activities (e.g., dancing, cycling, gardening, sports). Although the research was limited, it does not support the use of low-intensity walking as a primary mode of physical activity to reduce the risk of fall-related injuries and fractures among older adults (18,19), although walking may be included in multicomponent physical activity regimens. Unfortunately, insufficient information was available from the SR to determine the effects of individual elements (e.g., strength training, balance training) of the multicomponent training programs on the risk of fall-related injuries.

Effect modification by sociodemographic characteristics or preexisting disability. There was insufficient evidence available to determine whether the relationship between physical activity and risk of fall-related injuries and bone fractures varies by age, sex, race/ethnicity, socioeconomic status, or weight status or whether factors such as level of physical function ability and preexisting gait disability modify the relationship between physical activity and risk of injury due to a fall.

Physical activity and physical function in the general older population. The 2018 PAGAC Scientific Report cited strong evidence from RCT and cohort studies that aerobic, muscle-strengthening, balance, and/or multicomponent physical activity programs improved physical function and reduced risk of age-related loss of physical function in the general aging population (8). One high quality MA by Chase et al. (21) analyzed data from 28 RCT using objective composite measures of physical function, such as the short physical performance battery (SPPB), timed-up-and-go tests (TUG), the continuous scale physical performance test (CS-PPT), and the physical performance test (PPT). The summary effect size (ES) describing the magnitude of the relation between physical activity and physical function was 0.45 (95% CI: 0.27 to 0.64), with the higher quality studies reporting smaller effect sizes. The updated search identified nine SR/MA that supported the 2018 Scientific Report by also providing strong to moderate evidence demonstrating the benefits of physical activity to physical function in this population (22–30).

Dose–response. The 2018 PAGAC Scientific Report found strong evidence of an inverse dose–response relationship between volume of aerobic physical activity and risk of physical functional limitations in the general aging population. One review of 24 comparisons from prospective cohort studies with covariate adjustment classified dose of aerobic activity reported in cohort studies into four ordinal categories (0 = no activity; 1 = low activity; 2 = moderate activity; and 3 = vigorous activities and/or high activity volume) (31). With this analysis framework, virtually every study showed an inverse dose–response relationship of aerobic activity with risk of limitations in physical function (Fig. 3). The 2018 Scientific Report cited limited evidence of a dose–response relationship between either balance (32) or muscle-strengthening training and

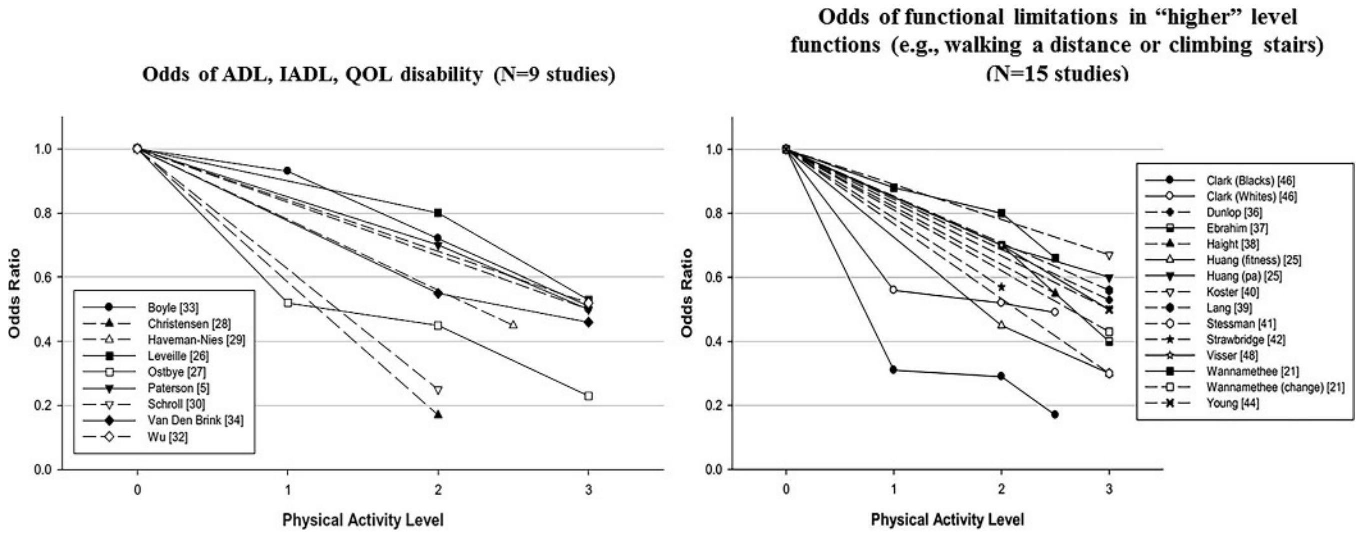

FIGURE 3—Results of a SR of the inverse dose–response relationship between volume of aerobic physical activity and risk of physical functional limitations in the general aging population. Categories of physical activity level were derived from prospective cohort studies with covariate adjustment: 0, no activity; 1, light activities only occasion walking or gardening; 2, moderate level of activity (volume = 3–5 d·wk^{-1} for 30 min·d^{-1}; and 3) = vigorous activities and/or high volume of systematic activity. The odds ratio is the odds of disability in the physical activity group relative to a comparison group. IADL, instrumental activities of daily living; QOL, quality of life score. Figure reproduced with permission from Paterson & Warburton, 2010.

physical function (21) in this same population. The updated search, however provided important additional information. Roberts et al. (29) examined the effects of different physical activity types and levels (determined from calculated MET-min and categorized as low, moderate, or high) on ADL function. Results from the pooled MA indicated that, compared with a control condition, there were beneficial effects of physical activity on ADL physical performance (standardized mean difference (SMD) = 0.72; 95% CI: 0.45 to 1.00; 29 studies) with the largest effects observed for moderate activity levels (SMD = 1.07; 95% CI: 0.44 to 1.70; nine studies), compared with low levels (SMD = 0.57; 95% CI:0.29 to 0.86; 20 studies). There were no studies of ADL performance that used high physical activity levels, and therefore a conclusion regarding their benefits could not be drawn. With regard to various levels of multitask activities (those activities that combine physical and mental tasks), the greatest difference in ADL performance between the exercise and the control groups were reported for the high level multitask group (SMD = 1.36; 95% CI: 0.46 to 2.26; six studies), followed by the moderate level group (SMD = 0.74; 95% CI: 0.41 to 1.06; 13 studies), and the low level group (SMD = 0.45; 95% CI: −0.01 to 0.91; eight studies).

Types of activity. The 2018 PAGAC Scientific Report cited strong evidence that, specifically, aerobic, muscle-strengthening, and multicomponent physical activity improved physical function in the general aging population, and moderate evidence indicating that balance training improved physical function in a dose–response manner among these same persons (8). The evidence linking physical activities such as tai chi exercise, dance training, active video gaming, and dual-task training to improvements in physical function in healthy aging were limited, however, due to the lack of studies at this time. Similarly, insufficient evidence was available to determine the effects of flexibility activity, yoga, and qigong exercise on physical function in the general aging population.

The updated search identified a MA by Farlie and colleagues (24) that examined the effects of four different types of balance training interventions [multidimensional (activities such as "functional exercises," tai chi, and ball games), control center of mass (COM), mobility, and reaching] on several dimensions of balance performance. Overall, the MA resulted in small to moderate effects in favor of programs that included multidimensional (SMD = 0.50; 95% CI: 0.36 to 0.65), reaching (SMD = 0.48; 95% CI: 0.33 to 0.64), COM (SMD = 0.42; 95% CI: 0.27 to 0.56) and mobility (SMD = 0.31; 95% CI: 0.20 to 0.43) balance training versus no balance training interventions. The authors noted, however, that there was substantial between-study heterogeneity among the interventions (I^2 range 50.4% to 80.6%).

Multitask activities with high levels of physical (speed, coordination, balance), mental and social demands (e.g., dancing, team sports, handball) appeared particularly effective in improving functional performance, relative to moderate or lower levels of such activities and compared with control conditions (29). Nordic walking also has demonstrated moderate effectiveness in improving dynamic balance (effect size (ES) = 0.30), functional balance (ES = 0.62), muscle strength of upper (ES = 0.66) and lower (ES = 0.43) limbs, and aerobic capacity (ES = 0.92) compared with no exercise comparison groups in healthy older people (23). An MA of 23 studies by Liu and colleagues (27) among community-dwelling older people with low physical function reported that progressive resistance exercise was effective in improving lower-body muscle strength and static standing balance; however multicomponent exercise was more effective in improving muscle strength, balance, and lower-body physical functioning, compared with progressive resistance exercise alone. Neither progressive resistance nor multicomponent exercise was effective in improving ADL, however.

Howe and colleagues (25) examined the effects of active computer gaming (ACG) on physical function in 1838 healthy people >65 yr of age. Their MA of 35 RCT reported significant moderate effects in favor of ACG over a control intervention on balance (SMD = 0.52; 95% CI: 0.24 to 0.79; 17 studies) and on functional exercise capacity when the volume of the ACG was >120 min·wk^{-1} (SMD = 0.53; 95% CI: 0.15 to 0.90; five studies). The authors noted, however, that the quality of the evidence for all comparisons was graded low or very low.

Finally, Weber et al. (30) reviewed 14 studies (six RCT) of interventions that integrated and embedded "functional exercise" into the daily activities of older people. The most frequently evaluated intervention in this review was the Lifestyle-integrated Functional Exercise (LiFE) program (33). "Functional exercises" are designed to improve lower-body strength, balance, and motor performance, as well as for increasing daily levels of physical activity. Examples of such include postures or walking with gradual reduction in the base of support (e.g., upgrading tandem stand to one-leg stand over time) and dynamic movements that perturb the center of gravity (stepping over obstacles). "Functional exercises" for improving lower-body strength include squatting, chair stands, and toe raises with a gradual increase to more intense and challenging activities (33). Importantly, the LiFE intervention has strategies for behavior change that are based on the habit reframing theory (34). Indeed, these exercises are linked to everyday tasks by using situational and environmental cues (e.g., tooth brushing, housework) as prompts to action, with the idea of performing the activities intentionally and consciously until they become a habit. Evidence from three RCT in the Weber et al. (30) review suggested that the LiFE intervention significantly improved balance, strength, and functional performance compared with either no intervention, low-intensity activities (e.g., walking), or structured exercise programs. Two of these RCT also reported a significant reduction in incident falls in participants in the LiFE group, compared with those in either a no intervention or a low-intensity activity group. Thus, although the data are limited, the LiFE approach appears to be a promising alternative or complement to traditional structured exercise programs.

In sum, our current findings pertaining to the effectiveness of different types of physical activity for improving physical function support those from the 2018 PAGAC Scientific Report, which cited strong evidence of the benefits of aerobic, muscle-strengthening, and multicomponent physical activity on improvements in physical function in the general aging population, and moderate evidence indicating that balance training improves physical function in these same persons. The evidence linking ACG (or active video gaming), Nordic walking, or functional exercise to improvements in physical function remains limited at this time.

Sociodemographic characteristics and weight status. Limited evidence from the 2018 PAGAC Scientific Report suggested that the relationship between physical activity and physical function did not vary by age, sex, or weight status in the general population of older adults (8). One MA reported sex and body mass index (BMI) were not significant effect modifiers of the relationship of physical activity on composite physical function scores (21). A MA of cohort studies reported the relationship between aerobic activity and ADL dependency did not differ significantly by age (75 yr and younger vs older than 75 yr) (35). The available evidence was insufficient to determine whether the relationship between physical activity and physical function varied by race/ethnicity and socioeconomic status in the general population of older adults. No relevant analyses were located in the updated search. We note, however, that several findings with "limited" evidence also have high public health importance. Adults age 75 yr and older have more age-related loss of physical function, are more likely to be women, and the majority have a BMI in the range of overweight-to-obese.

Effect modification by visual, cognitive, or physical impairments. None of the SR/MA identified in either search examined whether visual or cognitive impairments modified the effects of physical activity on physical function. Limited evidence suggested that physical activity has a stronger effect on physical function in older adults with limitations in physical function, compared with relatively healthy older adults. One MA compared the effect size in nonfrail adults (ES = 0.35; 95% CI: 0.17–0.54) with that in frail adults (ES = 1.09; 95% CI: 0.55–1.64) and found the effect size was significantly larger in frail adults ($P < 0.05$) (21). A MA identified from the updated search reported that the significant benefits of aerobic exercise training to improvements in peak aerobic capacity were observed in both healthy older people (MD = 1.72; 95% CI: 0.34 to 3.10; six studies) and in those with existing chronic conditions (MD = 1.47 (95% CI: 0.60 to 2.34; four studies) (22). This aerobic training involved walking, cycling, treadmill walking, walking/running on a mini-trampoline, or combinations of these activities performed three times per week over a range of 12 to 26 wk.

Physical Activity and Physical Function in Older People with Specific Chronic Conditions

This question builds upon Question 2 by addressing the relationship between physical activity and physical function in discreet populations of older people having selected chronic conditions. The chronic conditions were selected based on their prevalence in older age, as well as on the availability of published research linking physical activity to physical function within each condition (8).

Table 2 shows the level of evidence for the relationship between various types of physical activities and physical function in older people with specific chronic conditions from the 2018 PAGAC Scientific Report. The strongest evidence was observed for the benefits of multicomponent activities among people with frailty and with Parkinson's disease. Moderate evidence indicated that for community-dwelling older adults who sustain a hip fracture, extended exercise programs (which begin after formal hip fracture rehabilitation ends) was effective for improving physical function and that mobility-oriented physical activity improved walking function for individuals after a stroke.

Cardiovascular disease. In the 2018 PAGAC Scientific Report, there was limited evidence suggesting that physical activities such as muscle-strengthening and alternative/complementary exercises (tai chi, qigong, Baduanjin) improved physical function among older people with cardiovascular disease. The updated search identified no additional evidence of this relationship.

COPD. Limited evidence from the 2018 Report suggested that tai chi and qigong exercise improved one aspect of physical function (walking ability) in individuals with COPD (36,37). The updated search identified one SR/MA in people with severe COPD that supported the limited evidence reported in 2018 (38). This MA of 10 RCT reported that exercise training improved performance on the 6-min walk test (6MWT; SMD = 3.86; 95% CI: 2.04 to 5.67), compared with a control condition. The exercise training interventions comprised primarily leg exercises, cycling, and walking, with intensity of exercise ranging from 70% to 90% of maximal velocity achieved during incremental testing at baseline.

Cognitive impairment. Limited evidence from the 2018 PAGAC Scientific Report suggested that for individuals with cognitive impairment, physical activity programs improved physical function, including ADL measures. Two SR/MA examining the relationship between physical activity and physical function in older people with cognitive impairment were identified in the updated search (39,40). One of these MA (39) comprising 43 trials (N = 3988) reported significant differences between supervised exercise training and control conditions on improvements in performance on the 30-s sit-to-stand test (mean difference (MD) = 2.1 repetitions; 95% CI: 0.3 to 3.9; four trials), step length (MD = 5 cm; 95% CI: 2 to 8; five trials), Berg Balance Scale (MD = 3.6 points; 95% CI: 0.3 to 7.0; six trials), functional reach (MD = 3.9 cm; 95% CI: 2.2 to 5.5; six trials), TUG test (MD = −1 s; 95% CI: −2 to 0; 11 trials), walking speed (MD = 0.13 $m \cdot s^{-1}$; 95% CI: 0.03 to 0.24; seven trials), and the 6MWT (MD = 50 m; 95% CI: 18 to 81; seven trials) in this population. Importantly, about 45% of the training programs used multicomponent exercise with a resistance exercise component, while 23% relied on aerobic training.

Frailty. All of the 15 SR/MA included in the 2018 PAGAC Scientific Report cited that physical activity improved some or all measures of physical function in older people with frailty (8). A MA (41) of 19 RCT among community-dwelling older adults with frailty reported that overall, physical activity decreased the time needed to walk 10 m by 1.73 s. This has important clinical relevance for older people with frailty, as gait speed is a strong predictor of mortality risk and there is evidence that increments in speed as small as 0.1 $m \cdot s^{-1}$ significantly lowers that risk (42). The updated search identified five additional SR that support the strong evidence from the 2018 PAGAC Scientific Report (43–47). Most of these reviewed RCT and experimental studies examined multicomponent exercise involving resistance training, balance, gait, or endurance training (44–47). In a review of 16 studies involving 1350 frail older adults, Lopez and colleagues (45) reported that resistance training either alone or as part of multicomponent training improved maximal muscle strength between 6.6% and 37%. Similarly, the authors report gains in muscle mass (3.4% to 7.5%), muscle power (8.2%), and functional capacity (4.7% to 58.1%). Moreover, gait speed improved between 5.9% and 14.5%, as did score on the TUG (5.5% to 20.4%).

Hip fracture. Moderate evidence from the 2018 PAGAC Scientific Report indicated that older people who have sustained a hip fracture also benefitted from weight-bearing, multicomponent activity (8). The updated search identified only one SR/MA that investigated this relationship. The MA of RCT by Lee et al. (48) reported that progressive resistance exercise significantly improved overall physical function after hip fracture surgery compared with a control group (SMD = 0.408; 95% CI: 0.238 to 0.578; eight studies) and it was especially effective in improving mobility (SMD = 0.501; 95% CI: 0.297 to 0.705), ADLs (SMD = 0.238; 95% CI: 0.040 to 0.437), balance (SMD = 0.554; 95% CI: 0.310 to 0.797), lower-limb strength or power (SMD = 0.421; 95% CI: 0.101 to 0.741), and performance tasks (SMD = 0.841; 95% CI: 0.197 to 1.484).

Osteoporosis/osteopenia. Limited evidence from the 2018 PAGAC Scientific Report suggested that muscle-strengthening and agility activities performed on two or more days per week improved physical function in older people who are at risk of fragility fractures due to osteoporosis or osteopenia (8). The updated search identified one SR/MA examining this relationship that adds considerably to the level of evidence. Based on a MA of 25 RCT, Varaha et al. (49) reported that multicomponent exercise significantly improved timed mobility (SMD = −0.56; 95% CI: −0.81 to −0.32), balance (SMD = 0.50; 95% CI: 0.27 to 0.74), and self-reported functioning (SMD = −0.69: 95% CI: −1.04 to −0.34) compared with a control condition in 2,113 older people (95% of whom were women). Moreover, the results for multicomponent exercise (10 studies) were more pronounced than those for gait, balance, and functional tasks (four studies); strength/resistance training (nine studies); or tai chi (five studies) interventions, suggesting that multicomponent exercise was more effective in improving a broad range of functional outcomes in people with osteoporosis.

Parkinson's disease. The 2018 PAGAC Scientific Report cited strong evidence that physical activities, such as aerobic and resistance training, tango dancing, virtual reality training, yoga, and tai chi improved a number of physical function outcomes, including walking, balance, strength, and disease-specific motor scores in older people with Parkinson's disease, with effect sizes ranging from small (ES = 0.33; 95% CI: 0.17 to 0.49 for gait velocity) to moderate (ES = 0.72; 95% CI, 0.08–1.36 for the 6 min walk time) (8). Three additional SR on this relationship were identified in the updated search (50–52), two of which (51,52) included a MA. Overall, the newpapers supported the findings of the 2018 Report. One small MA (5 RCT; N = 159 participants) compared dance interventions (Tango or Irish) with other physical activity interventions (three RCT) or with no intervention (two RCT) (51). Dance practice at least three times per week promoted significant improvements in motor scores assessed with the Unified Parkinson's Disease Rating

Scale (UPDRS) III (SMD = −2.52; 95% CI: −4.59 to −0.45) and a significant decrease in TUG time (SMD = −1.15 s; 95% CI: −2.03 to −0.27 s) compared with other interventions. Dance also improved the UPDRS III score when compared with no intervention (SMD = −8.35; 95% CI: −13.79 to −2.91).

Stroke. In the 2018 PAGAC Scientific Report, moderate evidence indicated that mobility-oriented physical activity improved walking function for individuals after a stroke and that among stroke survivors, treadmill walking (especially with cadence cuing) improved walking speed by approximately 0.23 $m \cdot s^{-1}$ (8). Seven SR relating physical activity to improved physical function in people having had a stroke were identified from the updated search (53–59). Of these reviews, six included a MA (53–58). The interventions examined included aerobic exercise (54), circuit-based training (53), dual-task balance and mobility training (56), progressive task-oriented exercise (58), and treadmill training (57,59). Two novel MA examined the effects of circuit-based exercise (vs other types of exercise or no therapy) on various measures of physical function (53,55) and both reported that circuit-based training was equal or superior to other forms of therapy in improving measures of gait speed, balance, and functional mobility. In their MA (N = 10 studies; 835 participants), English and colleagues (55) reported that circuit training was superior to comparison interventions in improving walking capacity on the 6MWT (MD = 60.86 m; 95% CI: 44.50 to 77.17 m) and gait speed (MD = 0.15 $m \cdot s^{-1}$; 95% CI: 0.10 to 0.19 $m \cdot s^{-1}$). Interestingly, these same authors observed no difference in the effectiveness of circuit-training versus a control on walking endurance between stroke survivors who began training within 12 month of their stroke (MD = 46.56; 95% CI: 21.35 to 71.77) and those who started training 12 months or more after their stroke (MD = 71.15; 95% CI: 49.76 to 92.54). Additionally, superior benefits of circuit training were observed for scores on the TUG test and Activities of Balance Confidence, but not for the Berg Balance Score or the Step Test.

Visual impairments. Insufficient evidence was available from either search to determine the effects of physical activity on physical function in older adults with visual impairments.

DISCUSSION

This updated SR extends the findings of the 2018 PAGAC Scientific Report by providing new evidence that corroborates the benefits of physical activity to a lower risk of fall-related injuries, as well as to improved physical function among the general older population and among those with selected chronic conditions. The types of activities reviewed in the updated search are similar to those reviewed in the 2018 PAGAC Scientific Report with the addition of different types of balance training interventions, functional exercises that become embedded in everyday lifestyle activities, Nordic walking, and circuit-based training. Perhaps the most convincing evidence from the 2018 PAGAC Report, along with that from the updated search, relates to the greater benefits of multicomponent, relative to single-component, exercise to the prevention of fall-related injuries and to improvements in physical function in older age. Moreover, multicomponent and multitask activities that are incorporated into the daily routine may be a promising alternative to structured, single-task exercise programs for older adults.

One in four individuals ≥65 yr falls in the United States every year (60). Furthermore, falls are the leading cause of fatal injury and the most common cause of nonfatal trauma-related hospital admissions among older adults (60). Physical activity programs that emphasize combinations of moderate-intensity balance, strength, endurance, gait, and physical function training appear most effective in reducing the risk of fall-related injuries and fractures in older adults. Thus, the effectiveness of these programs (that were performed in community settings or at home) for risk reduction has significant public health relevance in older age, due to the high prevalence of falls and fall-related injuries and fractures among older adults, as well as the consequent morbidity, disability and reduced quality of life.

Age-related limitations in physical function are prevalent in older adults. The National Health Interview Survey ascertained the prevalence of physical limitations in 2001 to 2007, with limitations defined as great difficulty doing (or inability to do) basic tasks of life (e.g., walk a quarter of a mile, lift a 10-pound bag of groceries) (61). At that time, 22.9% of older adults ages 60 to 69 yr and 42.9% of adults ages ≥80 yr reported functional limitations. Older adults with lower levels of physical function generally have higher health care expenditures (60). In addition, about 80% of adults ≥60 yr of age have at least one chronic condition, and 77% have at least two. Moreover, approximately 20% to 30% of adults older than age 65 yr suffer from either mild cognitive impairment or dementia (60). Chronic diseases account for 75% of health care spending in the United States (60). Low levels of daily physical activity often co-exist with chronic disease, thereby accelerating the risk of functional decline, disability, and mortality. Ample evidence now indicates that physical inactivity is among the strongest predictors of physical disability in older people (4). Aerobic, muscle-strengthening, and multicomponent physical activity appear to have the strongest relationship to improvements in physical function in the general aging population, as well as among those with chronic conditions. Thus, such activities may delay or improve mobility disability, frailty, and loss of independence in aging.

Both the 2018 Scientific Report (8) and this umbrella review underscore the need for future research in several areas. For example, the relationship between the minimal effective dose of activity (150 $min \cdot wk^{-1}$ of moderate intensity activity) and health has been described in detail (3,8). There still is, however, a need to examine greater volumes and intensities of physical activity to establish safety thresholds for older people — especially for those with preexisting conditions or limitations. To accomplish this, studies need to examine several levels of activity and to monitor and report adverse events. Also, the feasibility and benefits of alternative and complimentary activities, rigorous multitask activities, as well as novel interventions that integrate "functional exercises" into everyday tasks, need to be examined further. Moreover, the effectiveness of any new intervention needs to be examined across different socioeconomic strata to address existing disparities in prevention strategies and in health among older people. Given the rapidly increasing trends in aging demographics in the United States, preventing or delaying fall-related injuries and loss of physical function and mobility has important public health benefits, and this may be especially so for older people with already established chronic conditions.

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This article is being published as an official pronouncement of the American College of Sports Medicine. This pronouncement was reviewed for the American College of Sports Medicine by members-at-large and the Pronouncements Committee. This article serves as an update to the topics covered in the 2009 ACSM position stand, "Exercise and Physical Activity for Older Adults" [*Med. Sci. Sports Exerc*. 2009;41(7):1510–30]. *Disclaimer:* Care has been taken to confirm the accuracy of the information present and to describe generally accepted practices. However, the authors, editors, and publisher are not responsible for errors or omissions or for any consequences from application of the information in this publication and make no warranty, expressed or implied, with respect to the currency, completeness, or accuracy of the contents of the publication. Application of this information in a particular situation remains the professional responsibility of the practitioner; the clinical treatments described and recommended may not be considered absolute and universal recommendations.

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AMERICAN COLLEGE of SPORTS MEDICINE.
PRONOUNCEMENT

Physical Activity to Prevent and Treat Hypertension: A Systematic Review

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ABSTRACT

PESCATELLO, L. S., D. M. BUCHNER, J. M. JAKICIC, K. E. POWELL, W. E. KRAUS, B. BLOODGOOD, W. W. CAMPBELL, S. DIETZ, L. DIPIETRO, S. M. GEORGE, R. F. MACKO, A. MCTIERNAN, R. R. PATE, and K. L. PIERCY, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Physical Activity to Prevent and Treat Hypertension: A Systematic Review. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1314–1323, 2019. **Purpose:** This systematic umbrella review examines and updates the evidence on the relationship between physical activity (PA) and blood pressure (BP) presented in the 2008 Physical Activity Guidelines Advisory Committee Scientific Report. **Methods:** We performed a systematic review to identify systematic reviews and meta-analyses involving adults with normal BP, prehypertension, and hypertension published from 2006 to February 2018. **Results:** In total, 17 meta-analyses and one systematic review with 594,129 adults ≥18 yr qualified. Strong evidence demonstrates: 1) an inverse dose–response relationship between PA and incident hypertension among adults with normal BP; 2) PA reduces the risk of cardiovascular disease (CVD) progression among adults with hypertension; 3) PA reduces BP among adults with normal BP, prehypertension, and hypertension; and 4) the magnitude of the BP response to PA varies by resting BP, with greater benefits among adults with prehypertension than normal BP. Moderate evidence indicates the relationship between resting BP and the magnitude of benefit does not vary by PA type among adults with normal BP, prehypertension, and hypertension. Limited evidence suggests the magnitude of the BP response to PA varies by resting BP among adults with hypertension. Insufficient evidence is available to determine if factors such as sex, age, race/ethnicity, socioeconomic status, and weight status or the frequency, intensity, time, and

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duration of PA influence the associations between PA and BP. **Conclusions:** Future research is needed that adheres to standard BP measurement protocols and classification schemes to better understand the influence of PA on the risk of comorbid conditions, health-related quality of life, and CVD progression and mortality; the interactive effects between PA and antihypertensive medication use; and the immediate BP-lowering benefits of PA. **Key Words:** BLOOD PRESSURE, CARDIOVASCULAR DISEASE, EXERCISE, HIGH BLOOD PRESSURE, PREHYPERTENSION

Cardiovascular disease (CVD) is the leading cause of death in the United States and the world, accounting for approximately one in three deaths (807,775 or 30.8%) in the United States and 17.3 million (31%) globally (1). Hypertension is the most common, costly, and preventable CVD risk factor (1). Nearly 70% of Americans have high blood pressure (BP) (i.e., preestablished to established hypertension) (1), according to the Joint National Committee Seven (JNC 7) BP criteria (2). Using JNC 7 BP thresholds, the lifetime risk for developing hypertension is 90%, and one in five people with prehypertension will develop hypertension within 4 yr (2–4). From 2010 to 2030, the total direct costs attributed to hypertension are projected to triple (US $130.7 to US $389.9 billion), whereas the indirect costs due to lost productivity will double (US $25.4 to US $42.8 billion) (1).

The American College of Cardiology (ACC)/American Heart Association (AHA) Task Force on Clinical Practice Guidelines recently redefined hypertension to a lower BP threshold of 130 mm Hg for systolic BP (SBP) or 80 mm Hg for diastolic BP (DBP) (5) versus the JNC 7 threshold of 140 mm Hg for SBP or 90 mm Hg for DBP (2). This change now classifies nearly half of US adults with hypertension as compared to 32% by the JNC 7 definition, underscoring the importance of hypertension as a public health problem. The authors of the recent ACC/AHA guidelines state that nearly all of those newly diagnosed with hypertension, due to the lower BP threshold, can treat their hypertension with lifestyle modification rather than medications (5). They also emphasize that decreasing the prevalence and improving the control of hypertension by increasing the use of lifestyle antihypertensive therapy, such as participation in habitual physical activity, would provide major societal public health and economic benefit (5).

In addition to the ACC/AHA, professional organizations throughout the world recommend physical activity to lower BP (6). Nonetheless, a systematic review of 33 meta-analyses on the BP response to exercise (7), and another on the existing professional exercise recommendations for hypertension (6), revealed significant shortcomings in this literature. Since the publication of the first Physical Activity Guidelines Advisory Committee (PAGAC) Report, 2008 (8), there has been a considerable expansion of knowledge about the relationships between physical activity and BP. The charge given to 2018 PAGAC was to make evidence-based conclusion statements based upon the newest, best informed science. To do this we conducted a systematic umbrella review of systematic reviews and meta-analyses on the relationship between physical activity and BP published since the 2008 PAGAC Report among adults with normal BP, prehypertension, and hypertension using methodology adhering to the best practices of systematic reviews (9). This manuscript presents the seminal portions of the sections on the role of physical activity in the prevention and treatment of hypertension in the 2018 PAGAC Report (9).

METHODS

This systematic review is reported consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (10,11). The purpose of this umbrella review was to identify systematic reviews and meta-analyses published since the 2008 PAGAC Report (8) that examined the relationship between physical activity and BP among adults with normal BP, prehypertension, and hypertension by the JNC 7 BP criteria because the literature reviewed was based upon this BP classification scheme (2). The specific questions addressed in this review are shown in Table 1. The methods are described in detail in the 2018 PAGAC Report (9), and the protocol is registered at PROSPERO 95748.

Search strategy and selection criteria. The searches were conducted in electronic databases (PubMed®, Cumulative Index to Nursing and Allied Health Literature, and Cochrane) and were supplemented by the authors who were experts in the area to provide additional articles identified through their knowledge of this literature. The studies were considered potentially eligible if they were systematic reviews, meta-analyses of randomized controlled trials (RCT), or pooled analyses published in English from 2006 until February 2018 and investigated the relationship between all types and intensities of physical activity and BP among healthy adults ≥18 yr with normal BP, prehypertension, and

TABLE 1. Questions related to the relationship between physical activity and blood pressure among adults with normal blood pressure, prehypertension, or hypertension* addressed by the 2018 Physical Activity Guidelines Advisory Committee.

Major questions

1. In people with normal blood pressure, prehypertension, or hypertension, what is the relationship between physical activity and blood pressure?
2. In people with hypertension, what is the relationship between physical activity and:
   (a) risk of comorbid conditions,
   (b) physical function,
   (c) health-related quality of life, and
   (d) cardiovascular disease progression and mortality?

Subquestions

a. Is there a dose–response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, socio-economic status, weight status, or resting blood pressure level?
c. Does the relationship vary based on frequency, duration, intensity, type (mode), or how physical activity is measured?

*Of note, we used the JNC 7 BP classification scheme (2) for data extraction purposes. The JNC 7 defines these BP classifications as follows: Hypertension is defined as having a resting SBP of ≥140 mm Hg and/or a resting DBP of ≥90 mm Hg, or taking antihypertensive medication, regardless of the resting BP level. Prehypertension is defined as a SBP from 120 to 139 mm Hg and /or DBP from 80 to 89 mm Hg. Normal BP is defined as having a SBP <120 mm Hg and DBP <80 mm Hg.

hypertension. Studies of non-ambulatory adults, hospitalized patients, or animals were excluded. Search terms included physical activity terms combined with BP terms. See Figure 1 for the systematic search and selection process, and the 2018 PAGAC Report for the detailed full search strategy (9).

Data extraction and methodological study quality assessment. The titles, abstracts, and full-text articles of the identified articles were independently screened by two reviewers. Disagreement between reviewers was resolved by discussion or a third person when necessary. We used the JNC 7 BP classification scheme for data extraction purposes because this literature was based upon this BP classification scheme (2). The JNC 7 BP definitions are as follows: Hypertension, resting SBP of ≥140 mm Hg and/or a resting DBP of ≥90 mm Hg, or taking antihypertensive medication, regardless of the resting BP level; Prehypertension, resting SBP from 120 to 139 mm Hg and/or DBP from 80 to 89 mm Hg; and Normal BP, a resting SBP <120 mm Hg and DBP <80 mm Hg. Two abstractors independently extracted data and conducted a methodological study quality assessment using a modified version of the Assessment of Multiple Systematic Reviews (AMSTAR) (12), specifically adapted for physical activity related health outcomes such as BP (AMSTARExBP) (7).

Grading of evidence. The 2018 PAGAC carefully deliberated the qualifying reviews, and then graded the evidence for the conclusion statements as strong, moderate, limited, or "not assignable" based on grading criteria that included applicability, generalizability, risk of bias/study limitations, quantity and consistency of results across studies, and magnitude and precision of effect. More detailed information about the grading of evidence rubric can be found in the 2018 PAGAC report (9).

RESULTS

Study and Sample Characteristics

Qualifying reviews included one systematic review of longitudinal studies with a minimum of 1 yr of follow up (13) and 17 meta-analyses of RCT (14–30) (see Supplemental Digital Content 1, Table of the qualifying meta-analyses and systematic review by physical activity type, http://links.lww.com/MSS/B522). The total sample size of this umbrella review was 594,129 adults ≥18 yr, ranging from 216 to 330,222 participants. The systematic review (13) included two large longitudinal prospective cohort studies that examined the influence of general and leisure-time habitual physical activity on CVD mortality among adults with hypertension (31,32); 15 of the meta-analyses included RCT that examined the BP response to an exercise training intervention among adults with normal BP (k = 7) (14,15,17–19,21), prehypertension (k = 5) (17–20,24), or hypertension (k = 15) (14–21,24–30) compared with a control condition among similar adults who were physically inactive at baseline; and two of the meta-analyses examined prospective cohort studies of adults initially free of hypertension for the influence of general and leisure-time habitual physical activity on the risk of the development of hypertension (22,23). When this information was disclosed, the samples in the qualifying reports were generally an

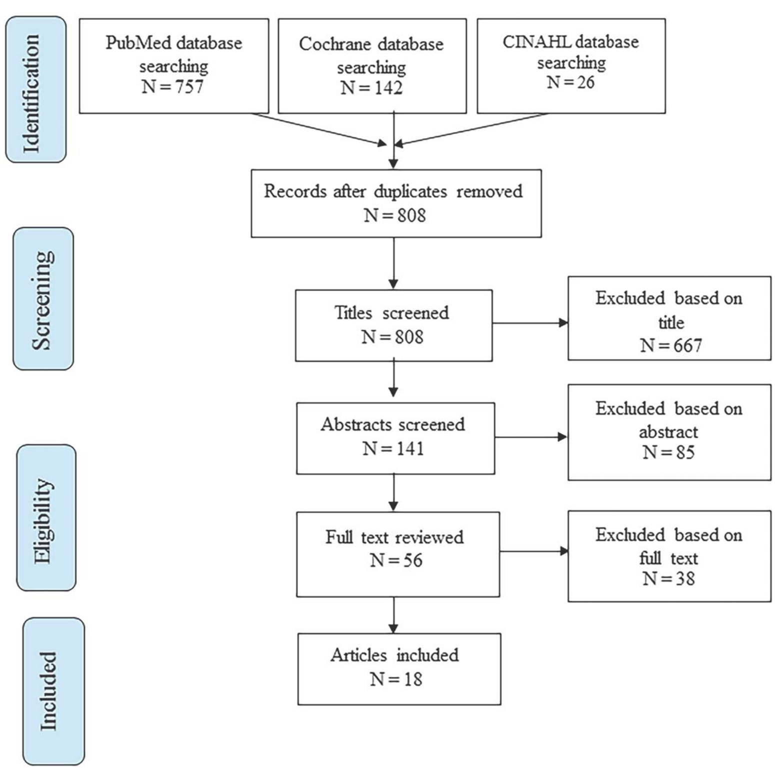

FIGURE 1—Flow diagram of search strategy and study selection. CINAHL, Cumulative Index to Nursing and Allied Health Literature.

equal mix of men and women, and mostly Caucasian followed by Asian and some African American, African, or Indian samples with a body mass index (BMI) that ranged from normal weight to obese. The overall methodological study quality of the qualifying reports was moderate as assessed by AMSTARExBP (7), with 83.3% of the included trials scoring poor to moderate and 16.7% high methodological study quality.

Evidence on the Overall Relationship between Physical Activity and BP

The risk of developing of hypertension or incident hypertension among adults with normal BP and prehypertension was defined in two ways. We regarded the BP response to an exercise training intervention ranging from low to vigorous intensity, and the association between habitual leisure-time physical activity and the risk of developing hypertension as the indicators of the risk of incident hypertension.

The prevention of incident hypertension. *The BP response to an exercise training intervention.* There were eight meta-analyses of RCT that examined the BP response to an exercise training intervention ranging from low to vigorous intensity among adults who were physically inactive at baseline and with prehypertension (17–19,24,25) and/or normal BP (14,15,17–19,21,24) (see Table, Supplemental Digital Content 1, Summary of the Included Systematic Reviews, http://links.lww.com/MSS/B522). Of the five meta-analyses involving adults with prehypertension, all reported a statistically significant reduction in SBP and four reported a statistically significant reduction in DBP. Of the seven meta-analyses involving adults with normal BP, three reported a statistically significant reduction and one reported a statistically significant rise in SBP, and six reported a statistically significant reduction in DBP. The magnitude of the BP reductions ranged from about 2 to 5 mm Hg for SBP and 1 to 4 mm Hg for DBP.

Habitual leisure-time physical activity and incident hypertension. We also regarded the association between habitual leisure-time physical activity and incident hypertension as an indicator of the BP response to physical activity. Huai et al. (22) examined this association among 136,846 adults with normal BP at baseline. After an average of 10 yr (2 to 45 yr) of follow up, 15,607 adults developed hypertension (11.4% of the sample). In this meta-analysis, high amounts (i.e., volume and/or intensity) of leisure-time physical activity were associated with a 19% decreased risk of incident hypertension compared to the referent group engaging in low amounts of leisure-time physical activity (relative risk [RR] = 0.81; 95% CI [Confidence Interval]: 0.76–0.85). Moderate amounts of leisure-time physical activity were associated with an 11% decreased risk of hypertension compared to the referent group engaging in low amounts of leisure-time physical activity (RR, 0.89; 95% CI, 0.85–0.94). *Strong evidence demonstrates that physical activity reduces BP among adults with prehypertension and normal BP. PAGAC Grade: Strong.*

The dose–response relationship between physical activity and incident hypertension. Two meta-analyses investigated the relationship of physical activity and incident hypertension among adults with normal BP (22,23). Of these two, Liu et al. (23) quantified the dose–response relationship between physical activity and incident hypertension among adults with normal BP (see Figure 2). Among 330,222 adults with normal BP, 67,698 incident cases of hypertension occurred (20.5% of the sample) after 2 to 20 yr of follow-up. The risk of hypertension was reduced by 6% (RR, 0.94; 95% CI, 0.92–0.96) at 10 MET·h·wk^{-1} of leisure-time light, moderate, and vigorous physical activity among adults with normal BP. The protective effect increased by about 6% for each further increase of 10 MET·h·wk^{-1}. For adults with 20 MET·h·wk^{-1} of leisure-time light, moderate, and/or vigorous physical activity, the risk of hypertension was reduced by 12% (RR, 0.88; 95% CI, 0.83–0.92); and for those for 60 MET·h·wk^{-1} of leisure-time light, moderate, and/or vigorous physical activity, the risk of hypertension was reduced by 33% (RR, 0.67; 95% CI, 0.58–0.78). The relationship between leisure-time physical activity and incident hypertension was linear, with no cutoff of benefit, and slightly weaker with

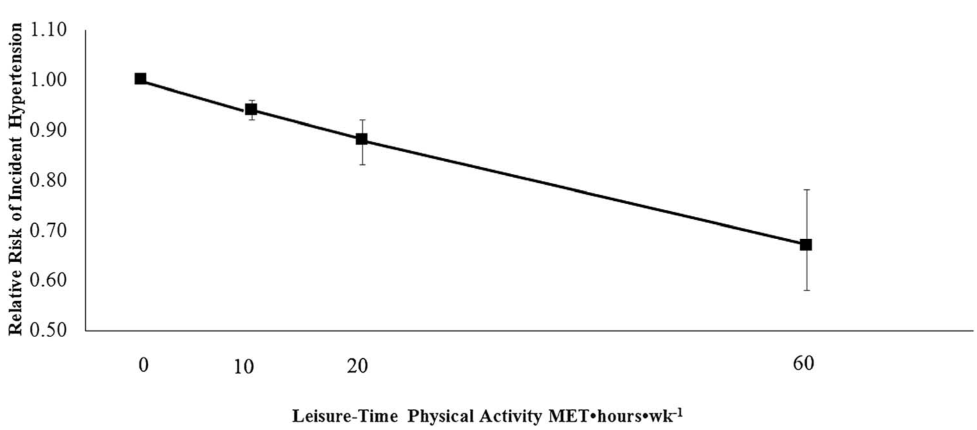

FIGURE 2—A meta-analysis of the inverse relationship between incident hypertension and leisure-time physical activity (MET·h·wk^{-1}) among adults with normal blood pressure. Adapted from Liu et al. (23).

(RR, 0.94; 95% CI, 0.92–0.96) than without (RR, 0.91; 95% CI, 0.89–0.93) BMI adjustment as a covariate. *Strong evidence demonstrates an inverse dose–response relationship between physical activity and incident hypertension among adults with normal BP. PAGAC Grade: Strong. However, the available evidence is insufficient to determine whether a dose–response relationship exists between physical activity and incident hypertension among adults with prehypertension. PAGAC Grade: Not Assignable.*

The treatment of hypertension. CVD progression was defined in two ways. Because BP is considered a proxy measure of CVD risk (20,33), we regarded the BP response to physical activity among adults with hypertension as an indicator of CVD progression, and the outcome of CVD mortality as an indicator of long-standing hypertension. The evidence on the BP response to physical activity is discussed first, and the evidence on CVD mortality outcomes follows.

The BP response to physical activity. There were 15 meta-analyses of RCT that examined the BP response to physical activity ranging from low- to vigorous-intensity among adults with hypertension compared with a control condition of adults who were physically inactive at baseline (14–21,24–30). Of these, 13 reported a statistically significant reduction in SBP and 14 reported a statistically significant reduction in DBP (see Table, Supplemental Digital Content 1, Summary of the Included Systematic Reviews, http://links.lww.com/MSS/B522). The magnitude of the BP reductions ranged from 5 to 17 mm Hg for SBP and 2 to 10 mm Hg for DBP. *Strong evidence demonstrates that physical activity reduces BP among adults with hypertension. PAGAC Grade: Strong.*

The relationship between physical activity and CVD mortality. There was one systematic review (13) that included two large longitudinal prospective cohort studies that addressed the impact of self-reported general and leisure-time habitual physical activity on CVD mortality among adults with hypertension followed from 5 to 24 yr (31,32). Hu et al. (31) investigated the associations among occupational, daily commuting, and leisure-time physical activity and CVD mortality among 26,643 Finnish men and women 25 to 64 yr who were overweight and had hypertension that were followed for 20 yr. The multivariate-adjusted hazard ratios of CVD mortality associated with low (almost completely inactive), moderate (some physical activity >4 $h \cdot wk^{-1} \approx 12$ $MET \cdot h \cdot wk^{-1}$ or more), and high (vigorous physical activity >3 $h \cdot wk^{-1}$ ≈ 18 $MET \cdot h \cdot wk^{-1}$ or more) leisure-time physical activity were 1.00, 0.84 (95% CI, 0.77–0.92), and 0.73 (95% CI, 0.62–0.86) among men, respectively; and 1.00, 0.78 (95% CI, 0.70–0.87) and 0.76 (95% CI, 0.60–0.97) among women, respectively (see Figure 3).

Furthermore, Vatten et al. (32) found that among men with a resting SBP between 140 and 159 mm Hg, whose status of medication use was not disclosed, compared with the referent group of men with a SBP between 120 and 129 mm Hg, men with a resting SBP between 140 and 159 mm Hg who were highly physically active (RR, 1.21; 95% CI, 0.97–1.52) reduced their risk of CVD mortality by 30% versus those who were physically inactive (RR, 1.73; 95% CI, 1.37–2.19). Among men with a resting SBP >160 mm Hg compared to the referent group of men with a SBP between 120 and 129 mm Hg, those who were highly physically active (RR, 1.82; 95% CI, 1.46–2.28) reduced their risk of CVD mortality by 19% versus those who were physically inactive (RR, 2.24; 95% CI, 1.78–2.83). In addition, among women with a resting SBP between 140 and 159 mm Hg compared to the referent group of women with a SBP between 120 and 129 mm Hg, those who were highly physically active (RR, 1.47; 95% CI, 1.04–2.09) reduced their risk of CVD mortality by 24% versus those who were physically inactive (RR, 1.93; 95% CI, 1.39–2.69). Among women with a resting SBP >160 mm Hg compared with the referent group of women with a SBP between 120 and 129 mm Hg, those who were highly physically active (RR, 1.77; 95% CI, 1.26–2.54) reduced their risk of CVD mortality by 27% versus those who were physically inactive (RR, 2.41; 95% CI, 1.76–3.30). Therefore, as SBP increases within hypertensive ranges, the risk of CVD mortality increases. However, the increased risk is attenuated with higher levels of physical activity. *Moderate evidence indicates an inverse, dose–response relationship between physical activity and CVD mortality among adults with hypertension. PAGAC Grade: Moderate.*

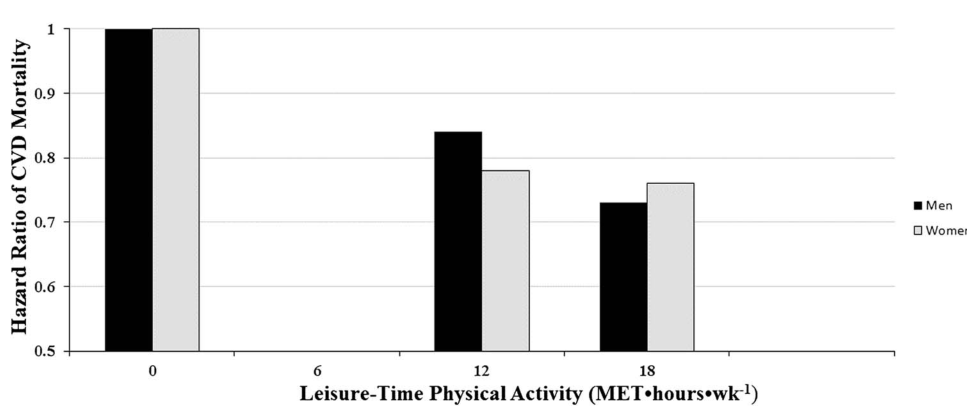

FIGURE 3—The inverse relationship between CVD mortality and leisure-time physical activity ($MET \cdot h \cdot wk^{-1}$) among adults with hypertension adapted from (31) in the systematic review of Rossi et al. (13).

Comorbid Conditions, Physical Function, and Health-related Quality of Life

Hypertension comorbidities include CVD, obesity, diabetes mellitus, chronic kidney disease, congestive heart failure, and the metabolic syndrome, among others. However, because of a lack of evidence, no conclusions could be drawn about whether a relationship exists between physical activity and risk of comorbid conditions, physical function, or health-related quality of life among adults with hypertension.

Evidence on Specific Factors

Age, sex, race/ethnicity, socioeconomic status, or weight status. Three meta-analyses found age not to be a significant moderator of the BP response to physical activity (17,18,23), but two of these contained samples with mixed BP levels, and the other did not stratify analyses by age. One meta-analysis reported that men exhibited BP reductions twice as large as did women following aerobic exercise training among samples with mixed BP levels (18), and another found no difference by sex (23). Race/ethnicity was poorly reported, and when reported in nine of the meta-analyses (20,22–24,26–30), the samples were largely white or Asian. One meta-analysis reported that nonwhite samples with hypertension experienced greater BP reductions than did white samples with hypertension (24).

Six meta-analyses reported the weight status of their samples which ranged from normal weight to obese (17,19,20,23,24,28). Cornelissen et al. (18) found the SBP reductions resulting from aerobic training tended to be larger with greater ($\beta 1 = 0.49$, $P = 0.08$) compared to less ($\beta 1 = 0.45$, $P = 0.06$) weight loss among 5,223 adults with mixed BP levels. Among a large sample of 330,222 adults with normal BP who were followed for 2 to 20 yr, Liu et al. (23) found that the inverse dose–response relationship between leisure-time physical activity and incident hypertension was slightly weaker with (RR, 0.94; 95% CI, 0.92–0.96) than without BMI adjustment as a covariate (RR, 0.91; 95% CI, 0.89–0.93), but these analyses were not stratified by BMI. No meta-analysis disclosed the socio-economic status of their sample. *The available evidence is insufficient to determine whether the relationship between physical activity and BP varies by age, sex, race/ethnicity, socioeconomic status, or weight status among adults with normal BP, prehypertension, and hypertension. PAGAC Grade: Grade not assignable. Also, the available evidence is insufficient to determine whether the relationship between physical activity and the CVD disease progression indicators of BP and CVD mortality vary by age, sex, race/ethnicity, socioeconomic status, or weight status among adults with hypertension. PAGAC Grade: Grade not assignable.*

Resting BP level. Of the six meta-analyses examining BP classification as a moderator of the BP response to physical activity (14,17–19,21,24), four (18,19,21,24) found that the greatest BP reductions occurred among samples with hypertension (5 to 8 mm Hg, 4 to 6% of resting BP level) followed by samples with prehypertension (2 to 4 mm Hg, 2 to 4% of resting BP level), and normal BP (1 to 2 mm Hg, 1 to 2% of resting BP level) (see Figure 4; see Table, Supplemental Digital Content 1, Summary of the Included Systematic Reviews, http://links.lww.com/MSS/B522). *Strong evidence demonstrates the magnitude of the BP response to physical activity varies by resting BP level, with the greatest benefits occurring among adults with hypertension followed by prehypertension and then normal BP. PAGAC Grade: Strong. However, limited evidence suggests the disease progression indicator of the BP response to physical activity varies by resting BP level among adults with hypertension. PAGAC Grade: Limited.*

Frequency, intensity, time, duration or how physical activity was measured. The frequency of the physical activity interventions was reported by 12 meta-analyses (15,17–21,23–26,29,30), and it ranged from 1 to 7 $d \cdot wk^{-1}$, with 3 $d \cdot wk^{-1}$ most common. The intensity of physical activity was reported in 13 meta-analyses (14–26), and ranged from low to vigorous intensity, with low to moderate most common. The time of the exercise session was reported in 11 of the meta-analyses (14,16,18–21,23,25,26,29,30), and ranged from 12 to 100 min, with 30 to 60 min per session most common. The duration of the physical activity intervention was reported in 14 meta-analyses with 1 to 4 to 5 months most common and duration of follow up ranging from 1 to 24 yr, (14,16–21,24–30). All 15 meta-analyses that examined the BP response to physical activity

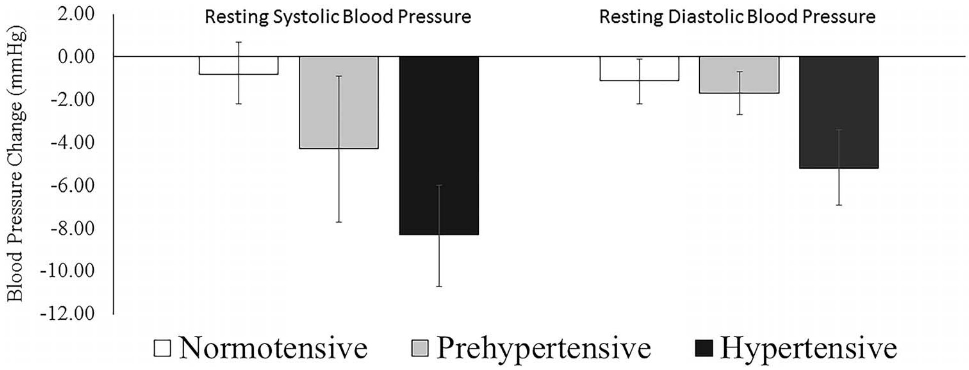

FIGURE 4—A meta-analysis of the BP response to 4 months of aerobic exercise training among adults with normal BP, prehypertension, and hypertension adapted from (18).

included interventions that were structured by the frequency, intensity, time, duration, and type of physical activity, but the details of these features were not well specified (14–21,24–30). None of these meta-analyses reported any physical activity measure outside of the structured physical activity intervention. Furthermore, the meta-analyses of general and leisure-time physical activity on either the influence of physical activity on incident hypertension (22,23) or the systematic review on CVD progression among those with hypertension (13) did not specify how physical activity was measured, although in most cases it appeared to be self-report. *Insufficient evidence is available to determine whether the relationship between BP and physical activity varies by the frequency, intensity, time, duration, or how physical activity is measured among adults with normal BP, prehypertension, and hypertension. PAGAC Grade: Not Assignable. In addition, insufficient evidence is available to determine whether the relationship between physical activity and the disease progression indicators of BP and CVD mortality varies by the frequency, intensity, time, duration, or how physical activity is measured among adults with hypertension. PAGAC Grade: Grade not assignable.*

The type of physical activity. There were five meta-analyses that examined the BP response to aerobic exercise training (16,18,21,25,28), three meta-analyses that examined the BP response to resistance exercise training [one acute (15) and two chronic (17,24)], one meta-analysis examined the BP response to combined aerobic and resistance exercise training (also referred to as concurrent exercise training) (19), and one meta-analysis examined the BP response to isometric resistance training (14) (see Table, Supplemental Digital Content 1, Summary of the Included Systematic Reviews, http://links.lww.com/MSS/B522). Cornelissen and Smart (18) examined aerobic exercise training performed, on average, at moderate to vigorous intensity for 40 min per session 3 $d \cdot wk^{-1}$ for 16 wk and reported SBP/DBP reductions of −8.3 (95% CI, −10.7 to −6.0)/−5.2 (95% CI, −6.9 to −3.4), −4.3 (95% CI, −7.7 to −0.9)/−1.7 (95% CI, −2.7 to −0.7), and −0.8 (95% CI, −2.2 to +0.7)/−1.1 (95% CI, −2.2 to −0.1) mm Hg among adults with hypertension, prehypertension, and normal BP, respectively (Fig. 4). MacDonald et al. (24) examined dynamic resistance training performed, on average, at moderate intensity for 32 min per session 3 $d \cdot wk^{-1}$ for 14 wk and reported SBP/DBP changes of −5.7 mm Hg (95% CI, −9.0 to −2.7 mm Hg)/−5.2 mm Hg (95% CI, −8.4 to −1.9 mm Hg), −3.0 mm Hg (95% CI, −5.1 to −1.0 mm Hg)/−3.3 mm Hg (95% CI, −5.3 to −1.4 mm Hg), and 0.0 mm Hg (95% CI, −2.5 to 2.5 mm Hg)/−0.9 mm Hg (95% CI, −2.1 to 2.2 mm Hg) among adults with hypertension, prehypertension, and normal BP, respectively. Corso et al. (19) examined combined aerobic and dynamic resistance exercise training performed, on average, at moderate intensity for 58 min per session 3 $d \cdot wk^{-1}$ for 20 wk and reported SBP/DBP changes of −5.3 mm Hg (95% CI, −6.4 to −4.2 mm Hg)/−5.6 mm Hg (95% CI, −6.9 to −3.8 mm Hg), −2.9 mm Hg (95% CI, −3.9 to −1.9 mm Hg)/−3.6 mm Hg (95% CI, −5.0 to −0.2 mm Hg), and +0.9 mm Hg (95% CI, 0.2 to 1.6 mm Hg)/−1.5 mm Hg (95% CI, −2.5 to −0.4 mm Hg) among adults with hypertension, prehypertension, and normal BP, respectively. *Moderate evidence indicates the relationship between resting BP level and the BP response to physical activity does not vary by traditional type (i.e., aerobic, dynamic resistance, combined) of physical activity among adults with normal BP, prehypertension, and hypertension. PAGAC Grade: Moderate.*

Carlson et al. (14) investigated the BP response among adults with hypertension (n = 61) and normal BP (n = 162) to four or more weeks of handgrip isometric resistance training at 30% to 50% maximal voluntary contraction, with four contractions held for 2 min with 1 to 3 min of rest between contractions. SBP, DBP, and mean arterial BP were reduced among the adults with hypertension, all of whom were on medication, by −4.3 mm Hg (95% CI, −6.6 to −2.2 mm Hg)/−5.5 mm Hg (95% CI, −7.9 to −3.3 mm Hg)/−6.1 mm Hg (95% CI, −8.0 to −4.0 mm Hg), and by −7.8 mm Hg (95% CI, −9.2 to −6.4 mm Hg)/−3.1 mm Hg (95% CI, −3.9 to −2.3 mm Hg)/−3.6 mm Hg (95% CI, −4.4 to −2.7 mm Hg) among adults with normal BP, respectively. These investigators were unable to explain reasons for the larger reductions in SBP among the adults with normal BP compared with adults with hypertension, and the reverse pattern of BP response for DBP and mean arterial BP. Therefore, no conclusions can be made about the antihypertensive benefits of isometric resistance training.

There were four meta-analyses that examined complementary and alternative types of physical activity (26,27,29,30) (see Table, Supplemental Digital Content 1, Summary of the Included Systematic Reviews, http://links.lww.com/MSS/B522). Xiong et al. (29) investigated the BP response to Baduanjin, an ancient Chinese mind-body exercise characterized by simple, slow, and relaxing movements, among 572 Asian adults with hypertension, and reported SBP/DBP reductions of −13.0 mm Hg (95% CI, −21.2 to −4.8 mm Hg)/−6.1 mm Hg (95% CI, −11.2 to −1.1 mm Hg) following 3 to 12 months of Baduanjin, respectively. Xiong et al. (30) investigated the BP response to Qigong, an ancient Chinese healing art that consists of breathing patterns, rhythmic movements, and meditation, among 2349 Asian adults with hypertension, and reported SBP/DBP reductions of −17.4 mm Hg (95% CI, −21.1 to −13.7 mm Hg)/−10.6 mm Hg (95% CI, −14.0 to −6.3 mm Hg), respectively, following 2 months to 1 yr of Qigong. Wang et al. (27) investigated the BP response to Tai Chi, an ancient Chinese exercise that combines deep diaphragmatic breathing with continuous body movements to achieve a harmonious balance between body and mind, among 1371 mostly Asian adults with hypertension. They reported SBP/DBP reductions of −12.4 mm Hg (95% CI, −12.6 to −12.2 mm Hg)/−6.0 mm Hg (95% CI, −6.2 to −5.9 mm Hg), respectively, following 2 to 60 months of all forms and types of Tai Chi. Park et al. (26) investigated the BP response to yoga, which incorporates meditation with physical movement, among 394 adults with hypertension. They reported SBP/DBP reductions of −11.4 mm Hg (95% CI, −14.6 to −8.2 mm Hg)/−2.4 mm Hg (95% CI, −4.3 to −0.4 mm Hg), respectively, among older adults 60 yr and older following 6 to 12 wk of yoga. These favorable findings of the antihypertensive effects of complementary and alternative physical activity types must be interpreted with caution due to the low study methodological quality of this literature, lack of disclosure of important study design considerations, considerable heterogeneity in this literature, inability to generalize findings to other racial/ethnic groups, and lack of long-term follow-up. *Moderate evidence indicates the relationship between physical activity and the disease progression indicator of BP does not vary by type of physical activity, with the evidence more robust for traditional types (modes, i.e., aerobic, dynamic resistance, combined) of physical activity than complementary and alternative types (modes, i.e., Baduanjin, Qigong, Tai Chi, Yoga) among adults with hypertension. PAGAC Grade: Moderate.*

DISCUSSION

A summary of the grading of the evidence-based conclusion statements on the relationship between physical activity and BP among adults with normal BP, prehypertension, or hypertension from this systematic umbrella review appears in Table 2. In total, four conclusion statements were strong, three moderate, one limited, and five were not assignable. The evidence was strong demonstrating that physical activity reduced BP among adults with normal BP, prehypertension, and hypertension. Indeed, of the four meta-analyses that included samples with normal BP, prehypertension, and hypertension (18,19,21,24), the investigative teams found that the greatest BP reductions occurred among samples with hypertension (5 mm Hg to 8 mm Hg, 4% to 6% of resting BP level) followed by samples with prehypertension (2 to 4 mm Hg, 2% to 4% of resting BP level), and normal BP (1 to 2 mm Hg, 1% to 2% of resting BP level). Consistent with the law of initial values (34), adults with hypertension experience BP reductions from exercise training that are approximately two times greater than the BP reductions among adults with prehypertension and approximately four to five times greater than the BP reductions among adults with normal BP. The BP reductions of this magnitude may be sufficient to reduce the resting BP of some of the samples with hypertension into prehypertensive and normotensive ranges; and the risk of coronary heart disease by 4% to 22% and stroke by 6% to 41% among adults with hypertension (2,35,36).

Surprisingly, the evidence regarding nearly all the effect modifiers we examined was insufficient so that a grade was not assignable. These effect modifiers included age, sex, race/ethnicity, socioeconomic status, or weight status; and the frequency, intensity, time, duration, or how physical activity was measured among adults with normal BP, prehypertension, and hypertension. In the few instances where these effect modifiers were examined as moderators of the BP response to physical activity, the findings were too disparate to synthesize because they were often not reported separately by BP classification but were reported for the overall sample that included adults with hypertension, prehypertension, and normal BP. We found strong evidence demonstrating the magnitude of the BP response to physical activity varies by resting BP level, with greater benefits occurring among those with higher resting BP. Therefore, inclusion of samples of mixed BP status (i.e., adults with normal BP, prehypertension, and hypertension)

TABLE 2. The grading of the evidence for the conclusion statements on the relationship between physical activity and BP and the effect modifiers organized by the questions being asked.

Conclusion Statement	PAGAC Grade
1. Strong evidence demonstrates that physical activity reduces BP among adults with prehypertension and normal BP.	Strong (14,15,17–19,21,22,24,25)
2. Strong evidence demonstrates an inverse dose–response relationship between physical activity and incident hypertension among adults with normal BP.	Strong (23)
3. The available evidence is insufficient to determine whether a dose–response relationship exists between physical activity and incident hypertension among adults with prehypertension, as the magnitude and precision of the effect cannot be ascertained from findings that are too scarce to synthesize.	Not assignable
4. Strong evidence demonstrates that physical activity reduces BP among adults with hypertension.	Strong (14–21,24–30)
5. Moderate evidence indicates an inverse, dose–response relationship between physical activity and CVD mortality among adults with hypertension.	Moderate (13,31,32)
6a. The available evidence is insufficient to determine whether the relationship between physical activity and BP varies by age, sex, race/ethnicity, socioeconomic status, or weight status among adults with normal BP, prehypertension, and hypertension.	Not assignable
6b. The available evidence is insufficient to determine whether the relationship between physical activity and the disease progression indicators of BP and CVD mortality varies by age, sex, race/ethnicity, socio-economic status, or weight status among adults with hypertension.	Not assignable
7a. Strong evidence demonstrates the magnitude of the BP response to physical activity varies by resting BP level, with the greatest benefits occurring among adults with hypertension followed by prehypertension and then normal BP.	Strong (18,19,21,24)
7b. Limited evidence suggests the disease progression indicator of the BP response to physical activity varies by resting BP level among adults with hypertension.	Limited
8a. Insufficient evidence is available to determine whether the relationship between BP and physical activity varies by the frequency, intensity, time, duration, or how physical activity is measured among adults with normal BP, prehypertension, and hypertension.	Not assignable
8b. Insufficient evidence is available to determine whether the relationship between physical activity and the disease progression indicators of BP and CVD mortality varies by the frequency, intensity, time, duration, or how physical activity is measured among adults with hypertension.	Not assignable
9a. Moderate evidence indicates the relationship between resting BP level and the BP response to physical activity does not vary by traditional type (i.e., aerobic, dynamic resistance, combined) of physical activity among adults with normal BP, prehypertension, and hypertension.	Moderate (18,19,24)
9b. Moderate evidence indicates the relationship between physical activity and the disease progression indicator of BP does not vary by type of physical activity, with the evidence more robust for traditional types (modes, i.e., aerobic, dynamic resistance, combined) of physical activity than complementary and alternative types (modes, i.e., Baduanjin, Qigong, Tai Chi, Yoga) among adults with hypertension.	Moderate (18,19,24,26,27,29,30)

underestimates the effectiveness of physical activity as antihypertensive lifestyle therapy.

The 2008 Scientific Report concluded that both aerobic and dynamic resistance exercise training of moderate-to-vigorous intensity produced small but clinically important reductions in SBP and DBP, with the evidence more convincing for aerobic than dynamic resistance training (8). Reflecting on the accumulating evidence over the past decade, we found moderate evidence indicating that the relationship between the BP response to physical activity is similar for aerobic, dynamic resistance, and combined aerobic and dynamic resistance exercise among adults with normal BP, prehypertension, and hypertension. Furthermore, there is promising, but limited, evidence that complementary and alternative types of physical activity are effective in lowering BP among adults with hypertension. Yet, very little research of high quality has been conducted in this area, and RCT are lacking that directly compare the BP-lowering effects of complementary and alternative to traditional types (aerobic, dynamic resistance, combined) of physical activity among adults with hypertension. Gaining this information will inform the public health recommendations on the types of physical activity that will optimize BP benefit and possibly provide adults with hypertension other effective exercise options to lower their high BP.

In conclusion, this systematic umbrella review provides strong, convincing evidence of the importance of physical activity in the prevention of the development of hypertension among adults with normal BP and prehypertension, and of its protective effects in the treatment of hypertension by attenuating the progression of CVD among adults with hypertension. These findings occurred in dose–response fashion with no cutoff to the amount of physical activity that confers benefit. Furthermore, we found moderate evidence that aerobic and dynamic resistance exercise training alone or combined were equally effective in lowering BP among adults with normal BP, prehypertension, and hypertension. Yet, important knowledge gaps remain regarding nearly all effect modifiers of the relationship between physical activity and BP that we examined, notably race/ethnicity. Due to the disproportionate burden of hypertension among African Americans (1,37,38), large RCT are needed that are sufficiently powered to perform stratified analyses between African Americans and other racial/ethnic groups to inform this important research gap. Future research is also needed that adheres to standard BP measurement protocols and classification schemes to better understand the influence of physical activity on the risk of comorbid conditions, health-related quality of life, and CVD progression and mortality; the interactive effects between physical activity and antihypertensive medication use; and the immediate BP-lowering benefits of physical activity.

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The results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate manipulation. The Committee's work was supported by the HHS. Committee members were reimbursed for travel and per diem expenses for the five public meetings; Committee members volunteered their time. Dr. Jakicic received an honorarium for serving on the Scientific Advisory Board for Weight Watchers International and was a coinvestigator on a grant awarded to the University of Pittsburgh by Weight Watchers International. The authors report no other potential conflicts of interest.

HHS staff provided general administrative support to the Committee and assured that the Committee adhered to the requirements for Federal Advisory Committees. HHS also contracted with ICF, a global consulting services company, to provide technical support for the literature searches conducted by the Committee. HHS and ICF staff collaborated with the Committee in the design and conduct of the searches by assisting with the development of the analytical frameworks, inclusion/exclusion criteria, and search terms for each primary question; using those parameters, ICF performed the literature searches.

This article is being published as an official pronouncement of the American College of Sports Medicine. This pronouncement was reviewed for the American College of Sports Medicine by members-at-large and the Pronouncements Committee. This article serves as an update to the topics covered in the 2004 ACSM position stand, "Exercise and Hypertension" [*Med. Sci. Sports Exerc*. 2004;36(3);533–53].

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PRONOUNCEMENT

Effects of Physical Activity in Knee and Hip Osteoarthritis: A Systematic Umbrella Review

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ABSTRACT

KRAUS, V. B., K. SPROW, K. E. POWELL, D. BUCHNER, B. BLOODGOOD, K. PIERCY, S. M. GEORGE, and W. E. KRAUS, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Effects of Physical Activity in Knee and Hip Osteoarthritis: A Systematic Umbrella Review. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1324–1339, 2019. **Introduction:** We conducted a systematic umbrella review to evaluate the literature relating to effects of physical activity on pain, physical function, health-related quality of life, comorbid conditions and osteoarthritis (OA) structural disease progression in individuals with lower-extremity OA. **Methods:** Our primary search encompassed 2011 to February 2018 for existing systematic reviews (SR), meta-analyses (MA) and pooled analyses dealing with physical activity including exercise (not mixed with any other intervention and compared to a no-activity control group). A supplementary search encompassed 2006 to February 2018 for original research related to physical activity (including exercise) and lower limb OA progression. Study characteristics were abstracted, and risk of bias was assessed. **Results:** Physical activity decreased pain and improved physical function (strong evidence) and improved health-related quality of life (moderate evidence) among people with hip or knee OA relative to less active adults with OA. There was no evidence to suggest accelerated OA progression for physical activity below 10,000 steps per day. Both physical activity equivalent to the 2008 Physical Activity Guidelines for Americans (150 $\text{min}\cdot\text{wk}^{-1}$ of moderate-intensity exercise in bouts ≥10 min) and lower levels of physical activity (at least 45 total minutes per week of moderate-intensity) were associated with improved or sustained high function. No SR/MA addressing comorbid conditions in OA were found. Measurable benefits of physical activity appeared to persist for periods of up to 6 months following cessation of a defined program. **Conclusions:** People with lower-extremity OA should be encouraged to engage in achievable amounts of physical activity, of even modest intensities. They can choose to accrue minutes of physical activity throughout the entire day, irrespective of bout duration, and be confident in gaining some health and arthritis-related benefits. **Key Words:** PAIN, FUNCTION, QUALITY OF LIFE, PROGRESSION, KNEE, HIP

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There are approximately 100 different arthritic conditions with a total of 54.4 million Americans estimated to have physician-diagnosed arthritis (1). Among these, osteoarthritis (OA) is the most common joint disorder in the US, affecting an estimated 30.8 million adults (13.4% of the civilian adult US population) (2). Osteoarthritis affects a broad spectrum of age groups in the US, including 2 million Americans under the age of 45 yr with knee OA (3). By the year 2040, an estimated 78.4 million (25.9% of the projected total adult population) adults 18 yr and older are expected to have physician-diagnosed arthritis (4), the majority of whom will have OA. Methodological issues, such as the current inability to reliably diagnose early nonradiographic OA and traditional accounting of OA in only a limited number of joint sites (hip and knee), make it highly likely that the real burden of OA has been underestimated (5). The risk of mobility disability (defined as needing help walking or climbing stairs) attributable to knee OA alone is greater than that attributable to any other medical condition in people 65 yr and older (6). As expected, based on these prevalence and disability figures, OA is associated with an extremely great economic burden—by one national estimate equal to US $185.5 billion in aggregate annual medical care expenditures (7).

To provide recommendations to the Department of Health and Human Services for updating the *Physical Activity Guidelines for Americans*, the Physical Activity Guidelines Advisory Committee (PAGAC) chose to investigate seven chronic conditions, among them OA (8). The choice of OA was predicated on the large portion of the general population having this chronic condition, the high disability associated with OA (9), and the potential public health importance of physical activity in people with OA. The overall goal of this systematic umbrella review was to evaluate the literature relating to effects of physical activity on 1) pain, 2) physical function, 3) health-related quality of life (HRQoL), 4) disease progression, and 5) risk of comorbid conditions in individuals with existing lower limb (hip and/or knee) OA. As a secondary goal, we also evaluated the literature for evidence of variation in the relationship of physical activity and these outcomes based on (a) the dose of physical activity exposure; (b) age, sex, race/ethnicity, socioeconomic status, or weight status; and (c) frequency, duration, intensity, mode (type), or means of measuring physical activity. This article represents the scientific research performed to inform the 2018 Physical Activity Guidelines for Americans (10) with an extension of the literature search by 1 yr through February 2018.

METHODS

The overarching methods used to conduct systematic reviews (SR) informing the 2018 Physical Activity Guidelines Advisory Committee Scientific Report (search strategy development, article triage, data abstraction, bias assessment, and quality control processes and methods for analysis) have been described in detail elsewhere (11). The searches were conducted of electronic databases (PubMed®, CINAHL, and Cochrane) and were supplemented by authors (experts in the area) to provide additional articles identified through their expertise and familiarity with the literature. The full search strategies are available online (12). The inclusion criteria were predefined and searches were registered in PROSPERO CRD42018092365. Studies were included if they were published in English; were meta-analyses (MA), SR or pooled analyses published from 2011 through February 2018, and investigated individuals of all ages with preexisting OA of the hip or knee; the association between all types and intensities of physical activity, including exercise, not mixed with any other interventions (such as diet); and one of the health outcomes of interest (pain, physical function, HRQoL, disease progression or risk of comorbid conditions). Physical activity was defined as bodily movement produced by skeletal muscles that results in energy expenditure. Exercise was defined as a form of physical activity that is planned, structured, repetitive, and designed to improve or maintain physical fitness, physical performance, or health. Physical function was defined as the ability of a person to move around and to perform types of activity; in the studies included in this summary, this was most often measured by a standardized instrument used routinely in OA clinical trials, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (13). Health-related quality of life was defined as a multidimensional concept including domains related to physical, mental, emotional, and social functioning.

Studies of nonambulatory adults, hospitalized patients, or animals were excluded. We also excluded studies of multimodal interventions not presenting data on physical activity alone and studies of single, acute sessions of physical activity. The titles, abstracts, and full-text of the identified articles were independently screened by two reviewers. Disagreement between reviewers was resolved by discussion or by a third member of the PAGAC committee.

The amended literature search yielded 20 MA and SR meeting the inclusion criteria for our analysis of OA and pain, physical function, and HRQoL outcomes (14–31); however, the studies identified included significant overlap. In an attempt to minimize redundancy, the Committee reviewed the overlap of studies within all the MA/SR; those with considerable overlap, with three or fewer unique additional studies, and that did not add additional information to the larger studies, were not retained for purposes of the final summary. This procedure resulted in retention of six MA (14–16,18,22,32) and three SR for the purposes of the summary related to OA pain, physical function, and HRQoL (17,33,34) (Table 1); from the amended search, one additional MA and two additional SR were added to the original search conducted as part of the governmental report.

Upon completion of triage based on the MA, SR, and pooled analyses, the authors observed a paucity of MA and SR dealing with physical activity and knee OA progression defined as structural worsening of OA based on imaging (radiographic or magnetic resonance imaging [MRI]), worsening function (based on patient-reported outcomes or gait speed) or

TABLE 1. Summary of included studies assessing the relationship of physical activity with pain, function and quality of life in individuals with lower-extremity OA (14–18,22,32–34).

Author (Year)	Type of Study; Joints; Mean Age and/or Range	Sample Size and No. Studies	Type(s) of Physical Activity	Outcome Measures	Effect Sizes (95% CI)*
Bartels (2016) (14)	MA; Knee & Hip; 68 yr	Total: 1190 participants from 13 studies Pain: 971 participants from 12 trials Physical Function: 1059 participants from 12 trials HRQoL: 971 participants from 10 trials	Range of motion, strength training, and aerobic exercise in a therapeutic/heated indoor pool	Pain: WOMAC, VAS, SF-36, HAQ, Lequesne algofunctional index, AIMS, KSPS, McGill Pain Questionnaire, ASES, SES, and NRS Physical Function: WOMAC, SF-36, PCS, HAQ, PDI, ASES HRQoL: SF-36/SF-12/SF-8, EuroQoL, KOOS Subscore: QOL, Quality of well-being, AIMS, others	**Pain:** **SMD −0.31 (−0.47 to −0.15)** **Physical Function:** **SMD −0.32 (−0.47 to −0.17)** **HRQoL:** **SMD −0.25 (−0.49 to −0.01)**
Bartholdy (2017) (33)	SR; Knee; 64 yr;	4699 participants from 45 studies	ACSM[a] Interventions (29% of included studies) and non-ACSM Interventions	Strength: knee extension Pain: WOMAC, NRS, KOOS, pain score, AIMS2, OASI, and VAS Physical Function: WOMAC, Lequesne Index, KOOS, functional incapacity score, SF-36 AIMS2, OASI, subjective rating of daily activity, and KOOS ADL	**Strength: SMD 0.448 (0.091 to 0.805)** Pain: SMD 0.106 (−0.239 to 0.451) Physical Function: SMD 0.153 (−0.243 to 0.549)
Beumer (2016) (15)	SR/MA; Hip; 52–77 yr	1213 participants from 19 studies	Land- and aquatic-based therapeutic strength and aerobic exercises	Pain: VAS, WOMAC	Pain: **(WOMAC): SMD −0.53 (−0.96 to −0.10)** **(VAS): SMD −0.49 (−0.70 to −0.29)**
Chang (2016) (16)	SR/MA; Knee; Mean age of study participants ranged from 61.15 to 79.01 yr	508 participants from 11 studies	Tai Chi Chuan	Pain: WOMAC Physical function: WOMAC, 6 min-walk test, stair climb test, and SAFE	Pain (WOMAC): **SMD −0.41 (−0.67 to −0.74)** Physical Function **(WOMAC): SMD −0.16 (−0.44 to −0.11)** **(6-min walking test): SMD −0.16 (−1.23 to 0.90)** **(Stair climb test): SMD −0.76 (−1.34 to 0.15)** **(SAFE): SMD −0.63 (−0.98 to −0.27)**
Escalante (2011) (17)	SR; Hip & Knee; Mean age range 54.4–74 yr (discoverable for 19 studies)	2145 participants from 20 studies	Land-based (strength, tai chi, aerobic, and mixed) and aquatic exercise	Physical function: 6 min walk test	Physical Function (6-min walk test): **Strength: SMD 0.31 (0.06 to 0.56)** **Pooled Tai Chi: SMD 0.66 (0.23 to 1.09)** **Pooled Aerobic: SMD 0.90 (0.70 to 1.10)** **Pooled Mixed: SMD 0.47 (0.032 to 0.62)** Pooled Hydrotherapy: SMD 0.00 (−0.38 to 0.39)

Fernandopulle, (2017) (32)	SR/MA; Hip & Knee; 54–73 yr	3233 participants from 27 studies	Land-based generic physical activity interventions on pain, physical function, and physical performance	Pain: pain intensity, VAS, WOMAC Physical Function: WOMAC, AIMS, KOOS, Japanese Knee OA measurement, customized measure of disability Physical Performance: 6MWT, TUG, timed stair climbing	Recreational Activity **Physical Function (WOMAC) at 3 months from randomization: SMD −9.56 (−13.95 to −5.17)** Conditioning Exercise **Physical Performance (6MWT) 6 months from randomization: SMD 42.72 (27.28 to 57.66)**; **Physical Function (WOMAC) 6 months from randomization: SMD −3.74 (−5.70 to −1.78);** Physical Performance (Timed-stair climbing test) at 6 months randomization: SMD −2.29 (−4.65 to .006); **Physical Performance (Timed-stair climbing test) at 18 months: SMD −0.49 (−0.75 to −0.23)** Walking **Physical Function at 6 months from randomization: SMD, −10.38 (−12.27 to −8.49);** Physical Function at 12 months from randomization: SMD, −0.03 (−0.035 to 0.28); Physical Performance 6MWT at 12 months from randomization: SMD, −1.88 (−43.46 to 39.71); Pain 3 months from randomization: SMD 0.19 (−0.31 to 0.68); Pain 6 months from randomization: SMD, −1.55 (−3.62 to 0.52)
Fransen (2015) (18)	SR/MA; Knee; Mean age range 55–73 yr	6345 participants from 54 studies Pain (immediately post-treatment): 3537 participants from 44 studies Physical Function (immediately post-treatment): 3913 participants from 44 studies HRQoL (immediately post-treatment): 1073 participants from 13 studies	Land-based strength and aerobic exercises (muscle strengthening, balance training, aerobic walking, cycling, Tai Chi)	Pain: WOMAC, global pain scores, Lequesne OA Index (2–6 months in and >6 months) Physical function: WOMAC, global disability scores, Sickness Impact profile (2–6 and >6 months) HRQoL: SF-12	Pain: **Pooled SMD 0.49 (0.39 to 0.59)**; 12 studies (1468 participants) **SMD 0.24 (95% CI, 0.14–0.35)** at 2–6 months post-exercise training; 6 studies SMD 0.08 (95% CI, −0.15 to 0.30) after more than 6 months post-exercise training Physical Function: **Pooled SMD 0.52 (95% CI, 0.39–0.64);** 10 studies (1279 participants) **SMD 0.15 (95% CI, 0.04–0.26)** at 2–6 months post-exercise training; seven studies **SMD 0.20 (95% CI, 0.08–0.32)** after more than 6 months post-exercise training HRQoL: **SMD 0.28 (0.15 to 0.40)**

(continued next page)

TABLE 1. *(Continued)*

Author (Year)	Type of Study; Joints; Mean Age and/or Range	Sample Size and No. Studies	Type(s) of Physical Activity	Outcome Measures	Effect Sizes (95% CI)*
Juhl (2014) (22)	SR/MA; Knee; 64.3 yr	4418 participants from 48 studies	Single or combination exercises (aerobic, resistance, and performance training)	Pain: WOMAC, VAS, SF-36, AIMS, BPI, KOOS, OASI Physical function: WOMAC, AIMS, Self-Reported from FAST, SF-36, KOOS, OASI	Pain: **Overall pooled SMD 0.50 (0.39 to 0.62); Aerobic Exercise SMD 0.67; Resistance Exercise SMD 0.62; Performance Exercise SMD 0.48** Physical Function: **Overall Pooled SMD 0.49 (0.35 to 0.63); Aerobic Exercise SMD 0.56; Resistance Exercise SMD 0.60; Performance Exercise SMD.56**
Young (2018) (34)	SR; Knee; Mean age range 54.4–70 yr	2173 participants from 24 studies (that included effect sizes related to knee OA)	To identify specific doses of exercise (aerobic, balance, and strength) related to improved outcomes of pain and function in individuals with common knee disorders	Pain: WOMAC, KOOS, VAS Physical Function: WOMAC, KOOS, Step Test, SF-36, 6MWT	Pain (Land based): WOMAC: SMD 0.28 to SMD 1.39; KOOS: SMD 0.64 to SMD 0.76; VAS: SMD 0.48 to SMD 2.44 Physical Function (Land based): WOMAC: SMD 0.01 to SMD 1.83; KOOS: SMD 0.45 to SMD 0.99; Step Test: SMD 0.45; SF-36: SMD 0.68 to SMD 1.49; 6MWT: SMD 0.58 Pain (aquatic based): KOOS: SMD 0.17 to SMD 0.58; VAS: SMD 1.78 to SMD 2.43 Physical Function (aquatic based): KOOS: SMD 1.19; SF-36: SMD 0.58; 6MWT: SMD 0.72

*Statistically significant results favoring exercise are shown in bold font (note sign can be positive or negative depending upon coding of data within the study).

[a]ACSM Interventions, a voluntary contraction against an external resistance typically performed in especially designed equipment or with free weights. The external load should be above 40% of 1 repetition maximum (1RM) corresponding to very light to light intensity, and the exercises performed in 2–4 sets of 8–12 repetitions; preferably to contraction failure or muscular exhaustion. The exercise program should consist of at least two to three sessions per week. Non-ACSM interventions, exercise interventions that in their description were considered not to follow all of the above definitions were categorized as “not-ACSM interventions,” and include all other types of interventions.

Additional Results for Juhl 2014.

Overall.

- When the studies that evaluated only a single exercise type were pooled, the SMD for pain 0.61 (95% CI, 0.48–0.75), and for the SMD for disability was 0.58 (95% CI, 0.40–0.75) but with large heterogeneity.
- Exercise programs that included a combination of resistance, aerobic, and performance exercise were not significantly better than control treatments in reducing pain (SMD 0.16 [95% CI, ⩾0.04 to 0.37], I2 = 44.0%) and had only a small effect in reducing disability (SMD 0.22 [95% CI, 0.08–0.37], I2 = 0%). The difference between exercise programs focusing on one type of exercise compared with programs mixing two or more types was significant for both outcomes (SMD for pain 0.45 [95% CI, 0.20–0.69], $P < 0.001$ and SMD for disability 0.36 [95% CI, 0.13–0.58], $P < 0.002$) in favor of using only one type of exercise.

Aerobic Training.

- The effect of aerobic exercise on pain relief increased with an increased number of supervised sessions (slope 0.022 [95% confidence interval 0.002,0.043]).

Resistance Training.

- More pain reduction occurred with quadriceps-specific exercise than with lower limb exercise (SMD 0.85 vs 0.39; $P = 0.005$) and when supervised exercise was performed at least three times a week (SMD 0.68 vs 0.41; $P = 0.017$).

Disease Severity.

- Stratified analysis showed similar effects for pain in patients with severe knee OA (SMD 0.60 [95% CI, 0.38–0.82], I2 = 36.1%) and those with mild/moderate knee OA (SMD 0.66 [95% CI, 0.34–0.99], I2 = 77.0%) ($P = 0.736$).
- Although exercise therapy seemed to reduce patient-reported disability less in patients with severe knee OA (SMD 0.39 [95% CI, 0.05–0.74], I2 = 73.6%) than in patients with mild/moderate knee OA (SMD 0.66 [95% CI, 0.32–0.99], I2 = 84.6%) ($P = 0.282$), the differences did not reach significance.

VAS, visual analog scale for pain; SF, Short Form (-8, -12, or -36 item) Health Survey; HAQ, Health Assessment Questionnaire; AIMS, Arthritis Impact Measurement Scales; KSPS, Knee Specific Pain Scale; ASES, Arthritis Self-Efficacy Scale; SES, Schmerzempfindungsskala; NRS, Numeric Rating System (of pain); PCS, Physical Composite Score; PDI, Pain Disability Index; EuroQoL, an instrument for measuring HRQoL; KOOS, Knee Injury and Osteoarthritis Outcome score; SAFE, Survey of Activities and Fear of Falling in the Elderly; OASI, Osteoarthritis Screening Index; FAST, Fitness Arthritis and Senior Trial; KOOS ADL, KOOS scale of activities of daily living; 6MWT, 6-min walk test; TUG, timed up and go test; BPI, Brief Pain Inventory; FAST, Fitness Arthritis and Seniors Trial.

progression to total joint arthroplasty (replacement) for OA. Based on the paramount importance of the issue of disease progression for individuals with OA, we elected to perform a separate literature search, using the same search strategy, process, and inclusion/exclusion criteria used for the pain, physical function and HRQoL outcomes but including two additional specific criteria: only inclusion of original research published from 2006 through February 2018 and only inclusion of the outcome of OA progression. Of note, we did not identify any studies examining the effects of physical activity on progression based on systemic biomarkers associated with disease state.

The search for MA, SR, and pooled analyses, and reports failed to identify any literature to address the question of the effects of physical activity on comorbid conditions in OA. The term comorbid condition referred to any other existing chronic condition identified by a medical diagnosis (e.g., coronary heart disease) or by clinical events (e.g., cardiovascular mortality); therefore, this question was not pursued.

The quality of each MA, SR and pooled analysis, summarized in Supplemental Digital Content 1 (see Table, Supplemental Digital Content 1, quality assessment chart, http://links.lww.com/MSS/B518), was assessed using $\text{AMSTAR}_{\text{ExBP}}$ (35), a modified version of "A Measurement Tool to Assess Systematic Reviews" (AMSTAR) (36,37); the majority of the studies met 11 of the 18 AMSTAR criteria. Risk of bias, or internal validity was assessed for each original study using an adapted version of the USDA NEL Bias Assessment Tool (BAT) (38) as summarized in Supplemental Digital Content 2 (see Table, Supplemental Digital Content 2, original research bias assessment chart, http://links.lww.com/MSS/B519); the majority of the studies met 8 of the 10 applicable criteria. The bias assessment of the original research and the full search strategy is available (12). Recently, the method of data extraction has been published in detail (11). Literature trees summarize the selection of MA, SR, and pooled analyses and reports in Supplemental Digital Content 3 (see Figure, Supplemental Digital Content 3, providing details of literature tree search for reviews related to OA pain, physical function, HRQoL, progression and risk of comorbid conditions, http://links.lww.com/MSS/B520) and original research related to OA progression in Supplemental Content (see Figure, Supplemental Digital Content 4, providing details of literature tree search for original research related to OA progression, http://links.lww.com/MSS/B521).

RESULTS

OA and Pain, Physical Function, and HRQoL as Outcomes

Most of the retained MA (six) and SR (three) publications evaluated randomized controlled trials (RCT) reviewing the effects of one or more modalities of exercise (land-based and aquatic, aerobic, muscle strengthening, and Tai Chi) on knee and hip OA. Most used the WOMAC scale—common in the OA research arena—to assess pain and physical function, and SF-12 to assess HRQoL. One SR examined land-based exercise studies exclusively (18); another examined pool-based exercise effects only (14). In sum, these references encompassed 261 studies related to knee and/or hip OA involving 25,924 individuals with pain, physical function or HRQoL as an outcome. A total of 240 studies involving 24,583 participants included knee OA; a total of 52 studies involving 4803 participants included hip OA.

Taken together, the evidence demonstrated that physical activity reduces pain and improves physical function and HRQoL for persons with lower limb OA. The effect sizes (based on standardized mean differences [SMD]) favored exercise: maximal SMD reported were 0.53 for pain (15), 0.76 for physical function (16) and 0.28 for HRQoL (18) (Table 1). For pain, physical function, and HRQoL, the effect sizes for those with hip OA did not vary from those with knee OA only. Although there were some modest differences in effect sizes across different exposures, in general, the reviews were consistent in finding that physical activity is associated with reductions in pain and improvements in physical function and HRQoL for both knee and hip OA, irrespective of the mode (aquatic vs land-based exercise) or muscle strengthening versus aerobic versus Tai Chi (Table 1). Following cessation of the intervention, the beneficial effects of physical activity persisted up to 6 months for pain, and beyond 6 months for physical function (18) (Table 1).

The findings on pain, physical function, and HRQoL are illustrated in Figures 1 and 2, which present results from one review addressing land-based exercise effects on the knee (from Fransen et al. (18)) and one review addressing aquatic exercise effects on the knee (from Bartels et al. (14)). In Figure 1, the direction to the left favors exercise (decreased pain and improved physical function), whereas, improved HRQoL is to the right. In Figure 2, the direction to the left favors exercise (decreased pain, improved physical function and HRQoL).

Mode and Dose of Exercise

Most studies of the effects of physical activity on pain, physical function, and HRQoL were RCT of one mode, intensity, or duration; there was significant heterogeneity for these factors among the studies included within each MA/SR. Limited information was available on dose–response or different modes (types of exercise). Overall, the literature search revealed four MA/SR (22) addressing mode and/or dose of exercise for OA (Table 1). One MA/SR of 48 RCT (4028 patients with pain data) (22) observed similar pain reduction for aerobic, resistance, and performance exercise (practicing a specific activity with the lower extremity); single-type exercise programs were more efficacious than programs that included different exercise types. The effect of aerobic exercise on pain relief increased with an increased number of supervised sessions; overall, more pain reduction occurred when supervised exercise was performed at least three times a week. The authors recommended supervised exercise three times a week, noting that such programs have a similar effect, regardless of patient characteristics, including radiographic disease severity and baseline pain.

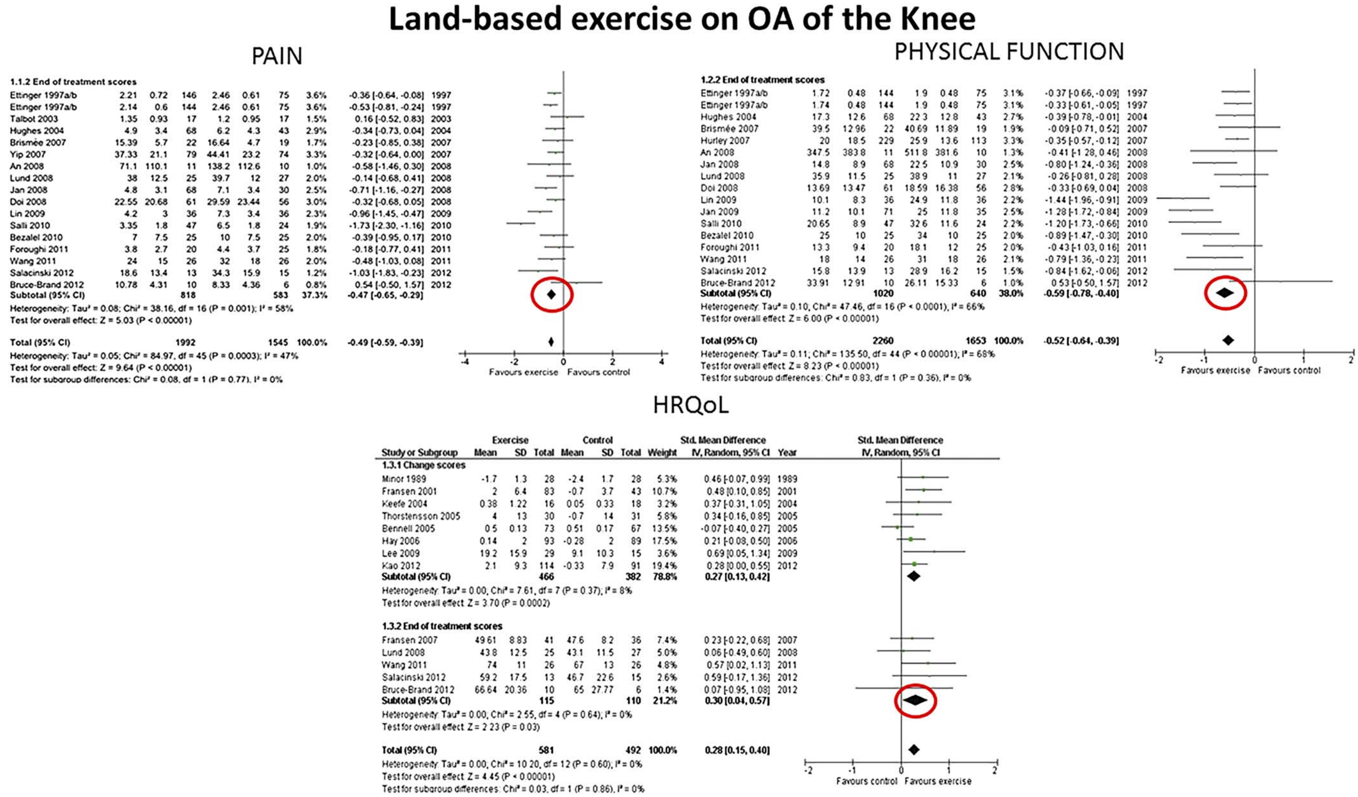

FIGURE 1—Effects of land-based exercise on pain, physical function and HRQoL in knee OA. Negative SMD represent improvements in pain and physical function (lower scores represent better pain and/or physical function) whereas positive SMD represent improvements in HRQoL (higher scores represent better HRQoL). Reproduced with permission from Fransen M, McConnell S, Harmer AR, et al. Exercise for osteoarthritis of the knee: a Cochrane systematic review. *Br J Sports Med.* 2015;49:1554–7. Copyright © 2015 BMJ Publishing Group Ltd.

Another SR, encompassing 45 trials (4699 participants), addressed mode and dose of exercise for knee OA (33). This review concluded that knee extensor strength significantly improved following American College of Sports Medicine (ACSM) recommendations (39) (described in Table 1 footer) versus all other types (i.e., any that did not deliver the intervention according to the ACSM recommendation) of strength training for older or sedentary patients. Although a dose–response association was identified between knee extensor strength gain and improvement in pain and physical function, there was no difference in pain and function outcomes comparing ACSM versus other types of exercise interventions.

A third SR, encompassing 24 trials (1747 participants), addressed dose of exercise for knee OA (34). Large differences among studies in the type, duration, and volume of exercise made it difficult to discern specific variables influencing the effects of treatment. A few generalizations based on self-reported pain and function were possible: 1) 24 or more total exercise sessions were most often related to large effect sizes (studies ranged from 3 to 108 sessions), 2) 8- and 12-wk exercise durations most often exhibited larger effect sizes (studies ranged from 4 to 36 wk), and 3) a frequency of one time per week exercise showed no effect.

A fourth MA/SR, encompassing 27 trials (3060 participants), addressed different modes of land-based exercise (recreational activities, walking or conditioning exercise consisting of a combination of strength training, flexibility, and aerobic interventions) (32). In contrast to studies lasting 12 months, walking and conditioning exercise lasting 6 months had a significant impact on physical function and/or physical performance (6-min walk test or timed stair climbing test) but not on pain. Conditioning exercise also had a moderate level of evidence for effectiveness on physical function in individuals with knee OA in both the short (6 months) and longer (18 months) terms. Adherence to the interventions is very likely to have an effect on the significance of the results.

Although not an MA or SR, and therefore not used in the PAGAC report, we found one original research article worth noting related to dose of exercise and function. In this study, Dunlop et al. (40) assessed the association of accelerometer measured physical activity and physical function in 1647 participants with lower-extremity symptoms in the OA Initiative (OAI) cohort. Moderate-to-vigorous physical activity (MVPA) was defined as greater than 2020 counts per minute corresponding to 3 METs or a level of exertion corresponding to a ~3.5 mph walk (41). Physical function based on measured (gait speed) and self-reported (SF-12) function was assessed 2 yr later. Improved or sustained high function was achieved by 34% of participants. Compared with participants performing ≤45 total minutes of MVPA per week (including bouts <10 min in duration), those performing >45 min·wk^{-1} were more likely to improve gait speed (relative risk [RR], 1.8;

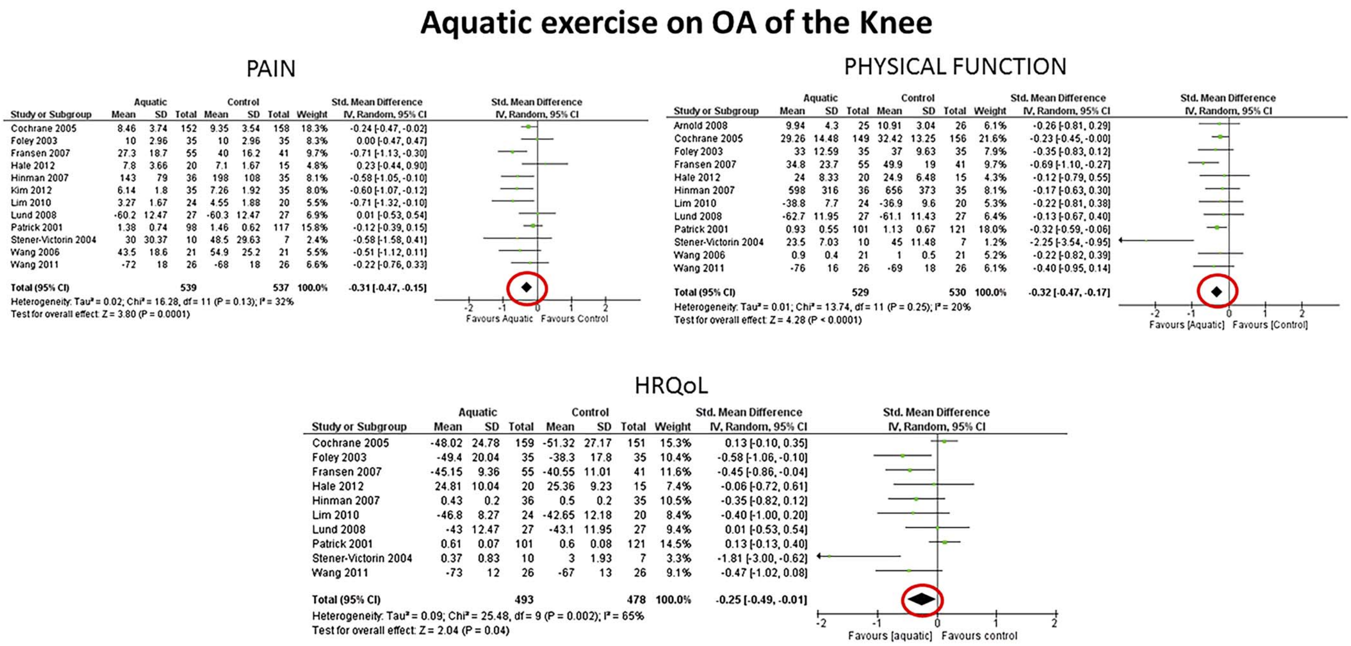

FIGURE 2—Effects of Aquatic Exercise on Pain, Physical Function and HRQoL in Knee OA. A multitude of measures were used in the included studies; standardized instruments used most often were WOMAC for pain and function and SF-36, SF-12 or SF-8 for physical function. Negative SMD represented improvements in pain, physical function and/or HRQoL (lower scores mean better pain, physical function and/or HRQoL). Reproduced with permission from Bartels EM, Juhl CB, Christensen R, et al. Aquatic exercise for the treatment of knee and hip osteoarthritis. *Cochrane Database Syst Rev.* 2016;3: CD005523. Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

95% confidence interval [CI], 1.6–2.1) and self-reported function (RR, 1.4; 95% CI, 1.3–1.6). Individuals performing or exceeding the 2008 Physical Activity Guidelines for Americans of >150 min·wk^{-1} of MVPA in bouts lasting ≥10 min also improved gait speed (RR, 1.4; 95% CI, 1.3–1.6) and self-reported function (RR, 1.3; 95% CI, 1.2–1.4). Results were consistent across varying knee OA severities. Thus, it is evident that important health improvements can be achieved even with levels of physical activity below those recommended by the 2008 Physical Activity Guidelines for Americans.

Demographic factors and weight status. Dunlop et al. (40) determined that the results for the intermediate level of physical activity (≥45 min·wk^{-1} moderate-vigorous activity) were consistent across sex, body mass index and age. However, effect modifications by sex, age, race/ethnicity and socioeconomic status were not addressed in any of the MA/SR identified for this umbrella review. Although a relationship between body mass index (BMI) and OA is generally well recognized (42), to our knowledge, there are no MA evaluating whether BMI modifies the physical activity–OA relationship.

OA Disease Progression as an Outcome

Existing SR and MA. A concern about the potential harm that high intensity and large amounts of weight-bearing exercise may cause for OA progression prompted a targeted review for this outcome.

We identified one SR/MA (29) that assessed the association of self-reported running or jogging (including running-related sports such as triathlon and orienteering) with knee OA onset or progression defined by any definition of diagnosed knee OA, radiographic or imaging markers of knee OA, knee arthroplasty for OA, knee pain and/or disability specifically associated with the knee (Table 2). Although this SR/MA included incident as well as progressive OA, the data are instructive for understanding the potential role of running in the development and/or progression of OA. With this evidence, the authors concluded that it was not possible to determine the role of running in knee OA. However, they noted that a key finding of their review was the result of their MA (2172 individuals) of three case-control studies (two of the three controlled for joint injury), which suggested that runners (running for 1 yr up to a lifetime) had around a 50% reduced odds of undergoing a total knee replacement for OA than nonrunners (pooled odds ratio, 0.46, $P = 0.0004$, Table 2). Evidence relating to symptomatic outcomes was sparse and inconclusive. Because retrospective case-control studies are subject to several types of bias, these data have to be interpreted with caution; these biases include recall and observer bias, bias related to choice of control groups, and selection bias. Selection bias could occur if individuals with joint symptoms or injury ceased their participation in physical activity and went on to eventual joint replacement; therefore, individuals with total knee replacement would be identified as having engaged in less physical activity leading to an apparent protective effect of physical activity on knee replacement.

We also identified one SR that included 49 studies (43) assessing the safety of physical activity in older adults with knee pain (summarized in Table 2). The SR (43) examined 49 longitudinal studies (comprising 48 RCT and one case

TABLE 2. Summary of included studies assessing the relationship of physical activity and OA progression in individuals with lower-extremity OA. (29,40,43–48).

Author (Year)	Type of Study, Joints, Mean Age and/or Range	Sample Size & Number of Studies	Type of Physical Activity	Outcome Measures	Measures of Association (95% CI)
Quicke (2015) (43)	SR, Knee, 45 yr or older	8920 participants from 49 studies 46 studies measured pain 43 measured physical function 3 measured TKR	Three months or more of physical activity intervention or exposure	OA Progression (structural OA biomarker imaging and TKR) between three and 30 months of physical activity intervention	There was no evidence of progression of structural OA by imaging or increased TKR at a group level (n = 8 TKR within the physically active groups compared to n = 10 TKR in the nonphysically active) The case control study concluded that increasing levels of regular physical activity was associated with lower risk of progression to TKR; OR, 0.91 (0.31 to 2.63) and OR, 0.56 (0.30 to 0.93) in men and women, respectively, with low cumulative hours of physical activity; OR, 0.35 (0.12 to 0.95) and OR, 0.56 (0.32 to 0.98) in men and women, respectively, with a high number of accumulative hours of physical activity
Timmins (2017) (29)	SR/MA, Knee, 28–69 yr	15 studies: 110 cohort and 4 case–control	Any form of running or jogging	OA Progression defined by one of the following outcomes and a minimum of 1 yr of running/jogging: 1. Any definition of diagnosed knee OA 2. Radiographic or imaging markers of knee OA 3. Knee arthroplasty for OA 4. Knee pain 5. Disability specifically associated with the knee	Findings of studies with a diagnostic OA outcome were mixed. Some radiographic differences were observed in runners, but only at baseline within some subgroups. MA suggested a protective effect of running against surgery due to OA: pooled OR, 0.46 (0.30 to 0.71)
Kwee (2016) (47)	ORes, Knee, 62.2 yr	100	Physical Activity Scale for the Elderly (PASE)	OA Progression was measured via cartilage damage progression in medial tibiofemoral compartment using 2-yr follow-up MRI in participants with denuded areas of subchondral bone (dAB) at the central weight-bearing medial femur (cMF) at baseline MRI examination	Standardized Regression Coefficient: Mean cMF.ThCtAB change: −0.15762 mm; cMF.dAB% change: 0.11479; MT.ThCtAB change: −0.08589; MT.dAB% change: 0.13846
Lin (2013) (48)	ORes, Knee, 52.8 yr	205 participants from the OAI without symptomatic or radiographic evidence of OA	Physical Activity Scale for the Elderly (PASE)	OA Progression was measured with MRI T2 relaxation time over a 4-yr period	T2 progression was increased in the highest tertile of physical activity compared to the mid-tertile at the medial tibia (P = 0.041), patella (P = 0.019), and average T2 of all knee compartments combined (P = 0.033). Participants with the lowest 15% PASE scores showed significantly higher T2 progression compared to the mid-level physical activity group at the lateral femur (P = 0.025), lateral tibia (P = 0.043), medial femur (P = 0.044), tibiofemoral compartment (P = 0.017), patellofemoral compartment (P = 0.016), lateral compartments (P = 0.003), and average of all compartments (P = 0.043)
Felson (2013) (45)	ORes, Knee, 61 yr	2,073 participants (3,542 knees)	Physical Activity Scale for the Elderly (PASE)	OA Progression was measuring with long limb radiographs. Participants were followed for 30 months (in MOST) and 48 months (in OAI), respectively, with at least one of the following incident outcomes: Symptomatic tibiofemoral OA (radiographic OA and knee pain) Tibiofemoral narrowing	Incident Tibiofemoral Symptomatic Knee OA: Lower 75%: OR, 1.0 Upper 25%: OR, 0.60 (0.03 to 1.3) Joint Space Loss: Lower 75%: OR, 1.0 Upper 25%: OR, 0.9 (0.05 to 1.5)
Oiestad (2015) (46)	ORes, Knee, 67 +/− 7.6 yr	1179 participants (2008 knees)	Steps/Day using a ccelerometer	OA Progression measured by radiographic and MRI assessment with a follow-up of 2 yr	Radiographic Worsening: <5859 steps per day: OR, 0.91 (0.64 to 1.27); 5859–7846 steps per day: OR, 1.0; >7846 steps per day: OR, 0.99 (0.69 to 1.42) Intensity minutes: OR, 1.01 (0.99 to 1.02); Lateral Cartilage Loss: <6078 steps per day: OR, 0.82 (0.45 to 1.51) 6078–7938 steps per day: OR, 1.0 >7938 steps per day; Medial Cartilage Loss: <6078 steps per day: OR, 1.37 (0.81 to 2.32); 6078–7938 steps per day: OR, 1.0; >7938 steps per day: 1.37 .80 to 2.33); MVPA minutes: OR, 0.99 (0.97 to 1.01)

Dore (2013) (44)	ORes, Knee, 51–81 yr	405 participants	Steps per day	OA Progression between objectively measured steps per day and knee structural change using MRI with approximately a 2.7-yr follow-up	≥10,000 steps per day increases BML: RR, 1.97 (1.19 to 3.27) ≥10,000 steps per day had a 1.52 times (1.05 to 2.20) greater risk of increasing meniscal pathology score, which increased to 2.49 (1.05 to 3.93) in those with adverse meniscal pathology at baseline. ≥10,000 steps per day was associated with a greater risk of increasing cartilage defect score in those with prevalent BML at baseline: RR, 1.36, (1.03 to 1.69) Steps per day was protective against volume loss in those with more baseline cartilage volume but led to increased cartilage loss in those with less baseline cartilage volume. (P = 0.046 for interaction)

TKR, total knee replacement; OR, odds ratio; ORes, original research; cMF.ThCtAB, mean cartilage thickness over total subchondral bone area at the central medial femur in mm; cMF. dAB%, % denuded area of subchondral bone (dAB) at the central medial femur; MT.ThCtAB, mean cartilage thickness over total subchondral bone area at the medial tibia in mm; MT.dAB%, % denuded area of subchondral bone (dAB) at the medial tibia; OAI, the Osteoarthritis Initiative cohort; BML, bone marrow lesion (MRI measure); SF-12, Short Form (12 item) Health Survey; PRO, patient-reported outcome;

control study) of 8614 total participants with knee pain and/or a diagnosis of knee OA ranging in radiographic severity from Kellgren and Lawrence (49) grades 1 to 4. All physical activity interventions were low-impact, most often combining muscle-strengthening, stretching, and aerobic elements for 3 to 30 wk. None of the primary literature studies in this SR dealt with hip OA. Comparing groups with greater amounts of low-impact physical activity to groups with the least amounts, this SR provided no evidence of serious adverse events defined as increased pain, decreased physical function, progression of structural OA on imaging or increased total knee replacement at a group level. In addition, although the total numbers were small and total follow-up brief, based on four RCT (985 participants), there were no more total knee replacements over a 2- to 24-month observation period within physical activity groups compared to non-physical activity groups (n = 8 vs n = 10 total knee replacements, respectively).

Original research. We identified five original research studies that examined the relationship between physical activity and disease progression (40,44–48) (Table 2); no additional studies were identified as part of the extended search for this summary. All studies were prospective cohort studies (published 2013 to 2016). The analytical sample size ranged from 100 (47) to 2073 (45); four were US studies (40,45–48), one Australian (44). Three studies used self-reported physical activity via the Physical Activity Scale for the Elderly (PASE) (45,47,48). Two studies had device-measured physical activity via accelerometer or pedometer (40,44,46). The five included studies determined OA progression based on change in radiographic imaging (34), change in MRI imaging (cartilage loss) (44,47,48) or both (46). Collectively, these five studies focused on one of three longitudinal cohort studies: the OAI (40,45,47,48), the Multicenter Osteoarthritis (MOST) study (34,35) and a longitudinal cohort study of 405 community dwelling adults from Australia (33). The OAI assessed physical activity with the PASE survey (34,36,37) and accelerometry (29); the MOST study and the Australian cohort assessed exposure by objective step count measures. Overall, the findings in these studies were mixed.

Three progression-related studies quantified physical activity with PASE at baseline and quantified OA progression by imaging (radiographic or MRI) outcomes. Kwee et al. (47) assessed 2-yr knee OA progression based on MRI of 100 participants in the OAI with symptomatic OA and baseline full-thickness cartilage defects of the knee; although OA progressed, there was no association of disease progression and levels of physical activity as measured by PASE (mean, 2-yr score 156; range, 42–334). Lin et al. (48) assessed 4-yr knee OA progression based on knee MRI (increasing T2 signal) of 205 asymptomatic individuals with (80%) and without (20%) risk factors for knee OA in the OAI. Greater OA progression was identified in the individuals with the 15% highest (score range, 242–368) and 15% lowest (score range, 31–120) PASE scores compared with the 70% mid-range (score range, 153–207) scores of the reference group. The moderate activity mid-range group consistently showed the lowest (best) T2 values at baseline and 48-month follow-up. This study supported a potential U-shaped relationship of physical activity and OA progression for individuals at high risk for radiographic OA (80% with risk factors) or who had radiographic OA (Kellgren Lawrence grade 1), although the overall proportion of this subset was not reported. Potential interactions of baseline MRI lesion severity and physical activity for OA progression were not evaluated. Felson et al. (45) assessed 30- to 48-month knee OA progression based on radiograph or symptoms of 2073 participants (3542 knees, 50% symptomatic) with or at high risk of knee OA; there was no relation of quartiles of PASE scores with any OA progression outcomes (radiographic joint space loss or incident symptomatic knee OA) and no difference by degree of knee malalignment. The upper quartile of PASE scores (median score 250 for women, 300 for men) corresponded to regular work with some walking, "walks outside the home 1–2 $h \cdot d^{-1}$ occasionally," light house or yard work in the prior 7 d but no extensive sports participation.

Two progression-related studies quantified physical activity with pedometers or accelerometers at baseline and quantified OA progression by imaging (radiographic or MRI) outcomes. Oiestad et al. (46) assessed 2-yr knee OA progression based on both knee radiographs (X-rays) and MRI (cartilage loss) of 1179 participants in the MOST study, at risk of or with mild knee OA with physical activity measured at baseline by accelerometer (steps). There were no significant associations between daily walking or more time spent walking at a moderate to vigorous intensity with radiographic worsening or cartilage loss. Dore et al. (44) assessed ~2.7-yr knee OA progression based on knee MRI (with four structural measures) of 405 Australian individuals (age, 50–80 yr) in a community-based sample with physical activity measured at baseline by pedometer. There was no association of steps and OA progression for individuals with baseline MRI joint pathology performing fewer than 10,000 steps per day. However, in the context of baseline joint pathology compared with the individuals performing fewer than 10,000 steps per day, there was greater OA progression (more meniscal pathology, more bone marrow lesions and/or lower cartilage volume by MRI) related to performing ≥10,000 steps per day (Fig. 3). Thus, the effect of physical activity was modified by baseline OA status. When steps were analyzed as a continuous variable, there was a significant association of steps and risk of progression of cartilage defects and bone marrow lesions; there was also an interaction of steps and baseline severity of OA for MRI-based cartilage volume and meniscal pathology. Taken together, these data support a potential J-shaped

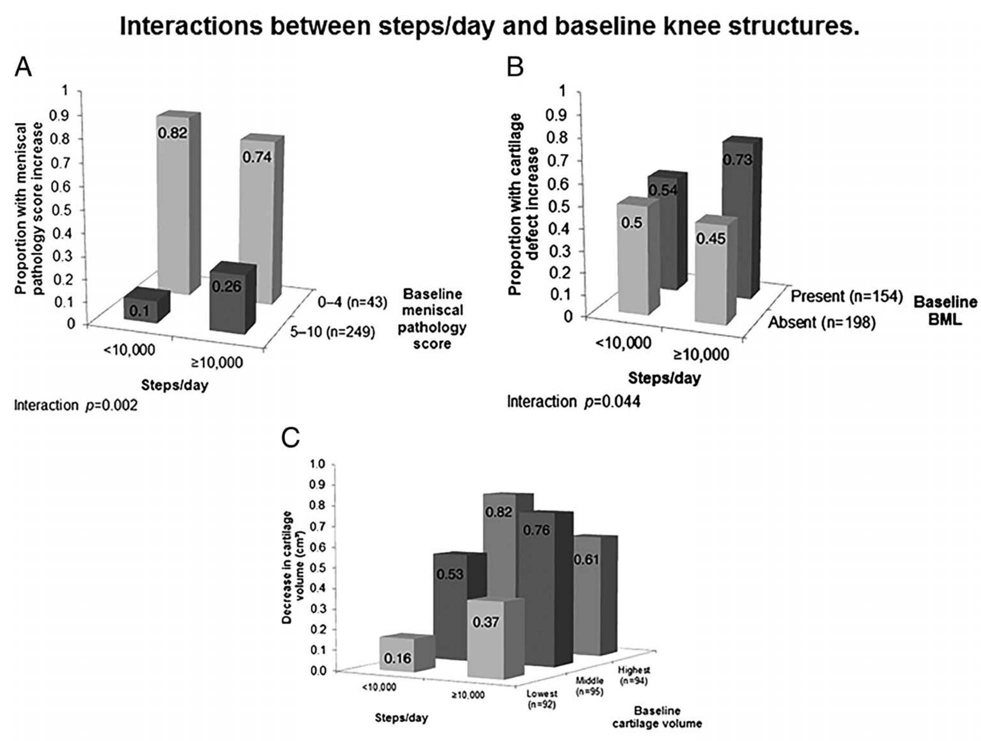

FIGURE 3—Interaction of underlying joint pathology by MRI and ambulatory physical activity amounts (step counts) on OA progression, as shown on MRI. Greater meniscal pathology scores, presence of BML and less cartilage volume all indicate more severe disease. BML are areas of increased signal adjacent to the subcortical bone at the medial tibial, medial femoral, lateral tibial, and lateral femoral sites and indicate more severe joint pathology. All figures show an interaction effect, wherein for those individuals with less baseline osteoarthritis pathology, steps are not related to pathology score increases. In contrast, in adults with greater baseline pathology scores, a greater percent of adults with more than 10,000 steps per day show worsening of pathology scores over time (26%) compared to adults with fewer than 10,000 steps per day (10%). BML, bone mineral lesions. Reproduced with permission from Doré DA, Winzenberg TM, Ding C, et al. The association between objectively measured physical activity and knee structural change using MRI. *Ann Rheum Dis.* 2013;72:1170–5. Copyright © 2013 BMJ Publishing Group Ltd.

relationship of physical activity and OA progression for those with preexisting OA.

DISCUSSION AND NEEDS FOR FUTURE RESEARCH

Over an entire week, as many as 40% of adults with lower-extremity joint conditions do not engage in even a single session of moderate physical activity lasting 10 min (40). However, as is clear from our review, regular exercise at amounts up to those consistent with the 2008 Physical Activity Guidelines for Americans—150 $\mathrm{min \cdot wk^{-1}}$ of moderate-intensity aerobic exercise, 2 $\mathrm{d \cdot wk^{-1}}$ of muscle-strengthening exercise—has a substantial beneficial impact on health of individuals with preexisting knee and hip OA. The evidence suggests that up to 10,000 steps per day of activity does not accelerate OA progression in individuals with preexisting OA. Land-based exercise appears to be as efficacious as water-based exercise for these outcomes. Benefits related to pain relief, physical function, and HRQoL appear to be applicable for aerobic exercise, muscle-strengthening exercise, and Tai Chi. Although not tested head to head, effect sizes for joint pain reduction by physical activity are comparable to those reported for analgesics (20). Although this review did not identify any MA/SR related to risk of comorbid conditions, a recent large cohort study (16,362 individuals age ≥55 yr; median, 13.5 yr follow-up) demonstrated that the presence and burden of radiographic hip and/or knee OA was significantly associated with increased risk (16%–25%) for incident diabetes (controlled for confounders) with 37% to 46% of this relationship explained by baseline limitations in walking (50). This excellent study begins to address the important question of physical activity and comorbidities in OA and underscores the necessity of further studies to determine means of counteracting the incidence or reversing established serious comorbidities, such as diabetes, in individuals with OA. A summary of the overall conclusions and grade of the evidence, based on a consensus of the 2018 PAGAC, are provided in Table 3.

There are a number of barriers to physical activity for individuals with OA. For people with lower-extremity joint symptoms, even 10-min bouts of activity can be a challenge. Moreover, greater knee pain and BMI can both contribute to poorer compliance with exercise (51). One study suggested a potential U-shaped, and another a J-shaped, dose–response relationship of physical activity with OA progression (40,44,48). Interestingly, this U-shaped dose–response relationship is supported by an MA of exercise studies in healthy animals (52).

Evidence addressing some of the barriers to physical activity for individuals with joint disease are provided by Dunlop et al. (40) where an intermediate level of accumulated physical activity—minimum of 45 $\mathrm{min \cdot wk^{-1}}$ of at least moderate intensity, irrespective of bouts—benefited function of individuals with lower-extremity OA. Given the ready accessibility to the general public of mobile health devices—including individuals with arthritis—it is useful for patients and arthritis health-related professionals to understand what is known about the relation of step counts to health outcomes in those with OA. The goal of 150 $\mathrm{min \cdot wk^{-1}}$ of MVPA (walking at least 3.3 mph) equates to ~2500 steps per day whereas the goal of 45 $\mathrm{min \cdot wk^{-1}}$ of MVPA corresponds to ~750 steps per day. Considering a background of daily activity of 5000 steps per day (53), a computed translation of these recommendations yields estimates of a total of ~7500 steps per day (corresponding to a ‘somewhat active’ lifestyle (54)), and ~5750 steps per day (also considered a ‘somewhat active’ lifestyle (54)), respectively. It is possible that background daily activity in some individuals with OA does not exceed basal activity levels of 2500 steps per day (54); under these circumstances, the corresponding minimal estimates of activity would be a total of ~5000 steps per day and ~3250 steps per day (considered a “sedentary” lifestyle). Interestingly, all these goals fall within the apparent safe range for individuals with more severe lower limb OA of less than 10,000 steps per day. In a large (n = 4840) community-based sample, benefits are similar for both bouted and nonbouted physical activity (55,56). Moreover, a marked mortality benefit accrues from as little as 40–80 $\mathrm{min \cdot d^{-1}}$ of moderate activity (56) defined as a threshold of 760 counts per minute using a waist-worn accelerometer—roughly equivalent to the level of exertion of activities of daily living. Taken together, these new insights provide encouraging news for individuals with OA for whom nonbouted activity and intermediate levels of activity below US guideline amounts are likely to be beneficial and more readily achieved on a regular basis.

Although umbrella reviews represent one of the highest levels of evidence synthesis currently available, they are subject to several limitations including: incomplete stratification of the evidence due to residual overlap within the included MA/SR; heterogeneity of exposures making it difficult to determine the exact relationships of physical activity and outcomes; and heterogeneity of studied populations potentially limiting the generalizability of results. In addition, this review was limited by the lack of studies related to HRQoL and OA progression and a lack of uniform definitions of OA—a current challenge to the OA research field as a whole. As a strength, this review has yielded insights into knowledge gaps that led us to formulate the recommendations described below for future research.

1. Conduct additional research to assess effect sizes of physical activity on OA to determine the clinical impact exercise may have on particular outcomes.
   Rationale: There is a particular need to conduct prospective longer-term RCT of physical activity to evaluate OA disease progression, with objective quantification of physical activity exposures with molecular and imaging disease status biomarkers as outcomes. In addition, more data are needed to address the critical issues of varying amounts and intensities of physical activity and their relationship to incidence and progression of OA (tibiofemoral and patellofemoral) in the absence of underlying injury. Because it often takes years for disease activity to result in

TABLE 3. PAGAC recommendations.

Research Questions	Evidence Grade[a]
Amounts of physical activity and comorbidities in individuals with OA	Not assignable
Amounts of physical activity and decreased pain and improved physical function in adults with OA of the knee and hip	Strong (evidence is unlikely to be modified by more studies for these outcomes)
Amounts of physical activity and improved HRQoL in persons with OA of the knee and hip	Moderate
Relationships vary by age, sex, race, ethnicity, socioeconomic status, or body mass index	Not assignable
Dose–response relationship between physical activity and improved pain, physical function and HRQoL in individuals with OA	Not assignable
Intensity or duration of aerobic and muscle-strengthening physical activity is related to improvement in pain and functional capacity in individuals with OA of the knee and hip	Limited
Dose–response relationship between physical activity and disease progression in individuals with OA	Moderate for safety (the relationship appears to be U-shaped; up to the range of 10,000 steps per day, ambulatory physical activity does not accelerate OA of the knee); Limited for adverse effects (range of more than 10,000 steps per day may have an adverse effect on progression of OA of the knee in individuals with existing OA of the knee)

[a]The 5 grading criteria serving as the determinants of the final Evidence Grade are described in Torres 2018 (Table 1); in brief they were 1) applicability, 2) generalizability (to the US population of interest), 3) risk of bias or study limitations (as determined by NEL BAT and/or AMSTARExBP), 4) quantity and consistency (of the results across the available studies), and 5) magnitude and precision of effect.

structural, detectable radiographic changes in the joint, sophisticated imaging modalities, such as MRI, and biological biomarkers of disease activity (circulating systemic or intra-articular) are needed to measure the outcomes. Recently (after the timeframe of the searches for this review), the first MA of synovial fluid, serum, and urine biomarkers in individuals with established knee OA was published (57). It concluded that 4 to 24 wk of exercise therapy (strengthening and or aerobic) was not harmful as it did not increase the concentration of molecular biomarkers related to inflammation and cartilage turnover, associated with cartilage breakdown. The overall quality of evidence was graded as low because of the limited number of RCT available underscoring the need for more biomarker research in this field.

2. Conduct research to clarify how OA progression is modified by baseline demographic and disease characteristics as well as pain responses to exercise.
   Rationale: For the outcome of disease progression induced by physical activity, some evidence suggests that baseline disease status plays a role in modifying the effect of physical activity; but this role has not yet been fully explained. In addition, although a relationship between BMI and OA is generally recognized, no studies have investigated through MA whether BMI modifies the physical activity–OA relationship. More studies on OA progression need to evaluate groups of individuals with clear evidence of OA (defined biochemically, by MRI or radiograph) at baseline as well as those "at risk" of OA.

3. Conduct direct head-to-head comparisons of the relative effectiveness of physical activity and analgesics for pain control in individuals with OA.
   Rationale: Our review of the literature revealed that the effect sizes for pain control from exercise interventions is very similar to that of analgesics, including narcotic analgesics (20). If true, this would be a critical observation with profound implications for patient care, especially as the effects of physical activity on OA-related pain seem to be durable for up to 6 months following cessation of an intervention. Determining the comparative effects of physical activity and analgesics on OA pain could contribute greatly to effective clinical management of OA and potentially to greater third-party payment of exercise treatments for OA.

4. Conduct research to determine the optimal physical activity dose, mode, intensity, duration and frequency to optimize efficacy and sustainability of physical activity for different types and severity of OA.
   Rationale: Different modalities or amounts of physical activity (using the same modality) have not been compared head-to-head to ascertain their relative effects on OA progression, as well as pain, physical function, and HRQoL. Dose–response investigations on the relationship of daily step counts and other device-based measures of physical activity and OA disease progression are particularly needed. Given that varying pain intensities and structural severities of OA have been associated with reduced compliance with exercise therapy, it is important to develop approaches to personalize physical activity prescriptions for individuals with OA to minimize discontinuation due to exacerbation of symptoms and/or disease progression.

5. Determine the capacity of individuals with OA to perform physical activity at intensities and amounts of exercise that are able to modify comorbidities.
   Rationale: Obesity is a risk factor for OA incidence and progression. Obesity is also a significant risk factor for OA-related comorbidities, including diabetes, cardiovascular disease, and cancer. However, few to no data address the relationships of physical activity and modification of OA-related comorbidities and mortality in those with OA. New longitudinal cohort studies, facilitated by device-based measures of physical activity, will be required to adequately address this question. In addition, more data are needed to determine whether those with advanced OA can safely exercise at intensities or amounts that are able to modify the risk of developing disease comorbidities without subjecting themselves to a greater risk of disease progression.

6. Develop biomarkers of exercise responsiveness and trajectories for different types and severity of OA, to determine who is likely to respond favorably to physical activity interventions versus who is at risk of disease progression.
   Rationale: As for many human conditions and physiologic states, even when controlling for possible effect modifiers, individuals with different OA characteristics (pain, physical function, HRQoL, and disease structural severity) demonstrate a range of individual responses to the same exercise exposure. Developing technologies (such as biomarkers) and approaches to better understand the demographic, physiologic, and molecular basis of disease will be valuable for predicting and monitoring responses to exercise and thereby for developing the best exercise regimen to elicit specific responses at the individual level.

CONCLUSIONS

Physical activity decreases pain, improves physical function and HRQoL among people with hip and/or knee OA relative to less active adults with OA. Given the strength of the evidence (261 studies of various physical activity modes of exposure including land and pool, aerobic, resistance and flexibility), it is highly unlikely that the conclusions will be modified by more RCT for these outcomes. There is currently no evidence to suggest accelerated progression of OA in individuals with preexisting joint pathology for physical activity below 10,000 steps per day. A total of at least 45 $\text{min}\cdot\text{wk}^{-1}$ of MVPA can improve or sustain function of individuals with lower-extremity OA. Thus, people with lower-extremity OA should be encouraged to engage in achievable amounts of physical activity, of even modest intensities, accrued throughout the entire day, irrespective of bouts, and be confident of gaining some health and arthritis-related benefits.

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PRONOUNCEMENT

Physical Activity Promotion: Highlights from the 2018 Physical Activity Guidelines Advisory Committee Systematic Review

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ABSTRACT

KING, A. C., M. C. WHITT-GLOVER, D. X. MARQUEZ, M. P. BUMAN, M. A. NAPOLITANO, J. JAKICIC, J. E. FULTON, and B. L. TENNANT, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE. Physical Activity Promotion: Highlights from the 2018 Physical Activity Guidelines Advisory Committee Systematic Review. *Med. Sci. Sports Exerc.*, Vol. 51, No. 6, pp. 1340–1353, 2019. **Purpose:** This article describes effective interventions to promote regular physical activity and reduce sedentary behavior that were identified as part of the *2018 Physical Activity Guidelines Advisory Committee Scientific Report.* **Methods:** A comprehensive literature search was conducted of eligible systematic reviews, meta-analyses, and relevant governmental reports published between 2011 and 2016. For the physical activity promotion question, articles were first sorted by four social ecological levels of impact (i.e., individual, community, communication environment, and physical environment and policy levels) and then further sorted into more specific categories that emerged during the review process. For the sedentary behavior reduction question, the literature was sorted directly into emergent categories (i.e., youth, adult, and worksite interventions). **Results:** Effective physical activity promotion strategies were identified at each level of impact, including those based on behavior change theories and those occurring at different settings throughout the community. Effective interventions also included those delivered in person by trained staff or peer volunteers and through different information and communication technologies, such as by phone, Web or Internet, and computer-tailored print. A range of built environment features were associated with more transit-based and recreational physical activity in children and adults. Effective sedentary reduction interventions were found for youth and in the workplace. **Conclusions:** A promising number of interventions with demonstrated effectiveness were identified. Future recommendations for research include investigating the most useful methods for disseminating them to real-world settings; incorporating more diverse population subgroups, including vulnerable and underrepresented subgroups; collecting

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cost data to inform cost-effectiveness comparisons; and testing strategies across different levels of impact to determine which combinations achieve the greatest effects on different modes of physical activity across the week. **Key Words:** PHYSICAL ACTIVITY, INTERVENTION, SYSTEMATIC REVIEW, SOCIAL ECOLOGICAL MODEL, PAGAC

Other articles in this issue describe a broad spectrum of evidence-based health benefits associated with regular physical activity and lower levels of sedentary behavior over the life course. The evidence clearly shows that physical activity provides a wide array of benefits—from reducing feelings of anxiety and depression and improving sleep and quality of life to lowering the risk of developing diabetes, heart disease, and many cancers. A large proportion of Americans, however, are not receiving the substantial benefits a physically active lifestyle can offer. In 2015, only about one half of US adults and one quarter of high school students and children in the United States reported meeting the age-specific federal guidelines for aerobic physical activity (1–3). Nearly one third of adults and one quarter of older adults (65+ yr of age) reported being inactive during their leisure time (1,4). These findings reflect the large burden of physical inactivity in the United States, which has been reported to be even higher when device-based measurement has been used (5). Furthermore, a large burden is found in a growing number of countries throughout the world (6). For individuals who are not yet participating in regular physical activity, there are a number of effective intervention strategies that individuals and communities can use to increase physical activity and reduce sedentary behavior.

The major goal of this article is to highlight the current evidence-based strategies and approaches for increasing regular physical activity and reducing sedentary behavior. This area was deemed of particular interest for the 2018 Physical Activity Guidelines Advisory Committee given it was not reviewed as part of the *2008 Physical Activity Guidelines Advisory Committee Report* (7). In light of the variety of intervention strategies and approaches used, the evidence for the current review was organized by level of impact using an adapted version of a social ecological framework (8) (see Fig. 1). Using this framework, the evidence was divided into four broad levels—individual, community, the communication environment (i.e., interventions delivered through information and communication technologies [ICT]), and physical environments and policy. The potential public health impacts of the described intervention strategies and approaches are also discussed, along with recommendations for future research and practice in physical activity promotion. Because the aim of the *2018 Physical Activity Guidelines Advisory Committee Report* was to evaluate the physical activity evidence as it pertains to *population health,* intervention-based clinical health impacts/clinical meaningfulness were not evaluated. Additionally, such clinical health impacts typically were not the focus of the reviews that were part of the evidence search.

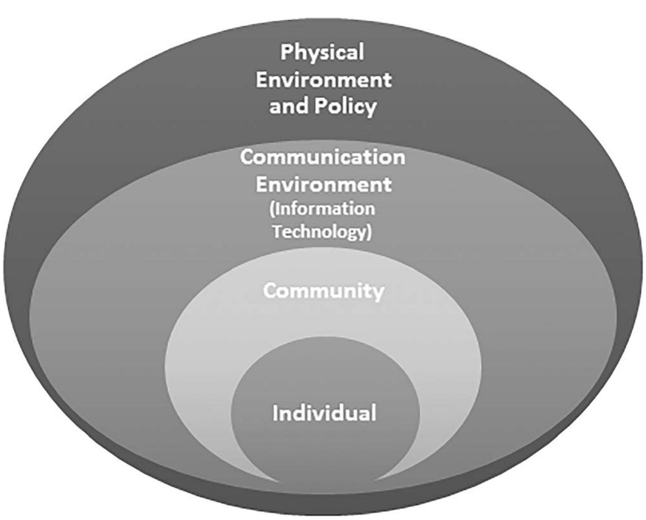

FIGURE 1—Social ecological framework.

METHODS

Questions of interest. The Physical Activity Promotion Subcommittee of the Physical Activity Guidelines Advisory Committee focused on two central questions to examine in the physical activity intervention area, as follows: 1) What interventions are effective for increasing physical activity at different levels of impact? 2) What interventions are effective for reducing sedentary behavior? The Committee also sought to determine whether intervention effectiveness varied by age, sex, race/ethnicity, or socioeconomic status, when such information was available. Thus, the Subcommittee charge was to identify those intervention areas for which effective interventions were available, as opposed to searching for any intervention areas for which the evidence did not support effectiveness.

Evidence review process. The evidence review process and methods are fully detailed in the *2018 Physical Activity Guidelines Advisory Committee Report* (9), and will be briefly described here. The protocol-driven methodology applied was aimed at minimizing bias and maximizing the identification of relevant and high-quality systematic reviews (10). Due to the size of the physical activity promotion evidence base, which spans at least six decades, includes review articles from both the US and non-US regions, and was not formally reviewed in developing the original 2008 US Physical Activity Guidelines (11), the focus of the evidence review was limited, due to pragmatic considerations, to systematic reviews, meta-analyses, and relevant governmental reports published from 2011 through 2016 and deemed of sufficient quality based on the Physical Activity Guidelines Advisory Committee's eligibility criteria (9). These criteria included publication language (English), publication status (i.e., peer-reviewed, high-quality report), research type (i.e., systematic review, meta-analysis, pooled analysis, relevant report), and study subjects (human) (10). Evidence sources published before or after the 2011 to 2016 period were unable to be included, and thus are not represented in the *2018*

Physical Activity Guidelines Advisory Committee Report. Although it is possible that reviewing additional literature through the beginning of 2018 could provide further insights, the nature of the evidence being accumulated in this field makes it less likely than other fields that the current evidence evaluation would have substantively changed. This is because of the broad heterogeneity of the physical activity promotion literature across a variety of factors (e.g., target populations, study designs and methods, physical activity types, intervention content, length and delivery channels). This, in turn, makes it less likely that any one additional study or review would be sufficiently rigorous and comprehensive to substantially change the evidence grades during that additional 16-month period. This point notwithstanding, the constrained period remains a limitation of the review process.

Additionally, studies included within the articles being evaluated typically reflected a mix of physical activity measures (i.e., self-report, device-based assessment), the types of primarily aerobic forms of physical activity being targeted (e.g., walking, moderate-to-vigorous forms of physical activity, aerobic activities combined with strengthening activities), and outcomes (e.g., total volume of activity, duration and/or frequency of moderate-to-vigorous activity, percentage of participants meeting guidelines). The review articles generally did not look at associations between specific types of physical activity measures and intervention outcomes, or how different types of physical activity outcomes were affected.

For efficiency, one comprehensive search was conducted which included global key word terms for both physical activity promotion and sedentary behavior reduction (see Fig. 2). Relevant review articles for each field were then sorted to specifically address each question of interest. For each question of interest (i.e., physical activity promotion, sedentary behavior reduction), eligible articles were next sorted into more specific categories (i.e., topic areas) that emerged as part of the review process. For the physical activity promotion question, articles were first sorted by the four social ecological levels of impact described earlier, and then further grouped into specific categories that emerged in examining each article (e.g., at the Community level, seven categories emerged). In light of the smaller overall evidence base available for the sedentary behavior reduction question, that literature was grouped directly in emergent clusters (as opposed to by level of impact) of youth, adult, and worksite interventions.

When available, information was abstracted from the reviews for between- and within-group comparisons, the magnitude of effect, type and amount of physical activity, and physical activity intensity and frequency. For most systematic reviews, which constituted the majority of articles evaluated, such information, including effect size estimates, was often inadequately described

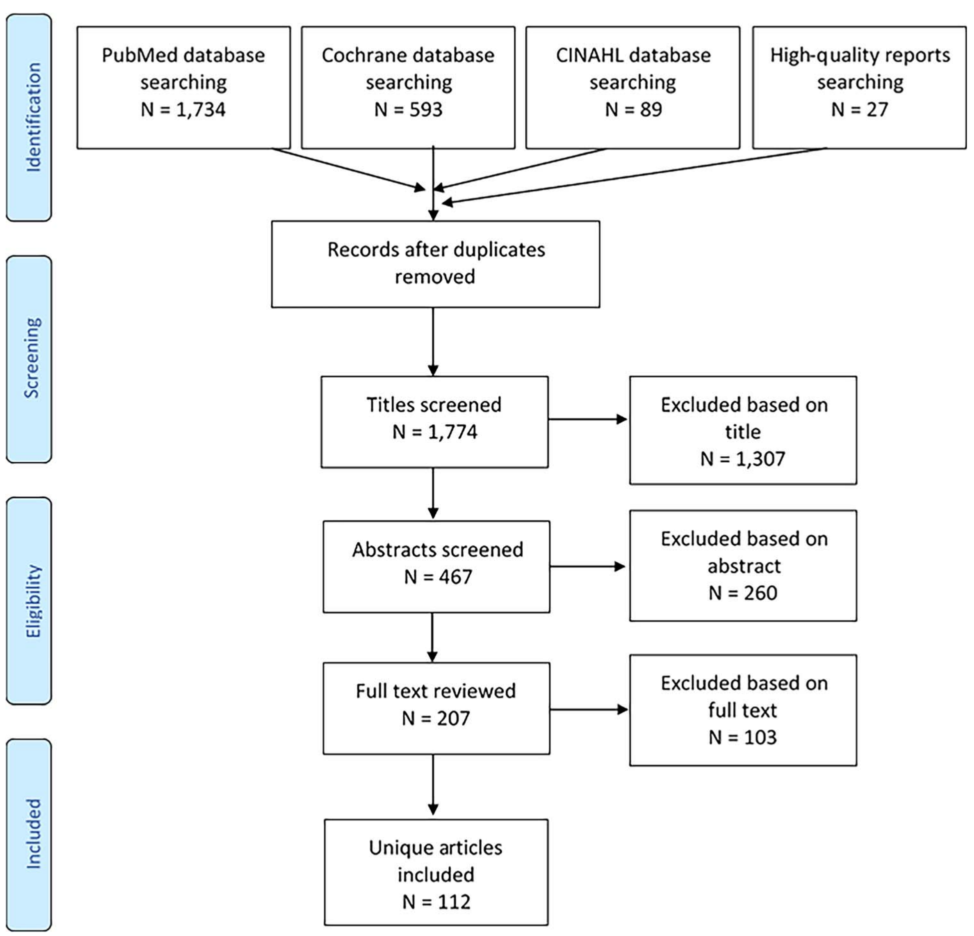

FIGURE 2—Evidence review flowchart.

or missing. When effect size estimates were available, we included them in the findings of this article. A standard evidence-grading rubric was utilized across all Committee topic areas which consisted of evidence grades of strong, moderate, limited, and grade not assignable (9). The collective scientific expertise of the Committee members was utilized in making final determinations with respect to applying the rubric in arriving at evidence grades, commensurate with the formal charge of the Committee. The Physical Activity Promotion Subcommittee assigned evidence grades of "Strong" or "Moderate" when the body of systematic evidence was reasonably large (e.g., typically more than one rigorous systematic review or a published meta-analysis, with articles usually including more than 10 studies) and indicated a consistent effect across rigorously designed studies (e.g., experiments). "Strong" was distinguished from "Moderate" based on the larger pool of more rigorously designed studies available (e.g., experimental designs) and typically longer intervention periods (e.g., greater than 6 months) (9). Because both strong and moderate evidence grades reflect sufficiently consistent bodies of literature supporting the use and deployment of the interventions involved, they constitute the focus of this article.

RESULTS

Number of Articles Included in the Review

For both questions, a total of 1778 eligible systematic reviews, meta-analyses, and governmental reports (all referred to as "articles" in this article) were evaluated for relevance in addressing questions 1 and 2. Of this total, 96 articles were deemed relevant to address question 1 related to physical activity promotion, and 18 articles were deemed relevant to address question 2 related to sedentary behavior reduction.

Results of the Evidence Review: Interventions to Promote Physical Activity

Categories for which consistent strong or moderate evidence support was found for physical activity intervention effectiveness are provided in Table 1 and described briefly below by levels of impact. Promising, but currently understudied, strategies within each level are listed within each level of impact but, due to space constraints, are not described in detail. The "Online-Only Supplementary Material" included in the *2018 Physical Activity Guidelines Advisory Committee Report* contains detailed information about all articles that were considered by the Committee.

Individual-Level Strategies and Approaches

Much of the original physical activity promotion literature dating back to the mid-twentieth century has been comprised of individual-level interventions consisting of person-to-person or small group-based programs. The literature evaluated as part of the 2011 to 2016 comprehensive evidence review resulted in five individual-level intervention categories, with four of those categories containing a sufficiently consistent and rigorous evidence base to be highlighted here. The fifth category, interventions for postnatal women, was identified as an area with limited evidence from systematic reviews and meta-analyses that warranted further study.

Application of behavioral theories and models to inform interventions. The current evidence base supports the application of behavioral theories and models (e.g., Social Cognitive Theory, the Transtheoretical Model, Theory of Planned Behavior, Self-Determination Theory) and strategies drawn from such theories in developing effective programs at the individual level as well as at other levels of impact (9). For example, a meta-analysis of 82 randomized controlled trials (RCT) of theory-based interventions in more general adult populations reported an overall average effect size of 0.31 (95% confidence interval [CI], 0.24–0.37) relative to controls (34). Among the most commonly reported behavior change techniques associated with physical activity change were self-monitoring of behavior and intention formation. Several techniques within theory-based behavioral interventions were identified as areas warranting additional study, including providing rewards (conditional and unconditional) for exercise session attendance and understanding the effects of achieving physical activity goals across a variety of age groups.

Interventions specific to youth and older adults. Notably, the evidence base at the individual level has expanded well beyond the general adult populations constituting the early targets of intervention to important population subgroups, including youth and older adults. Robust evidence exists for individual-level interventions aimed specifically at youth (9). Effective programs often have included in-person education and experiential activities (i.e., exercise classes), which can be enhanced through incorporating the family as part of the intervention (14). Examples of such interventions include in-person and Web-based education, hands on experiential activities (e.g., supervised exercise, dance, or sports and recreational activities), and replacing sedentary behaviors with increased physical activity (14).

Interventions aimed specifically at older adults have been shown to be effective in promoting increased physical activity across intervention periods of a year or more (9). Among the types of strategies that have been reported to be effective among older adult samples are individual or group-based advice and counseling, problem-solving around barriers to physical activity, social support, modeling and similar demonstrations of the physical activities being targeted, and use of rewards linked to behavior change (13).

Extending the Reach of Individual-Level Interventions—Peer-Led Interventions

While in-person individual-level approaches provide a flexible means for tailoring programs to the needs of each person, they often require a level of staff time and support that can be costly and/or infeasible to deliver to larger groups of people or in certain contexts (e.g., under-resourced communities). The growth of information and communication technologies

TABLE 1. Strategies and approaches with evidence of effectiveness for the general population and selected populations.[a]

Category	Intervention Approaches	Evidence Type (Number of Studies)	Selected Effect Sizes[b]
Physical activity promotion interventions			
Individual			
Behavior change theories and models	Behavior change theories and techniques (general adult as well as more specific populations)	1 SR (12) 1 MA (11)	One meta-analysis reported a positive effect of providing lottery and escalating incentives on exercise session attendance when compared with no incentive for short-duration interventions lasting 4 to 26 wk; pooled results showed an increase in exercise attendance of 11.55%; 95% CI, 5.61%–17.50% (12).
Interventions specific to older adults	Effective strategies include identifying & problem-solving around age-specific PA barriers, social support, modeling of PA behaviors, rewards linked with PA behavior change	2 SR (158 and 18) 1 MA (24)	Interventions had a small effect on physical activity d = 0.14 (95% CI, 0.09–0.20, P < 0.001) (13).
Interventions specific to youth	Effective strategies include in-person education & experiential strategies (e.g., exercise classes) Above can be enhanced through family inclusion	2 MA (47 and 58)	1. Significant effect sizes for interventions targeting individuals only (g = 0.27; 95% CI, 0.12–0.42), which were further enhanced when individual interventions also included families (g = 0.44; 95% CI, 0.23–0.66) or school and print or digital media (e.g., newspaper, radio; g = 0.30; 95% CI, 0.04–0.57) (14). 2. Family-based physical activity interventions found a small but significant effect size favoring the intervention group (SMD, 0.41; 95% CI, 0.15–0.67) (15).
Peer-Led	Peer-led behavioral self-management interventions (older adults and individuals with chronic disease)	1 MA (21)	Moderate effects for increases in physical activity overall among the 17 studies where effects sizes were available (SMD, 0.4; 95% CI, 0.22–0.55, P < 0.001) (16).
Community			
Community-wide	Community-wide interventions that use intensive contact with the majority of the target population	2 SR (16 and 33) 1 MA (10) PAGMR	Effect sizes not mentioned in PAGAC chapter.
School interventions	Multiple-component programs occurring during school hours aimed at physical activity across the school day in primary school-age (typically ages 5 to 12 yr) and adolescent youth Revising the structure of physical education (PE) classes to increase in-PE physical activity in primary school-age and adolescent youth	5 SR (range, 8–129) 2 MA (13 and 15) AHA PAGMR	1. CATCH and SPARK trials: Results showed that vigorous physical activity was significantly higher among intervention students (mean (M) = 58.6 min) compared to controls (M = 46.5 min) (P < 0.003) (17). Students spent more minutes per week being physically active in teacher- and specialist-led classes compared to controls (33 min, 40 min, and 18 min, respectively, P < 0.001), although PA did not increase outside of school (18). 2. Absolute difference of 10.37% (95% CI, 6.33–14.41) of lesson time spent in moderate-to-vigorous physical activity in favor of the interventions over controls. This estimated difference of 10.37% of lesson time corresponds to 24% more active learning time in the intervention groups compared with the control condition (SMD, 0.62; 95% CI, 0.39–0.84) (19).
Communication environment (information and communication technologies)			
Wearable activity monitors	Wearable activity monitors, including step counters (pedometers) and accelerometers, when used in conjunction with goal-setting and other behavioral strategies (general population of adults and those with type 2 diabetes or with overweight or obesity)	4 SR (range: 5–14) 3 MA (11 for each)	1. Accelerometry interventions across 12 trials resulted in a small but significant increase in physical activity levels (SMD, 0.26; 95% CI, 0.04–0.49). The additional benefit of activity monitors when compared with an active comparison arm (e.g., a physical activity intervention without activity monitors) is less clear (SMD, 0.17; 97% CI, −1.09 to 1.43) (20). 3. Type 2 diabetes: step-counter use significantly increased physical activity by a mean of 1822 steps per day (7 studies, 861 participants; 95% CI, 751–2894 steps per day). use of a step-counter in combination with setting a specific physical activity goal resulted in significantly more steps per day compared to control arms (weighted mean difference (WMD) of 3200 steps per day; 95% CI, 2053–4347 steps per day), whereas step-counter use without a goal did not significantly increase physical activity relative to control arms (WMD of 598 steps per day; 95% CI, −65 to 1260 steps per day). Use of a step diary or log also was related to a statistically significant increase in physical activity (WMD = 2816 steps per day), whereas when a step diary was not used, physical activity did not increase significantly (WMD = 115 steps per day) (21).

			4. Overweight/Obesity: a significant positive intervention effect for steps per day was found for behavioral physical activity interventions that included an activity monitor when compared with waitlist or usual care interventions (n = 4) (SMD, 0.90; 95% CI, 0.61–1.19, P < 0.0001). A similar intervention comparison also found a significant positive effect for total moderate-to-vigorous physical activity minutes per time unit (n = 3) (SMD, 0.50; 95% CI, 0.11–0.88, P = 0.01). In a meta-analysis of a similar intervention comparison (i.e., the addition of an activity monitor to an existing intervention versus when it was not added) using the mean difference for walking MET-minutes per week as the outcome and involving only two studies (both of which included women only), a statistically significant positive effect was found (mean difference for walking MET-minutes per week = 282; 95% CI, 103.82–460.18, P = 0.002) (22).
Telephone-assisted interventions	Telephone-assisted interventions (general adult population, including older adults)	2 SR (11 and 27)	Effect sizes not mentioned in the PAGAC chapter. "The majority of high-quality studies in this area produced effect sizes indicating a moderate or better intervention effect (i.e., d > 0.5). The evidence indicates that longer-duration interventions (i.e., 12 months or more) are associated with greater effectiveness."
Web-based or Internet-delivered interventions	Internet-delivered interventions that include educational components (general adult population)	3 SR (range: 7–15) 1 MA (34)	1. Overall effect size estimates indicate a small but positive intervention effect on physical activity in the general adult population (d = 0.14). Studies that initially screened participants and enrolled only those classified as sedentary or insufficiently active produced larger effects (d = 0.37) relative to studies that did not screen participants for physical activity level (d = 0.12). The meta-analysis, which targeted either physical activity only (n = 21) or physical activity and additional health-related behaviors, such as nutrition or weight management behaviors (n = 13), found that the two different types of interventions produced similar effect sizes (23). 2. In a systematic review of nine web-based physical activity interventions in individuals with type 2 diabetes, six studies reported significant short-term increases (less than 6 months, typically) in physical activity when compared with a control arm. The overall magnitude of the physical activity increases reported in this review ranged from 3% to 125% (24). 3. In a systematic review of seven self-guided web-based physical activity intervention trials among patients with a range of chronic disease conditions (e.g., multiple sclerosis, heart failure, type 2 diabetes mellitus, physical disabilities, metabolic syndrome), three studies reported significant physical activity improvements relative to controls, while four studies reported nonsignificant differences between groups. Effect sizes ranged from 0.13 to 0.56, with wide variability in physical activity change across studies (25).
Computer-tailored print interventions	Computer-tailored print interventions that collect user information through mailed surveys that is then used to generate computer-tailored mailings containing personalized physical activity advice and support (general adult population)	2 SR (11 and 26)	The majority of studies in this area produced effect sizes that were small (i.e., Cohen's d ranging from 0.12 to 0.35) when compared to minimal or no-intervention control arms. (F11–57)
Mobile phone programs	Mobile phone programs consisting of or including text-messaging (general adult population) Use of smartphone applications (children and adolescents)	5 SR (range: 9–30) 3 MA (range: 11–74)	1. General adult population: text messaging interventions aimed at general adult populations found significant positive effect sizes, relative to controls, that were on average 0.40 or greater, with a median effect size in one systematic review of 0.50 (26). 2. Smartphone apps – youth: Interventions have been reported to have small to moderate effects in both girls and boys, with one systematic review reporting Cohen's d coefficients ranging from −0.36 to 0.86. As part of these meta-regression analyses, investigators were able to explain 45 percent of the variability in physical activity effect size among children and 62 percent of the variability in physical activity effect size among adolescents (27).
Physical environment and policy			
Point-of-decision prompts to promote stair use	Point-of-decision prompts to use stairs versus escalators or elevators (adults)	2 SR (6 and 67) AHA	In one systematic review of 67 studies, 77 percent reported increases in stair use. For those studies with significant effects (n = 55 studies), the percent stair use increase ranged from 0.3 percent to 34.7 percent. When odds ratios were reported, they ranged from 1.05 (95% CI, 1.01–1.10) to 2.90 (95% CI, 2.55–3.29) (28).

(continued next page)

TABLE 1. *(Continued)*

Category	Intervention Approaches	Evidence Type (Number of Studies)	Selected Effect Sizes[b]
Built environment characteristics that support active transport	Built environment characteristics and infrastructure that support active transport to destinations (e.g., Safe Routes to School programs, street connectivity, a mix of residential, commercial, and public land uses) (children, adults, and older adults)	3 SR (range: 12–42) 1 MA (42) AHA The Guide to Community Preventive Services	1. RESIDE study: each unit increase in perceived safety from crime was associated with 3.2 min·wk^{-1} more of transport physical activity. In addition, the association remained similar (3.6 min·wk^{-1} increases with unit increases in perceived safety from crime) when also controlling for built environmental characteristics such as residential density, streets connectivity, and number of local destinations (29). 2. Youth: positive associations found between land-use mix and children's physical activity (OR ranged from 1.8 (95% CI, 1.05–3.42) to 3.46 (95% CI, 1.6–7.47)). (AHA Scientific Statement) 3. Older adults: A meta-analysis of 42 quantitative studies found significant positive associations among a number of environmental variables and active transport behaviors, including residential density and urbanization, walkability, easy access to building entrances, and access to and availability of services and destinations. A weak, negative association was found between neighborhood disorder (e.g., litter, vandalism and decay) and total walking for transport (30).
Community design and characteristics that support recreational physical activity	Community design and characteristics that support physical activity, such as having safe and readily usable walking and cycling infrastructure and other favorable built environment elements (children and general adult populations)	1 SR (600) AHA The Guide to Community Preventive Services	1. RESIDE study: each unit increase in perceived safety from crime was associated with 13.5 min·wk^{-1} more of recreational physical activity over a 7-yr follow-up period. This amount of increase remained similar (13.7 min·wk^{-1}) when also controlling for additional built environmental characteristics (i.e., residential density, streets connectivity, and mix of local destinations) (29). 2. Adults: the largely cross-sectional studies reviewed by the AHA Scientific Statement generally indicated a significant relationship between neighborhood aesthetics and leisure-time physical activity, walking, or meeting physical activity recommendations (ORs ranged from 1.13 to 2.6). Absence of heavy traffic was associated with more walking and leisure-time physical activity (OR = 1.22; 95% CI, 1.08–1.37). (AHA Scientific Statement)
Access to indoor and/or outdoor recreation facilities or outlets	Having access to indoor (e.g., gyms) and/or outdoor recreation facilities or outlets, including parks, trails, and natural or green spaces (children and general adult populations)	3 SR (range: 12–90) AHA	Greater access generally was shown to be related to more physical activity among adults (OR 1.20; 95% CI, 1.06–1.34). (AHA Scientific Statement)
Sedentary behavior reduction interventions			
Youth	Reductions in television viewing and other screen-time behaviors in primarily school-based settings (youth) through school-based counseling, parental involvement, tailored feedback, and use of screen allowance devices at home	5 SR (range: 10–22) 4 MA (range: 13–34)	1. As a whole, the studies reviewed showed small but consistent effects on sedentary behavior reduction (e.g., mean difference was −20.44 min·d^{-1}; 95% CI, −30.69 to −10.20) (31). 2. School-based interventions focused primarily on reducing screen time in children through in-class or after-school curricula, and typically included messages targeting screen time as well as other health behaviors (e.g., exercise, diet). Such interventions had small but consistent effects in reducing sedentary time, particularly for those lasting longer than 6 months (e.g., mean difference was −0.25 h·d^{-1}; 95% CI, −0.37 to −0.13) (32).
Worksite	Interventions targeting sedentary behavior in worksites (adults), including physical changes to workstations	2 SR (15 and 40) 2 MA (8 and 21)	Interventions that focused on providing educational or motivational support showed only small and inconsistent effects on sedentary behavior (e.g., mean difference was −15.52 min per 8-h workday [95% CI, −22.88 to −8.16]). Interventions that targeted physical changes to work stations (i.e., predominantly the addition of sit-stand workstations, with a few that used treadmill desks or portable pedal machines) had consistently medium to large effects (e.g., mean difference was −72.78 min per 8-h workday [95% CI, −104.92 to −40.64]). Additionally, these effects were stronger when these types of work station changes were combined with educational and behavioral support (e.g., mean difference was −88.80 min per 8-h workday [95% CI, −132.69 to −44.61]) (33).

[a]Intervention categories derived from a comprehensive search of eligible systematic reviews and meta-analyses along with selected governmental reports identified during a 2011–2016 evidence search.
[b]Effect sizes are from articles mentioned in manuscript. Due to space limitations, not all articles included in the Committee Report were captured in the article; however, a full list of all systematic reviews, meta analyses, and effect sizes can be found in *2018 Physical Activity Guidelines Advisory Committee Report*.
SR, systematic review; MA, meta-analysis; PAGMR, Physical Activity Guidelines Midcourse Report; AHA, American Heart Association Scientific Statement.

(described in a subsequent section) as well as peer-led programs can provide a level of personalized advice and support in a manner that may reduce costs and enhance reach to a wider and more diverse audience. For example, there is consistent evidence supporting the effectiveness of peer-led behavioral self-management interventions such as the Chronic Disease Self-Management Program in attaining meaningful increases in physical activity among older adults and persons with chronic conditions, particularly over the short-term (e.g., 3 months) (16). Examples of original research supporting the longer-term effectiveness (1 yr or longer) of peer-engaged in-person or phone-delivered physical activity interventions in healthy midlife and older adults also are available (35,36). However, it is also important to further evaluate the impacts of such physical activity programs on important health outcomes of interest, such as physical function, which a recent meta-analysis in this area suggested may be more difficult to attain with such interventions (37).

Community-Level Strategies and Approaches

Community interventions can be aimed at the entire community (i.e., community-wide) or at particular community settings. Among the settings that have been frequently targeted for physical activity intervention are educational, housing, recreational, worksite, primary care, and faith-based settings. They offer potentially convenient locations for reaching diverse groups of people and, depending on the setting or location, provide a means for targeting different age groups using a range of strategies (38).

As noted earlier, the Committee's evidence review focused on those eligible systematic reviews, meta-analyses, and government reports published between 2011 and 2016. The available evidence during that time frame allowed us to identify robust evidence supporting contact-intensive community-wide interventions and interventions occurring in school settings. Meanwhile, other community setting reviews captured during the 2011 to 2016 review period (i.e., childcare and preschool settings, faith-based interventions, primary care settings, worksites, nurse-delivered interventions in home or other community settings), while promising, presented less rigorous intervention evidence. We present highlights from the two areas (contact-intensive community-wide interventions and school settings) that received particularly rigorous evidence support during the targeted review period.

Community-wide interventions. Community-wide interventions that use intensive contact with the majority of the target population over time can increase physical activity across the population (9). Although a large number of community-wide interventions that included physical activity promotion have occurred throughout the world, a relatively smaller number have been able to report sufficiently intensive contact with the majority of community members over time to produce significant physical activity increases across the target population. One example is a study conducted in China (39) that reported a significant increase in community-wide physical activity levels in three urban areas of Hangzhou city. The types of intervention strategies that were used included door-to-door distribution of instructions and information, identification and support of community members at increased chronic disease risk, and health counselor advising. The effectiveness of this type of community-wide intervention has been supported by a recent 5-yr cluster-randomized trial evaluating the effects of a community-wide intervention on population-level physical activity among midlife and older adults in Japan (40). The percent of adults achieving recommended levels of regular physical activity in the communities randomized to the social marketing-based intervention (n = 9) increased by 4.6 percentage points over 5 yr relative to the control communities (n = 3). The intervention, which consisted of targeted educational outreach, information delivery through different media channels, and different types of social support, was effective in promoting aerobic, muscle strengthening, and flexibility activities in those communities in which these different physical activity types were specifically targeted. Of note, however, in the intervention community in which all three types of physical activity were targeted simultaneously, less positive change occurred relative to those communities targeting fewer physical activity types (40). Although promising evidence for positive physical activity changes in some portions of the community has been reported in other studies in the United States and elsewhere, it remains a challenge to reach broad segments of communities with sufficient intervention duration and intensity to produce sustainable changes, particularly when interventions often include strategies to improve other risk factors beyond physical activity (9).

Overall, there is an extensive literature evaluating community-wide as well as setting-specific community interventions for physical activity promotion (9,41). The robustness of the evidence overall could be improved by using more rigorous study designs and assessment strategies, longer intervention time frames, and consistent applications of intervention fidelity processes and procedures (9).

School interventions. Among the most robust literature available in the physical activity promotion field is that aimed at promoting physical activity in school settings (41). Effective multicomponent school-based interventions, such as CATCH (17) and SPARK (18), include structural changes in physical education (PE) classes, classroom activity breaks, activity sessions occurring before and after school, active transport to and from school, behavioral skill-building to promote physical activity participation, and the provision of after-school spaces and equipment for physical activity (17,18). Such interventions have been found to significantly increase physical activity during school hours relative to controls in primary school and adolescent youth (9). A number of studies also have shown that implementing a well-designed PE curriculum with appropriately trained teachers can improve amounts of within-class moderate-to-vigorous physical activity. For example, a meta-analysis in this area (19) reported a 24% increase in active learning time during PE in the intervention groups relative to controls irrespective of age, sex, and intervention duration (standard mean difference [SMD], 0.62; 95% CI, 0.39–0.84).

Communication Environment-Level Strategies and Approaches

The communication environment includes a large and growing group of ICT that have been used increasingly to promote regular physical activity. The ICT strategies are typically tested with individuals but can be deployed widely within a larger communication and technology environment, thus having the potential for broad reach. Given this observation along with the unique delivery channels represented in this emerging field, we chose to treat ICT interventions as a distinct level of impact (8). Such interventions have the potential for providing more dynamic intervention delivery (e.g., "just-in-time" strategies) than those accessed in the more traditional in-person interventions found at the individual level. Typical delivery channels used include technologies such as wearable activity monitors, cell or smart phones, and the Internet. Among the advantages of ICT intervention approaches are their ability, similar to the individual-level approaches highlighted earlier, to personalize information, behavior change strategies, and support to the varying contexts and needs of individual users while providing a means for readily documenting the information delivered and responses received. For example, the passive sensing capabilities of smartphones and similar mobile devices can provide near continuous, lower burden physical activity tracking abilities, as well as a means for capturing social and environmental contextual information that allow delivery of "just in time" personalized advice and support (42). In addition, in light of accelerating smartphone ownership (69%) in the US population and other developed countries (43), as well as in a growing number of developing economies worldwide (46% own smartphones) (43), the population reach of mobile device-based interventions can potentially rival or eclipse community interventions.

The evidence evaluated during the 2011 to 2016 comprehensive review that focused on ICT interventions was organized into seven categories, with five of those categories containing a sufficiently consistent and rigorous evidence base to be highlighted here. The two categories not included, which represent areas needing further systematic study, were active video games promoting active play or exercise and interventions delivered via social media. A recent meta-analysis of 18 RCT of active video games focusing on healthy, community-dwelling older adults suggested that use of such games can promote short-term mobility and balance gains in healthy populations (44). However, their impacts in older adults with balance or mobility limitations are less clear. In addition, while program adherence rates were reported overall to be reasonably high, intervention durations in this area remain brief (i.e., from 3 to 20 wk) (44). With respect to social media, a recent systematic review of physical activity interventions using a specific social media platform—Facebook—found that only two of eight interventions reviewed resulted in significant physical activity increases relative to controls (45). As represented in this review, this nascent intervention field continues to suffer from weak designs, lack of theory-based content, small sample sizes, and short follow-up periods (45).

Wearable activity monitors. The evidence reviewed supports the use of wearable activity monitors, such as step-counters and accelerometers, when used jointly with specific behavioral strategies such as goal-setting, behavioral coaching, and/or group-based support for increasing regular physical activity in general adult populations as well as some specific adult subgroups. In general adult populations, a meta-analysis of 12 trials using activity monitors reported a significant, albeit small, increase in physical activity levels relative to minimal-attention or usual care controls (SMD, 0.25; 95% CI, 0.04–0.49) (20). In this review, setting a specific physical activity goal appeared to enhance physical activity outcomes irrespective of whether it was a self-chosen goal versus a goal specified by the intervention team (e.g., a 10,000-step goal) (20). The importance of setting a specific physical activity goal in combination with an activity monitor was also supported in a meta-analysis of patients with type 2 diabetes (21). In this meta-analysis, setting a specific physical activity goal resulted in a significant mean increase of 3200 steps per day relative to controls, whereas step-counter use without a goal did not increase physical activity significantly relative to control. Use of a step diary also was efficacious in increasing physical activity (21). Significant positive effects of behavioral interventions that included activity monitors in comparison with waitlist or usual care interventions were also found in a meta-analysis of adults with overweight or obesity (22).

Among some of the challenges accompanying wearable activity monitor use are the timing of their use in physical activity programs (e.g., during the adoption vs maintenance phases of behavior change) (46), and methods for extending the duration of use.

Telephone-assisted interventions. Decades of physical activity intervention work have supported the use of physical activity advice and support delivered by phone for general adult as well as older adult populations, with effect sizes in the moderate range or stronger (i.e., $d > 0.5$) (47). Longer-term interventions (i.e., 12 months or longer) have been associated with greater effectiveness, and at least two large-scale dissemination studies targeting diverse groups of midlife and older adults and including trained community staff as well as volunteers have reported physical activity increases of a magnitude similar to those obtained in RCT (47–49). Of interest, a review of a small number of trials that combined physical activity and dietary interventions in general adult and older adult populations suggested that including a dietary intervention might at times hamper physical activity change (47). This finding was supported in a subsequent RCT in which the timing of the introduction of these two health behavior interventions was manipulated systematically (i.e., sequential or simultaneous ordering) (50). Greater increases in physical activity occurred when the physical activity intervention was initiated from the beginning, as opposed to when it was added following initiation of a dietary intervention (50).

Web-based or Internet-delivered interventions. Systematic reviews and meta-analyses of interventions delivered remotely over a web page or the Internet and that include educational components have reported small but positive intervention effects in general adult populations (6); for example, one meta-analysis found a *d* = 0.14 when comparing such interventions with control arms (23). Larger effect sizes have been reported for studies which screened out already active individuals (*d* = 0.37) (23), while targeting physical activity alone or in combination with other health behaviors (i.e., dietary behaviors, weight management behaviors) produced similar effect sizes (23). Web-based or Internet interventions may also result in significant short-term physical activity increases (i.e., typically less than 6 months) in persons with type 2 diabetes when compared with controls (24), although this literature is less well developed and more variable than the literature for general adult populations.

Computer-tailored print interventions. These programs collect user information via mailed surveys, which is then used to develop computer-tailored mailings that include personalized physical activity advice and support (51). Current evidence indicates that, in general adult populations, such interventions have a positive, albeit small effect (*d* = 0.12 to 0.35) on physical activity levels, particularly in the short-term (i.e., 6 months or less) (51). Commonly used tailoring variables upon which to personalize the mailed advice were psychosocial and behavioral variables (e.g., perceived barriers to activity; motivational readiness to change) (51).

Mobile phone interventions. In generally healthy adult populations, the relatively small number of mobile phone interventions that include or focus primarily on text-messaging have reported significant positive effects, relative to controls, on physical activity levels (9). Some of the effect sizes reported in the available reviews have been notable (i.e., an average of 0.40 or greater) (26). In a number of studies, text-messaging was used primarily to provide simple cues or messages related to becoming more active (9).

While no reviews of text-messaging interventions in youth were found during the 2011 to 2016 search period, reviews were identified evaluating the efficacy of physical activity smartphone apps in youth. Occurring in school and other community settings and across diverse countries, the evidence indicates small to moderate effects on physical activity levels in boys and girls, although at least one systematic review reported Cohen's *d* coefficients of 0.36 to 0.86 (27). When types and combinations of behavioral strategies were evaluated systematically, differences were found in children relative to adolescents. For example, while general encouragement, modeling and instruction predicted positive physical activity effects in children (27), providing teens with specific instruction tended to reduce the effects of the intervention (27).

While no systematic reviews were found during the search period evaluating smartphone apps in adults, a recent systematic review and meta-analysis of 18 RCT in this area indicated some promising results for adults, with small to moderate increases in device-based physical activity when measured in minutes per day (SMD, 0.43; 95% CI, 0.03–0.82) (52). However, most studies included additional intervention components (e.g., counseling sessions), which could result in larger effects than if the smartphone app was offered alone (53).

Physical Environment and Policy-Level Strategies and Approaches

Physical environment-level approaches can be defined broadly as the evaluation and targeting of features in the built environment that may affect physical activity levels, including pedestrian or bicycling infrastructure, ready access to stairs, and access to indoor and outdoor recreational facilities, including parks, trails, and gyms (9). Policy-level approaches, meanwhile, include local ordinances and laws, as well as organizational policies and practices that can influence physical activity (9). Over the last several decades there has been an increase in research worldwide evaluating the associations between physical environment factors and levels of physical activity (38). In addition to the large number of cross-sectional observational designs that have been used in this field, more rigorous longitudinal and natural experimental designs have been added more recently to the literature (29,38). Environmental and policy-level evidence can set the stage for intervention approaches that can span large portions of the population, therefore having a potentially larger impact and "reach" than interventions at other levels of impact (e.g., the individual-level). However, environmental and policy approaches are also, by their often complex and multifactorial nature, constrained by the real-world challenges that can make it difficult to implement as well as evaluate them. These challenges notwithstanding, four approaches at this level, described below, have achieved consistent evidence support and are important public health strategies to consider in the physical activity area.

Point-of-decision prompts promoting stair use. Systematic reviews of short-term point-of-decision studies (typically ranging from 4 to 12 wk) conducted in a variety of community settings (e.g., shopping malls, transit hubs, worksites) have reported increases in stair use in the majority of studies evaluated (e.g., 77% of 67 studies reviewed) (28). Most of the studies reviewed used quasi-experimental designs (e.g., interrupted time series, controlled before-and-after studies) (28). Percent stair use increases have ranged from 0.3% to 34.7% (28). Some studies suggest that responses to the prompts may vary by age, sex, and weight status (9).

Built environment characteristics that support active transport to destinations. The evidence reviewed reported that street connectivity, a mix of commercial, residential and public land uses, and similar types of characteristics, along with Safe Routes to School programs, are positively associated with greater walking and cycling for transport among adults, older adults, and children relative to environments lacking such elements (9,38). For instance, the results of a large natural experiment (RESIDE) (29) found increases across a 7-yr period in active transport among residents moving to neighborhoods that they perceived as safer for walking and bicycling relative to those who did not move to such neighborhoods. The importance of walkability and similar environmental features for active transport and other forms of physical activity additionally has been supported by a recent large-scale study of US smartphone app users (42). This study showed that women may be particularly sensitive to the effects of walkability features in terms of their daily physical activity levels.

Community design and characteristics that support recreational physical activity. Readily usable and safe walking and cycling infrastructure and related built environment features (e.g., sidewalks, street connectivity, absence of heavy traffic) are also positively associated with greater amounts of recreational physical activity among both children and adults relative to environments without such infrastructure. For example, one meta-analysis reported that absence of heavy traffic was associated with significantly more walking and leisure-time physical activity in adults (odds ratio, 1.22; 95% CI, 1.08–1.37) (54).

Access to indoor and/or outdoor recreation facilities or outlets. The evidence review additionally showed that access to indoor (e.g., gyms or fitness centers) or outdoor recreational facilities (e.g., parks, trails, open streets programs which temporarily reduce motor vehicle access in specified locations) is positively associated with greater physical activity among both children and adults compared to environments without such facilities or outlets (9). For example, a meta-analysis reported that greater access to such facilities among adults was related to more physical activity, with an odds ratio of 1.20 (95% CI, 1.06–1.34) (54). In addition, some intervention studies have shown that combining a built environment approach (e.g., building a new footpath) with a public education or skills-building program has resulted in increased physical activity levels (55).

Policy-specific approaches to physical activity promotion. In contrast to the built environment arena, little evidence was found during the 2011 to 2016 evidence search period evaluating the impacts of specific policies related to land use, urban sprawl, and similar environmental design factors on physical activity levels. Only one review was found during this search period that focused specifically on policy approaches for physical activity programs (56), and this review was primarily descriptive in nature. It identified land use policies and school physical activity policies as among the most promising types of policies that have been studied to date. In a review that included five studies of urban sprawl and physical activity, 80% found a relationship between less sprawl and more physical activity of different types (e.g., active transport, recreational, total physical activity) (38), and one prospective study reported positive impacts over time of urban sprawl mitigation policies on physical activity (57).

SUMMARY OF KEY INTERVENTION COMPONENTS FOR PHYSICAL ACTIVITY PROMOTION AT EACH LEVEL

For investigators designing and implementing physical activity interventions, a number of key intervention components were highlighted above. At the individual level, self-monitoring of behavior and intention formation are commonly related to increased physical activity. At the community level, door-to-door distribution of instructions and information, identification and support of community members at increased chronic disease risk, and health counselor advising can be important components, as can well-structured PE classes and environmental changes in school settings. At the communication environment level, goal setting was found to be particularly important, and assessing perceived barriers to activity and motivational readiness to change are useful. At the physical environment/policy level, street connectivity, a mix of commercial, residential, and public land uses and similar types of built environment characteristics, along with Safe Routes to School programs, are positively associated with greater walking and cycling for transport among adults, older adults, and children relative to environments lacking such elements.

RESULTS OF THE EVIDENCE REVIEW: INTERVENTIONS TO REDUCE SEDENTARY BEHAVIOR

A summary of the intervention categories for which sufficiently consistent evidence was found supporting sedentary behavior reduction among youth and in worksites is summarized in Table 1 and briefly described below. Interventions to reduce sedentary behavior among adults were identified as an area warranting further study. Given the relative newness of this area, the size of the evidence base was smaller than that for physical activity interventions (9). However, the evidence available tended toward more rigorous methods (i.e., meta-analyses of RCT).

Youth interventions. The 2011 to 2016 evidence review found support for sedentary behavior interventions in youth which typically were delivered in school settings, generally lasted at least 6 months, and targeted primarily reductions in television viewing and other screen-time activities (9). Combinations of strategies were often used in these studies consisting of school-based counseling, parental involvement, tailored feedback regarding screen-time activities, and the use of screen allowance devices to limit TV and video game viewing time. Taken together, the reviews indicated small but consistent self-reported sedentary behavior reduction effects (e.g., a mean reduction of about 20 $\text{min}\cdot\text{d}^{-1}$) irrespective of whether the intervention was delivered alone or as part of a multiple behavior change program (31). A more recent review of 0- to 5-yr-old children showed similar reductions in sedentary time (i.e., mean difference of 18.91 fewer sedentary minutes per day relative to control; 95% CI, −33.31 to −4.51) (58). It was unclear from the evidence reviewed whether such consistent reductions in sedentary behavior would be sufficiently large to produce positive health effects in this age group.

Worksite interventions. We found consistent evidence supporting the effectiveness of sedentary reduction interventions with worksite populations that performed their work duties typically while seated (9). This was particularly the case for interventions that targeted physical changes to work stations (e.g., sit-stand workstations), which reported medium to large effect sizes based on device-measured sedentary behavior (i.e., mean difference of 72.78 fewer sedentary minutes per 8-h workday relative to control, 95% CI, −104.92 to −40.64) (33). Such effects were strengthened when the workstation changes were combined with educational (e.g., e-newsletters), social (e.g., workgroup contests), and other environmental (e.g., managerial support, signage) support strategies (e.g., mean difference of −88.80 min per 8-h workday relative to control) (33). Evidence of efficacy in the meta-analyses also appeared to be somewhat diminished when walking workstations and cycle ergometers were used (59).

Methodological constraints included small sample sizes and short-term intervention durations (3 to 6 months) (59). However, these constraints have been addressed in recent trials using cluster-randomized designs that demonstrated similar effect sizes to those observed in the meta-analyses (60,61). In addition, a recently published cluster-randomized trial resulted in reductions in body fat percentage at the end of the multicomponent intervention (62).

DISCUSSION AND FUTURE RECOMMENDATIONS

The above highlights from the *2018 Physical Activity Guidelines Advisory Committee Scientific Report* underscore the range of effective interventions for promoting regular physical activity at different life stages. Of particular note are the promising number of technology-based approaches that can effectively promote short-term physical activity increases. An ongoing challenge for the field as a whole is to identify the best methods for promoting *sustained* physical activity for different population groups within different environmental and cultural contexts as well as life stages. One way to increase sustained physical activity is to target several levels of the social ecological framework within the same intervention. Unfortunately, such multilevel interventions have not been commonplace to date. In addition, while the type and nature of the physical activity (e.g., intensity, duration, frequency, its enjoyability and related factors) can influence the effectiveness of an intervention for different population groups, few of the reviews, meta-analyses, and reports that were evaluated presented systematic information on the associations of such program factors with intervention success. The field as a whole would benefit from further research in this area.

The evidence also supports the effectiveness of those sedentary behavior reduction approaches that have received systematic study to date. Such evidence notwithstanding, there remains much that we need to know about how to most efficiently and effectively promote these key health behaviors among the significant proportion of the population who are substantially sedentary or insufficiently active on a regular basis. Among other important areas for further systematic investigation are the following:

- Incorporate more diverse population subgroups, including broader age groups, men as well as women, diverse racial/ethnic groups, and vulnerable and underrepresented population groups (e.g., lower-income residents, patient subgroups).
- Develop efficient methods for collecting cost data on all interventions being tested to inform cost-benefit and cost-effectiveness comparisons across the field as a whole (63).
- Study the most effective methods for disseminating to real-world settings those physical activity interventions that work, a number of which have been highlighted in this review. As part of this dissemination process, it is critical that specific efforts are made to reach traditionally underserved segments with interventions adapted to their needs. Doing this can help to ensure that all population groups can benefit from interventions shown to be effective. Additionally, it will be important to systematically evaluate such dissemination efforts to better capture actual intervention effects when delivered in the community (48).
- As a complement to dissemination approaches, conduct implementation research as a means of identifying methods for enhancing the uptake and implementation of programs shown to be effective to ensure that they maintain their effectiveness when delivered at scale.
- Test strategies across different levels of impact, as has been done in school settings, to determine which combinations achieve the greatest effects on different modes of physical activity across the week and in different population groups.
- Test methods for sustaining physical activity increases over time and across different contexts, given that inactivity is most appropriately conceptualized as a “chronic condition,” as opposed to an acute condition that can be “cured” with a finite intervention without targeting maintenance.
- Continue the systematic work aimed at increasing our understanding of the most effective strategies and mechanisms of action underlying physical activity interventions. An example of such an approach, based on international scientific consensus-building and evidence review and analysis, aims to build a taxonomy of behavior change techniques for physical activity and other health behaviors (64). Such a taxonomy can serve as the starting point to identify the most effective strategies and mechanisms for behavior change for different population groups, contexts, and outcomes.

Finally, although this article highlights those interventions reviewed for which the evidence supported intervention effectiveness, many such interventions were noted to have small to moderate effects in increasing physical activity. Among the aims of the future recommendations described above are to help facilitate the development of increasingly robust multicomponent and multiple-level interventions that can strengthen intervention effects among different population segments. This point notwithstanding, it has been noted that even small effects of an intervention can translate into meaningful public health impacts when the intervention is disseminated effectively across a large segment of the population (65,66). This observation underscores our call for an increased focus on broad dissemination of the group of interventions that show effectiveness, even if an intervention might alone produce a reasonably small individual-level effect. With careful attention to ensuring that all groups benefit from the knowledge that has been gained in the physical activity promotion field, the untapped promise for the nation's health offered through a physically active lifestyle can be more fully realized.

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