PART G. NEEDS FOR FUTURE RESEARCH

Table of Contents

OVERARCHING RESEARCH NEEDS

Following are a set of questions the Committee believes are most important and critical for informing the scientific foundation for the next set of physical activity guidelines.

- Determine the independent and interactive effects of physical activity and sedentary behavior on multiple health outcomes in youth, adults, and older adults.

  Rationale: Preliminary evidence from one 2016 review and meta-analysis indicates a significant interaction among physical activity (measured as moderate-to-vigorous physical activity) and sedentary time on all-cause mortality.[1] The extent to which physical activity, at the workplace or during leisure time, can compensate for increases in sedentary time—for individuals of all ages—is a timely, important and popular question.

- Determine the role and contribution of light-intensity activity alone or in combination with moderate-to-vigorous physical activity to health outcomes.

  Rationale: The importance of light physical activities to health outcomes has been an interest for a long time. However, the scientific community has been limited by survey tools that poorly quantify physical activity. The development and wide use of wearable monitors that permit quantification of light physical activity and total physical activity now permit and promote a new series of investigations critical to the understanding of the role of total range of physical activity on health. The role of steps and step counting to measurement of physical activity exposure and promotion derives from this issue.

- Identify effective intervention strategies for increasing physical activity through actions in multiple settings in youth, adults, and older adults. How does the effectiveness of interventions differ by sex, age, race/ethnicity, socioeconomic, and other factors?

  Rationale: Once guidelines are established, developing effective strategies to help individuals achieve the goals remains a most critical step in improving the general health of our communities. However, effective intervention strategies necessarily vary by an individual's personality, culture, environment, socioeconomic status, medical condition, fitness level, and other personal factors.

Understanding these intervention modifiers will be critical to developing strategies for effective means to increase physical activity for communities.

- Strengthen the understanding of dose-response relationships between physical activity and multiple health outcomes in youth, adults, and older adults, and especially during the life transitions between these categories.

  Rationale: Before the widespread adoption of device-based measures of physical activity, it was almost impossible to obtain reliable data on the various components of physical activity contributing to health effects in large populations. Most of the relevant information on dose-response with respect to intensity, frequency, duration, and longevity of physical activity interventions on health effects comes from small controlled training trials that can carefully control the exposure parameters of interest. To understand the effects of the frequency, intensity, time, and type (FITT) exposure parameters at the population level will require use of devised-based measures of physical activity incorporated into longitudinal study designs, whether they be controlled randomized trials or longitudinal cohort studies.

- Expand knowledge of the extent to which the relationships between physical activity and health outcomes are modified by demographic factors including sex and race/ethnicity.

  Rationale: The health effects of physical activity have been conducted in samples that were not fully representative of the population (e.g., only females or males; mostly non-Hispanic white race/ethnicity). Very significant health disparities have been linked to race, ethnicity, and socioeconomic status. Studying whether (and how) physical activity mitigates race-based health disparities in a number of conditions—heart disease, cancer, obesity, type 2 diabetes, Alzheimer's disease, and many others—could have far-reaching public health implications. In the future, more studies should be designed specifically to consider differential effects across demographic sub-groups.

- Develop instrumentation and data collection systems that will enhance physical activity surveillance systems in the United States.

  Rationale: Based on the information and evidence described in this report, bouts of moderate-to-vigorous physical activity of less than 10-minutes have value and may be included in the

accumulated total, and light-intensity physical activity is a beneficial behavior for individuals who are highly sedentary and perform no or little moderate-to-vigorous physical activity. Therefore, these aspects of physical activity, which are most accurately measured by devices, are important to capture across the U.S. population. Information relevant to physical activity promotion, such as the presence of supportive programs (community or site-specific), policies, or environmental supports, are also important to monitor. Instrumentation and data collection systems are needed to enhance the collection of this information. Research is needed to determine the most appropriate metrics and data collection methods to capture this information for surveillance or for large-scale surveys.

CHAPTER 1. PHYSICAL ACTIVITY BEHAVIORS: STEPS, BOUTS, AND HIGH INTENSITY TRAINING

Question 1. Step Count Per Day and Question 2. Bout Duration

1. Conduct additional longitudinal research, either in the form of prospective studies or randomized controlled trials, to examine the dose-response relationship between:

    a) Steps per day and health outcomes, and

    b) Whether physical activity accumulated in bouts of less than 10 minutes in duration enhances health outcomes.

    Rationale: This information is critical for setting target volumes of physical activity using steps per day as the metric and for firmly establishing that steps per day predicts 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.

    The majority of studies reviewed supporting the health benefits of physical activity accumulated in bouts of less than 10 minutes in duration used a cross-sectional design, with none of the randomized studies reporting on the effects of physical activity accumulated in bouts of less than 10 minutes. Having this knowledge will inform potential cause and effect rather than simply associations.

2. Include measurement methods in prospective and randomized controlled studies that will examine:

a) Whether the rate of stepping and the length (bouts) of continuous steps influence the relationship between steps per day and disease outcomes

b) Whether physical activity performed in a variety of bout lengths has differential effects on health outcomes

Rationale: The studies reviewed used simple pedometers providing accumulated steps and could neither address patterns nor intensity of steps per day. Additional physical activity assessment methods collecting these data should provide a better target for recommending physical activity volume. Based on the studies reviewed, randomized studies did not report on physical activity accumulated in bouts less than 10 minutes in duration, and only two prospective studies were identified that reported on physical activity accumulated in bouts less than 10 minutes. This may be a result of the methods used to assess physical activity in randomized and prospective studies, and suggests the need to include physical activity assessment methods that allow for these data to be available for analysis.

Question 3. High Intensity Interval Training

1. Conduct longer-term randomized controlled trials to assess the adherence to and the effects of high intensity interval training, compared to other types of physical activity programs, on physiological, morphological, and cardiometabolic health outcomes. They should address issues of dose-response and be of at least 6 months in duration. These randomized controlled trials should include diverse groups of adults who have overweight or obesity and/or who are at high risk of cardiovascular disease or type 2 diabetes. They should systematically assess adverse events, including musculoskeletal injuries, attributable to high intensity interval training, compared to other types of exercise training, among adults with a wide variety of health and disease characteristics.

   Rationale: Most high intensity interval training intervention periods are less than 12 weeks, which may be insufficient time to assess the magnitude and sustainability of clinically-important changes in some physiological, morphological, and cardiometabolic health outcomes. The willingness and ability of individuals to adhere to high intensity interval training programs is currently unknown. Prescriptively designing these studies to include participants who have overweight or obesity and/or who are at high risk of cardiovascular disease or type 2 diabetes is important to inform health promotion practitioners and policy leaders on the utility of recommending high intensity interval

training for health among a large proportion of the U.S. adult population. At present, evaluation of the safety of high intensity interval training among adults with varied health and disease characteristics is compromised by the limited data available, in part, due to the low proportion of studies reporting adverse events.

CHAPTER 2. SEDENTARY BEHAVIOR

1. Conduct research using prospective cohorts on the interactive effects of physical activity and sedentary behavior on all-cause and cardiovascular disease mortality and incident cardiovascular disease, especially on the role of light-intensity physical activity on attenuating the relationship between sitting and mortality.

   Rationale: Evidence on the role of physical activity in displacing the mortality risks associated with sedentary behavior is limited. A better understanding of these interactive effects will allow for more specific recommendations regarding the amount and intensity of physical activity required to maximize health benefits among people with higher or lower levels of sedentary behavior. Given that associations between specific risk factors and cancer mortality are affected by cancer screening and treatment availability and efficacy, studies of the associations between sedentary behavior and all-cancer mortality are not a priority.

2. Conduct research using prospective cohorts on the role of bouts and breaks in sedentary behavior in relation to all-cause and cardiovascular disease mortality.

   Rationale: The preponderance of the existing evidence on prospective associations between sedentary behavior and health is based on the association between daily or weekly duration of sedentary behavior. More research is needed on the relationship between patterns of sedentary behavior and mortality and other health outcomes, especially the role of sedentary bouts and breaks. This information will contribute to the development of recommendations on how sedentary behavior patterns should be modified to maximize related health benefits. Given that associations between specific risk factors and cancer mortality are affected by cancer screening and treatment availability and efficacy, studies of the associations between sedentary behavior and all-cancer mortality are not a priority.

3. Conduct research on how factors such as sex, age, race/ethnicity, socioeconomic status, and weight status relate to the association between sedentary behavior and cardiovascular disease incidence and cardiovascular disease mortality.

   Rationale: Compared to the evidence base for all-cause mortality, fewer studies have addressed issues of effect modification by these factors on the relationship between sedentary behavior and cardiovascular disease incidence and mortality. This information will help determine how generalizable the potential benefits of reducing sedentary behavior are in preventing cardiovascular disease and whether different recommendations are required based one's sex, age, race/ethnicity, socioeconomic status, or weight status. Given that associations between specific risk factors and cancer mortality are affected by cancer screening and treatment availability and efficacy, studies of the associations between sedentary behavior and all-cancer mortality are not a priority.

4. Conduct research using prospective cohorts to disentangle the independent effects of sedentary behavior and adiposity on risk of type 2 diabetes.

   Rationale: Given that the association between sedentary behavior and type 2 diabetes is attenuated when body mass index is a covariate in the statistical models, this suggests that body mass index may be in the causal pathway between sedentary behavior and risk of type 2 diabetes. However, further research is required to understand the nature and direction of this relationship to better understand whether the relationship between sedentary behavior and type 2 diabetes is truly causal.

5. Conduct randomized controlled trials to test the health effects of interventions to replace time spent in sedentary behaviors with standing and light-, moderate-, and vigorous-intensity physical activity.

   Rationale: The preponderance of the evidence on the health effects of sedentary behavior has come from observational epidemiological studies. To develop public health guidelines and develop effective intervention strategies, more evidence is required on the positive and negative consequences associated with replacing sedentary behavior with greater intensity activities for short or long durations.

CHAPTER 3. BRAIN HEALTH

1. Conduct randomized controlled trials of moderate-to-vigorous physical activity across the lifespan, including in youth, to better understand its effects on cognitive development, quality of life and health-related quality of life, state and trait anxiety, and sleep outcomes.

   Rationale: Despite considerable research focused on the importance of physical activity on brain health in adults and older adults, the paucity of knowledge during other periods of the lifespan should be addressed to better understand physical activity effects on cognition, quality of life, affect, anxiety and depression, and sleep outcomes, and how they may change, across the entire lifespan. Physical activity may beneficially affect measures of brain health in common childhood disorders such as attention deficit hyperactivity disorder and autism spectrum disorder, but the impact on these conditions, or the long-term impact of physical activity during childhood on adult outcomes are largely unknown.

2. Conduct randomized controlled trials that manipulate the physical activity dose in a systematic fashion to improve the understanding of the dose-response relationship and durability of physical activity effects on brain health. Conduct these studies in healthy children and adults, and also in populations with conditions and impairments of brain health (e.g., dementia, sleep disorders, mood disorders).

   Rationale: To date, little evidence exists to draw strong conclusions about the optimal intensity, duration, and frequency of physical activity to enhance brain health (i.e., cognition, quality of life, anxiety, depression, sleep). This work is critically needed to better inform the public and practitioners about the amount of activity needed to observe changes in brain health outcomes in healthy individuals and in individuals with cognitive, sleep, or mood disorders. Although the current literature base does not allow for a firm understanding of a dose-response relationship between either acute or chronic physical activity on brain health, recommended doses of physical activity (e.g., moderate-to vigorous-intensity) have demonstrated positive effects on brain health across the lifespan.

3. Conduct randomized controlled trials of both light and moderate-to-vigorous physical activity in individuals with cognitive (e.g., dementia), mood (e.g., anxiety, depression), sleep (e.g., insomnia), and other mental health disorders (e.g., schizophrenia) to better understand its effects on brain

health in these conditions, including aspects of quality of life and health-related quality of life. Further, conduct randomized controlled trials and observational studies in individuals at different stages or severity of impairment, including studies in individuals at risk of disease (e.g., genetic risk) as well as individual with comorbid conditions (e.g., anxiety and depression) to examine whether physical activity delays or prevents disease onset and progression, or interacts with common treatments used by individuals with disorders and diseases.

Rationale: Knowledge of this area varies across impairments, with some diseases and disorders having significantly more research than others (e.g., depression). Yet, even in the context of some of these more common conditions, there is a paucity of research on some outcomes that are highly relevant for optimal functioning, such as the impact of physical activity on sleep, cognitive, and quality of life in individuals with depression. In addition, little is known about the effects of physical activity on conditions that often co-occur, like anxiety and depression. Other conditions that are also associated with impaired brain health (e.g., autism spectrum disorder, cancer, traumatic brain injury) have received little focus to date. Research in this area would contribute to a better understanding of etiologic subcategories of cognitive, sleep, mood, and other mental health conditions such as Alzheimer's disease and related dementias, and Lewy Body, Vascular, and Mixed Dementias, which are increasingly recognized and diagnosed within the domains of impaired mental and neurological health in aging.

4. Conduct randomized controlled trials of physical activity that examine brain imaging and other biomarker metrics across the lifespan and in conditions characterized by cognitive, mood, and sleep impairments.

   Rationale: These studies could yield a better understanding of circulating biomarkers (e.g., neurotrophins) associated with brain health, and the relative roles of genetic (e.g., *ApoE4* gene) and environmental risk factors (e.g., stroke risk factors, traumatic brain injury) as covariates influencing the response to physical activity. To date, although candidate biomarkers and environmental risk factors have been identified, little systematic study in humans has emerged in the literature especially in relation to markers associated with affect, anxiety, depression, and sleep.

5. Conduct studies to monitor sedentary time and conduct randomized controlled trials that systematically reduce sedentary behaviors to improve the understanding of the impact of varying contexts, patterns, and durations of sedentary behavior on brain health outcomes (e.g., depression symptoms) throughout the lifespan and in populations with brain health disorders and diseases.

   Rationale: The understanding of the effects of sedentary behavior on brain health is in its infancy. Given that recent evidence indicates that sedentary behavior is distinct from physical inactivity, a greater understanding of the effect of sedentary behavior on brain health may inform and target interventions aimed at improving brain health across a variety of populations, including school-aged children, middle-aged adults, and older adults, as these populations spend considerable time during their day engaged in sitting and other sedentary behaviors. In addition, portable health technologies that continuously measure physical activity, estimate its intensity, and characterize sleep behavior, may offer inroads to better understand such relationships, and perhaps test novel interventions using connected health approaches.

6. Conduct appropriate analyses to examine effect modification by demographic factors. Such analytical approaches require studies that include large samples and substantial variation in sample characteristics (i.e., race/ethnicity, socioeconomic status).

   Rationale: Although some understanding of the effects of physical activity during the developing years and in aging has emerged, evidence for other demographic factors has not been demonstrated in a systematic fashion, affording little opportunity to form strong conclusions about any potential effect of these factors. Findings that incorporate other demographic factors stand to generalize the physical activity-brain health literature, improving understanding of this relationship more broadly across the U.S. population, deepening understanding of health disparities, and informing interventions aimed at improving brain health.

7. Conduct randomized controlled trials and prospective observational studies that will improve understanding of the latency and persistence of the improvements in brain health following both acute and regular physical activity. These studies should have larger sample sizes, longer follow-up periods, and a broader range of instruments and outcomes relevant for brain health (e.g., mental subdomain of health-related quality of life, affect).

Rationale: To date, the temporal dynamics of the effects of physical activity on brain health are poorly understood. Yet, it is known that individuals start and stop exercise regimens on a regular basis and such variability in the consistency of physical activity may differentially influence the impact of physical activity on brain health outcomes. It is possible that the persistence of the effects might also depend on the dose of activity (frequency, intensity, time, type), the age of the individual, the presence of a disorder or disease, or other factors. Enrolling samples of sufficient size to support mediator analyses (i.e., exploration of putative mechanisms through which the interventions operate) will provide useful information for adapting the interventions to optimize uptake among different subgroups as well as to identify key elements that are essential to improving brain health.

8. Conduct randomized controlled trials and prospective observational research on the impact of muscle-strengthening exercises (often referred to in the literature as resistance training) and other forms of physical activity (e.g., yoga, tai chi), and other modes of activity on brain health outcomes.

   Rationale: Most research in this area has been conducted using aerobic exercise approaches (e.g., brisk walking). Given the effects of muscle-strengthening exercises and the increased popularity of many other forms of physical activity (e.g., yoga, tai chi) and the evolving evidence of their influence on multiple health outcomes, it will be important to understand how these different modalities differentially influence cognition, quality of life, affective, anxiety, depression, and sleep outcomes.

CHAPTER 4. CANCER PREVENTION

1. Conduct epidemiologic studies of effects of physical activity on risk of cancer for specific cancer sites that have not been adequately studied, preferably large prospective cohort studies.

   Rationale: Very little evidence exists on the relationship between physical activity and the risk of cancer at several sites, particularly the rare cancers. Therefore additional pooled datasets and meta-analyses may be needed. Additional studies would provide the data necessary for the useful insights that would be possible through analyses of pooled datasets and meta-analyses.

2. Conduct epidemiologic studies of effects of physical activity on risk of cancer in specific race, ethnic, and socioeconomic groups.

Rationale: Few studies have had sufficiently large numbers of participants from specific racial, ethnic, or socioeconomic subgroups to assess the effects of physical activity on risk of developing cancer. This additional research is particularly important, as many groups are at high risk of cancer (i.e., African Americans are at increased risk for colon, prostate, and breast cancers), are typically diagnosed with more advanced disease (i.e. individuals from low socioeconomic groups or others without access to medical care), and are often insufficiently active.

3. Conduct studies to test effect modification by age on the associations between physical activity and cancer risk.

   Rationale: Some evidence suggests that risk for some cancers such as colon and breast is increasing in younger age groups, who are also less active today than in previous generations. It would be important to know whether physical activity can be protective in this younger age group.

4. Conduct epidemiologic studies, preferably prospective cohort studies, to determine effects of specific types of physical activity on cancer risk.

   Rationale: Few data are available on the associations of specific activities on cancer risk. It would be useful to know whether moderate-intensity activities such as walking are sufficient to provide protection. Also, insufficient data exist on associations of other activities such as muscle-strengthening activity on cancer risk.

   Conduct epidemiologic studies, preferably prospective cohort studies, to more precisely determine dose-response effect of physical activity on cancer risk.

   Rationale: All data in available studies have been from self-reported recall of usual activities. Collecting data with device-based measures of activity will be important, as will determining precise measures of dose of activity.

5. Conduct randomized controlled clinical trials testing exercise effects on cancer incidence.

   Rationale: All available data are from observational studies, which could suffer from confounding effects of other variables. Randomized trials in high risk individuals could be more cost-effective, as trials with smaller sample sizes or shorter follow-up durations might be feasible.

CHAPTER 5. CARDIOMETABOLIC HEALTH AND PREVENTION OF WEIGHT GAIN

1. 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, hypertension, and type 2 diabetes across a wider spectrum of exposure.

   Rationale: Only limited evidence is currently available on the effect of physical activity less than 150 minutes per week on prevention of weight gain, hypertension, and type 2 diabetes. Thus, limited data are currently available to inform whether lower amounts of physical activity can be effective for preventing these conditions. Having this knowledge is important and will inform public health recommendations regarding the minimum physical activity exposure that can be effective for preventing weight gain or the development of obesity, hypertension, and type 2 diabetes.

2. 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, hypertension, and type 2 diabetes varies by age, sex, race/ethnicity, socioeconomic status, or initial weight status.

   Rationale: Only limited evidence is currently available on whether the influence of physical activity on weight gain or risk of hypertension or type 2 diabetes 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. Having this information will inform public health recommendations regarding whether physical activity exposure to prevent weight gain 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. 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 varies by these factors.

3. 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, hypertension, and type 2 diabetes.

Rationale: Limited evidence is available on whether the influence of physical activity on weight gain, hypertension, or type 2 diabetes 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, hypertension, or type 2 diabetes 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.

4. 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.

   Rationale: The majority of the studies examined regarding weight gain either did not report that diet and eating behavior were measured or considered in the analysis. Given that both dietary factors, primarily energy intake, and energy expenditure from physical activity can influence body weight regulation, it is important to understand whether the physical activity exposure necessary to limit weight gain will vary based on diet or eating behavior patterns.

5. Within research that is conducted, disclose the standard criteria and methods that were used to determine the blood pressure status of the study sample to better isolate samples with hypertension from those with normal blood pressure and prehypertension, and report results separately by blood pressure classification.

   Rationale: Strong evidence demonstrates the magnitude of the blood pressure response to physical activity varies by resting blood pressure, with greater benefits occurring among adults with prehypertension than normal blood pressure. However, study samples often include mixed samples of adults with hypertension, prehypertension, and normal blood pressure, and findings are frequently not reported separately by blood pressure classification. Consistent with the law of initial values, this practice underestimates the blood pressure benefits of physical activity. In addition, samples with prehypertension are underrepresented as they are often mixed with samples with hypertension. Reporting findings by blood pressure classification will inform public health recommendations on the magnitude and precision of the blood pressure reductions that result from physical activity among adults with normal blood pressure and prehypertension.

6. Conduct randomized controlled trials to examine the influence of types of physical activity other than aerobic, dynamic resistance, or combined aerobic and dynamic resistance physical activity on blood pressure and other health outcomes among adults with normal blood pressure and prehypertension.

   Rationale: Limited evidence on these topics is available among adults with normal blood pressure and prehypertension. Gaining this information will inform the public health recommendations on the types of physical activity that optimize blood pressure benefit.

7. Conduct experimental research that examines both the acute (i.e., short-term or immediate, referred to as postexercise hypotension) and the chronic (i.e., long-term or training) blood pressure response to physical activity among adults with prehypertension and normal blood pressure.

   Rationale: Insufficient evidence exists on the acute blood pressure response to physical activity despite primary-level reports suggesting a close relationship between the blood pressure response to acute and chronic exercise. Developing a better understanding of acute blood pressure responses will inform public health recommendations on possible behavioral strategies to increase adherence to physical activity for blood pressure benefit.

8. Conduct observational and experimental research examining the relationship between physical activity and blood pressure using the 2017 *Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults* new blood pressure classification scheme.[2]

   Rationale: The literature that was reviewed to answer this question was based upon The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)[3] blood pressure classification scheme. The new guideline increases the number of people with hypertension, eliminates the category of prehypertension, and adds the category of elevated blood pressure. The relationship between physical activity and blood pressure according to this new blood pressure classification scheme remains to be determined.

CHAPTER 6. ALL-CAUSE MORTALITY AND CARDIOVASCULAR DISEASE

Several advances in our understanding of the relationships among physical activity and these outcomes have occurred since the Physical Activity Guidelines Advisory Committee Report, 2008.[4] Most of the literature upon which the conclusions were based used survey data and questionnaire data; physical activity exposures were assessed using self-reported estimates of time spent in aerobic continuous moderate-to-vigorous physical activity accumulated in bouts of at least ten minutes. Therefore, all other components across the physical activity spectrum—sedentary behavior, light-intensity physical activity, and any moderate-to-vigorous physical activity in bouts less than 10 minutes –was considered "baseline" physical activity. Researchers have begun to incorporate device-based measures of physical activity into their 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 effects of episodes of moderate-to-vigorous physical activity of less than 10 minutes on health outcomes. These issues are addressed in *Part F. Chapter 1. Physical Activity Behaviors: Steps, Bouts, and High Intensity Training*.

More research is needed in these areas:

1. Conduct research on the role of light intensity physical activities 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 or wearables) to measure physical activity into all clinical drug trials with all-cause mortality, cardiovascular disease mortality, or incident cardiovascular disease as outcomes.

   Rationale: As reported in this chapter, the benefits of moderate-to-vigorous physical activity on all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease (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 in intensity (i.e., light intensity). The development of device-based measures of physical activity (pedometers, accelerometers, and other wearables) provides the scientific imperative to begin to explore the relations of all intensities and amounts of physical activity—light- to vigorous-intensity; small to

large total amounts. These studies are beginning to appear.[5-9] Unfortunately, there are not enough studies on the relation of light-intensity physical activity, total physical activity, or step counts per day to provide enough information for meta-analyses to be performed in these areas for the outcomes of interest here. Therefore, this is a major future research need in this area.

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

   Rationale: Whether high 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[10, 11]; however, there seems to be a U-shaped relationship with life-long volume of training.[11] These findings may explain the hint of an increased cardiovascular risk in long-term athletes. Clearly, this issue demands more study in athletic populations.

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

   Rationale: The second edition of the Scientific Report continues to rely on studies of aerobic ambulatory moderate-to-vigorous physical activity, primarily collected via survey, to understand the relationship of physical activity to all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease. 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 equally to 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 individuals who want to exercise for health, we need better understanding of the relative contributions of a general range of options.

CHAPTER 7. YOUTH

1. 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 in children and adolescents at each developmental stage.

   Rationale: Few studies have been designed to directly examine dose-response relationships between physical activity and health outcomes in young persons. This gap constitutes a major limitation in the process of identifying the types and amounts of physical activity needed to produce health benefits at each developmental stage.

2. Undertake randomized controlled trials and prospective observational studies to determine whether the health effects of physical activity during childhood and adolescence differ across groups based on sex, age, maturational status, race/ethnicity, and socioeconomic status.

   Rationale: Few studies have been designed to directly examine the extent to which the health effects of physical activity may differ across demographic subgroups. This gap substantially limits the ability to determine whether the dose of physical activity needed to produce health benefits varies across population sub-groups. Studies aimed at elucidating the extent to which race/ethnicity modifies the effects of physical activity on health outcomes should consider social, cultural, and biological factors that may influence an effect modifying role of race/ethnicity.

3. Conduct experimental and prospective observational studies to examine the health effects of physical activity in children and adolescents with elevated risk status based on adiposity, cardiometabolic health, and bone health.

   Rationale: Most children and adolescents fall within the normal, healthy range on key health indicators, and consequently increased physical activity is unlikely to enhance their already normal status. However, children at elevated risk may manifest improved status with increased physical activity. A considerable volume of research has been conducted in children and adolescents with overweight and obesity, but more research is needed with young persons who have elevated cardiometabolic and bone health risk.

4. Examine the effects of novel forms of physical activity, including high intensity interval training and exergaming, on health outcomes in youth. Both experimental and prospective observational studies should be conducted.

   Rationale: Certain forms of physical activity are particularly prevalent among children and adolescents, and more research is needed to determine the extent to which these forms of physical activity affect key health outcomes.

5. Develop valid instruments for measuring physical activity and examine the health effects of physical activity in very young children between birth and 2 years.

   Rationale: In part because of a lack of validated measures of physical activity in very young children, knowledge of the relationship between physical activity and health outcomes in children between birth and age 2 years is very limited.

6. Undertake studies, using longitudinal research designs, to examine the relationship between specific forms of sedentary behavior (e.g., sitting time, screen time) and health outcomes in children and adolescents using both self-report and device-based assessment of sedentary behavior.

   Rationale: Current research on the relationship between sedentary behavior and health is limited by a dearth of studies using device-based measures of time spent in sedentary behavior. Many studies have focused on television viewing as an indicator of sedentary behavior, but television viewing is confounded by exposures other than sedentary time. Research is needed to differentiate between the health effects of time spent sedentary and time spent in specific behaviors that typically include sedentary time.

7. Conduct intervention studies to test the effects of reducing sedentary behavior on health outcomes in children and adolescents.

   Rationale: Very few studies have examined the health effects associated with reduction of time spent in sedentary behavior among children and adolescents. The findings of such studies would inform the process of identifying the levels of time spent in sedentary behavior that may be associated with negative health outcomes. Further, these studies would determine the extent to

which reduction of time spent in sedentary behavior influences time spent in moderate-to-vigorous and light-intensity physical activity.

8. Examine the interactive effects of sedentary behavior and physical activity of varying intensities on health outcomes in children and youth.

   Rationale: The relationship between physical activity and health outcomes in children and adolescents may be modified by amount of time spent in sedentary behavior. That is, youth who spend large amounts of time in sedentary behavior may require higher levels of physical activity to produce a particular health outcome. Studies should be undertaken to directly examine this issue.

9. Undertake prospective observational studies to examine the effects of physical activity during childhood and adolescence on health outcomes later in life.

   Rationale: Large-scale cohort studies that have followed children into adulthood and have used state-of-the-art measures of physical activity are rare, particularly in the United States. Accordingly, knowledge of the long-term impact of physical activity status early in life on health outcomes later in life is very limited. Further, the findings of such studies could inform development of physical activity guidelines for individuals in transitional periods, such as early adulthood.

10. Determine in children and adolescents the impact of genetic profiles on behavioral and physiological responses to physical activity and on the health effects of physical activity.

    Rationale: Studies in adults have shown that the health effects of physical activity are moderated by genetic profile such that a given dose of physical activity produces widely varying effects on indicators of health. Our knowledge of the relationship between physical activity and health in children and adolescents would be enriched by undertaking similar studies in young persons. Such studies could expand knowledge of how genes and the environment may interact in influencing indicators of health in young persons.

CHAPTER 8. WOMEN WHO ARE PREGNANT OR POSTPARTUM

1. Conduct observational and experimental studies of the effects of vigorous-intensity physical activity before and during pregnancy on maternal and fetal outcomes.

   Rationale: The safety and benefits of moderate-intensity physical activity during pregnancy and the postpartum period are now generally accepted. The safety and benefits of vigorous-intensity (absolute and perceived) physical activity are less well-documented and this type of activity may be discouraged by some health care providers. For women who have not been physically active, a program of moderate-intensity physical activity would be recommended. On the other hand, substantial numbers of women participate regularly in vigorous physical activity (e.g., running, stationary cycling, rowing) before pregnancy and 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 and maximal threshold levels for safety.

2. Continue to conduct large-scale observational studies to investigate longitudinally the relationship between various types and volumes of physical activity before and during pregnancy and during the postpartum period on short- and long-term weight status.

   Rationale: Although it is established that habitual moderate-intensity physical activity of a volume in the recommended target zone is associated with reduced weight gain during pregnancy, information about the relationship between various types and volumes of physical activity and weight change during pregnancy and the postpartum period would help guide the development of clinical and public health recommendations.

3. Conduct experimental and observational studies to investigate the effects of various types, intensities, and volumes of regular physical activity on quality of life and symptoms of anxiety and depression and during pregnancy, and quality of life and symptoms of anxiety during the postpartum period.

   Rationale: Although strong evidence demonstrates that regular moderate-intensity physical activity reduces depressive symptoms during the postpartum period, little information exists about the role of physical activity on perceived quality of life and symptoms of anxiety and depression symptoms during pregnancy and quality of life and symptoms of anxiety during the postpartum period.

Emerging evidence suggests that maternal mental health affects the health of the developing fetus. Knowledge about the benefits of even low doses of physical activity, as well as about the benefits of various modes of physical activity for women with anxiety or depression can help to promote a healthy pregnancy for both mother and fetus.

4. Conduct experimental and observational studies to determine the influence of regular physical activity on quality of sleep during pregnancy and the postpartum period.

   Rationale: Although regular physical activity is known to improve sleep and feelings of quality of life in the general population, little is known about the effect of regular physical activity on quality of sleep during pregnancy and the postpartum period. Getting enough sleep, especially during the postpartum period, is a common problem for new mothers. If women during pregnancy and postpartum benefit from acute episodes and regular participation in physical activity as do those in the general population, it could improve overall level of energy and quality of life.

5. Conduct large observational studies to determine whether specific types, intensities, and doses of physical activity affect maternal and fetal outcomes, such as preterm birth, low birth weight, and preeclampsia differentially.

   Rationale: Most of the experimental research on physical activity during pregnancy relies on the 2008 Physical Activity Guidelines[12] or the 2015 American College of Obstetricians and Gynecologists[13] recommendations of 150 minutes per week 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. The veracity of the observation needs to be determined, and, if confirmed, it will be important to determine whether the results are caused by the nature of the activities or the setting or perhaps other confounding factors (socioeconomic status, education level, age). Observing the impact of varying types, intensities, and doses of physical activity in varying domains (leisure-time, occupational, household, transportation) on a range of maternal and fetal outcomes would significantly advance current knowledge and inform both clinical and public health practice.

6. Conduct observational and/or experimental research that has adequate statistical power to determine whether the associations between physical activity and maternal or fetal outcomes vary by age, race/ethnicity, socioeconomic status, or weight status.

   Rationale: Most of the studies reviewed in this report were not designed or powered to test for effect modification by various sociodemographic factors or by body weight. Such information is important for making more specific physical activity recommendations for various population sub-groups in efforts to reduce health disparities among pregnant women.

CHAPTER 9. OLDER ADULTS

1. Conduct large-scale randomized controlled trials of older adults at high risk of falls designed with fall-related injuries and bone fractures as the primary outcomes of interest.

   Rationale: The incidence of fall-related injury or bone fracture is typically a secondary outcome of interest for randomized controlled trials designed to assess the effect of physical activity on the rate of falling. This issue results in insufficient sample sizes across studies to assess injurious falls and fractures, increases the potential for selection or information bias, and results in inadequate collection of pertinent injury-related data.

2. Conduct large observational and experimental studies to investigate further the dose-response relationships between physical activity (aerobic, muscle-strengthening, balance, and multicomponent) and fall-related injuries and bone fractures.

   Rationale: Currently, little information is available regarding the dose-response relationship between physical activity and fall-related injuries in older adults. Such information in necessary for setting minimum activity thresholds for effectiveness and maximum thresholds for safety.

3. Conduct large-scale randomized controlled trials comparing various doses of balance training and muscle-strengthening training on physical function in the general population of older people.

   Rationale: Little information is currently available on the amount of balance and muscle-strengthening training necessary to maintain or to improve physical function among generally healthy older people. Such information is important for attenuating the aging-related decline in

physical function, thereby delaying the onset of frailty and maintaining physical independence in aging.

4. Conduct large-scale randomized controlled trials to determine the effects of tai chi, qigong, dance, active video gaming, and yoga on physical function in healthy older adults, as well as those with different chronic conditions.

   Rationale: These activities have only recently been considered as effective strategies for maintaining and improving physical function in older people. These forms of physical activity may be especially beneficial for those with already-existing chronic disease and/or limitations to mobility. Such research should address: 1) the types or modes of such activity that are most effective for specific chronic conditions; and 2) the minimal effective doses of these activities for improving physical function.

5. Conduct prospective cohort studies of physical activity and physical function in older adults that include objective measures (e.g., heart rate monitors) of relative intensity of activity.

   Rationale: The relationship of relative versus absolute intensity to the health benefits of regular physical activity remains unclear. Epidemiologic (i.e., observational) studies using objective monitoring would: 1) allow for more robust analyses of how intensity affects health benefits, and 2) facilitate integration of findings from observational studies (which typically measure intensity of activity using absolute intensity) with those from randomized controlled trials (which typically measure intensity of activity using relative intensity).

6. Conduct more meta-analyses with meta-regressions to determine the extent to which the heterogeneity of results often observed among different studies of physical activity and physical function can be explained by variation in the tests used to measure physical function.

   Rationale: Composite measures of physical function (such as the combination of measures resulting in a single score used in the Diong et al[14, 15] paper) tend to result in stronger effect sizes with physical activity, compared with single measures. This may be due to the fact that physical function comprises a constellation of attributes that may not be adequately captured by a single measure. Moreover, comparison among studies is difficult due to differences in how physical function is characterized and assessed (performance measures versus self-reported activities of daily living

function or quality of life). Such meta-analyses would allow investigators to derive a single best composite measure to be used consistently in future studies of physical function.

7. Conduct more experimental research on dual-task training that clearly describe the dual-task training procedures and the parameters of the secondary task. In addition, these studies should provide evidence of whether dual-task costs were reduced by training and whether dual-task training transfers to untrained tasks.

   Rationale: Dual-task training is a relatively new area of research in aging, and the methodologic quality of the studies reviewed for this report ranged from poor to moderate. To ensure internal validity and reproducibility, future research in this area should provide as much detail as possible in describing the methods and should consider multiple outcome tasks (trained and untrained) in the analysis.

8. Conduct large-scale randomized controlled trials and/or meta-regression analyses to establish dose-response effects of aerobic and resistance training on physical function for people with chronic obstructive pulmonary disease, frailty, osteoporosis, cognitive impairment, Parkinson's disease, visual impairments, and following hip fracture or stroke.

   Rationale: Currently, little information is available regarding the dose-response relationship between aerobic and strengthening activities and physical function in specific vulnerable subgroups of older adults. These modes of activity are proven effective in minimizing the age-related decline in physiological reserve and function among the general aging population, and thus may be especially important for older people with chronic conditions that limited their mobility. Such information in necessary for setting minimum activity thresholds for effectiveness and maximum thresholds for safety.

9. Conduct large-scale randomized controlled trials to investigate the optimal dose and mode of physical activity necessary to improve and maintain balance function and reduce injury-related falls and fractures in persons with frailty, hip fracture, osteoporosis, Parkinson's disease, visual impairments, and stroke.

Rationale: Balance is essential for maintaining physical function and mobility, particularly among people with existing functional and mobility limitations due to frailty, osteoporosis, Parkinson's disease, visual impairments, or following hip fracture or a stroke. Currently, little information is available regarding the types or optimal dose of exercise for improving balance function. Such information in necessary for setting minimum activity thresholds for effectiveness and maximum thresholds for safety.

10. Conduct large-scale randomized controlled trials with 6- and 12-month post-intervention follow-up assessments to determine the effects of physical activity on activities of daily living mobility, instrumental activities of daily living, free-living physical or ambulatory activity and social participation for older individuals with chronic disease. These individuals are at accelerated risk of functional decline, disability, and social isolation.

    Rationale: Little evidence currently exists on how improvements in strength, balance, and endurance following a physical activity intervention to improve physical function translate into everyday improvements in activities of daily living function and social participation, especially after the formal intervention period is over. Such knowledge would provide important information on how improvements in physiologic function can contribute to and sustain certain behavioral aspects of healthy aging (such as self-care, independence, social engagement) and quality of life.

11. Conduct large cohort and experimental studies to determine the dose-intensity and timing of physical activity necessary to prevent functional decline or to improve physical function across the spectrum of cognitive dysfunction and dementia.

    Rationale: Limited evidence currently exists about the impact of physical activity training on physical function limitations that often co-occur with cognitive dysfunction and dementia. Cognition and mobility are intimately linked, and improving physical function through physical activity in a cognitively impaired population might have broad effects for independence and activities of daily living.

12. Conduct large-scale observational or experimental studies with adequate statistical power to determine whether the relationship between physical activity and risk of fall-related injuries or loss of physical function in older people varies by race/ethnicity, sex, socioeconomic status, or level of existing impairments across the aging spectrum.

    Rationale: The vast majority of available research has been conducted on older white women, thereby limiting the generalizability of the findings to this demographic subgroup alone. Moreover, the potential impact of these influential factors often is not considered in statistical analyses, thus limiting the ability to determine whether effect modification exists at all. Results from this type of research would provide stronger scientific foundations for local, state, and national government, medical, and community wellness entities committed to reducing possible health disparities among various demographic sectors. This research would also support public and private partners in developing effective physical activity programs and policies to help individuals maintain their health and function through older age.

CHAPTER 10. INDIVIDUALS WITH CHRONIC CONDITIONS

This section is organized into two parts. First, five cross-cutting needs for research are discussed that integrate similar research needs relevant to more than one chronic condition (involving conditions reviewed by this chapter or chronic conditions generally). Then, research needs specific to each chronic condition are listed. Research needs within each topic area are listed in order of priority. .

Priority Research Needs on Preventive Effects of Physical Activity in Individuals with Chronic Conditions

For the five research priorities in this section, research designs should generally include and compare self-report and device-based measures of physical activity. All the questions in this chapter found insufficient evidence to determine whether method of measurement of physical activity influences reported relationships between physical activity and health outcomes.

1. Conduct research on how characteristics of aerobic activity, muscle-strengthening activity, balance training, and combined activity (e.g., dose, duration, intensity, frequency, and type) influence the relationship between physical activity and health outcomes in individuals with chronic conditions.

Rationale: A basic element of public health recommendations in physical activity is to specify the frequency, duration, intensity, types, and amounts of physical activity that provide health benefits. Hence, it is remarkable that the reviews of this chapter provided so few data on how these characteristics of physical activity influence health effects. For example, in osteoarthritis, no reviews were located comparing the relative effects of different types of physical activity or of different amounts of physical activity. Yet this chapter has some provocative findings illustrating the importance of research in this area. For example, in type 2 diabetes, research indicated: (1) muscle-strengthening activity and aerobic activity have independent effects on hemoglobin A1C (indicating the importance of combined activity), and (2) vigorous-intensity activity is more efficient in lowering hemoglobin A1C (larger effect on hemoglobin A1C for a given volume of aerobic activity) than moderate-intensity activity. The increased interest in health benefits of light-intensity activity makes it an even higher priority to conduct randomized trials comparing different intensities and types of physical activity, and to conduct long-term cohort studies that provide dose-response data. For uncommonly performed types of activity (e.g., balance training), cohort studies are not feasible, so dose-response randomized trials are needed. To some extent, such as in individuals with hypertension, studies are needed to understand how characteristics of physical activity influence acute physiologic and health effects of activity.

2. Conduct research in individuals with chronic conditions on the effects of physical activity in reducing risk of developing additional chronic conditions (co-morbidities).

   Rationale: The introduction of this chapter explains the public health importance of preventing multiple chronic conditions. In essence, as the number of chronic conditions afflicting a person increases, generally physical function worsens, health-related quality of life decreases, and cost of medical care increases. Despite a broad search for preventive effects of physical activity on reduced risk of any co-morbid condition, this chapter could make only a few conclusions related to prevention of co-morbidity. This lack of evidence is despite higher risk of co-morbid conditions in some chronic diseases, as illustrated by the higher risk of cardiovascular disease in individuals with spinal cord injury. Whereas the incidence of a few chronic conditions may be high enough to study in randomized controlled trials, generally prospective cohort studies are needed of long-term effects of physical activity on risk of common co-morbidities.

3. Conduct research on the secondary prevention effects of physical activity in individuals with chronic conditions, that is, research on how physical activity reduces risk of progression of the chronic condition and mitigates the effects of the chronic condition on physical function and health-related quality of life.

   Rationale: The amount of information located on secondary prevention by the evidence reviews varied substantially by chronic condition. Except for osteoarthritis, in individuals affected by the chronic conditions of this chapter, high-quality randomized controlled trials of effects of exercise on physical function and health-related quality of life are needed, including longer term studies (e.g., 4-6 months) that have adequate statistical power. For effects of physical activity on progression, generally prospective cohort studies are needed. For example, cohort studies are needed on effects of physical activity in type 2 diabetes on risk of neuropathy, nephropathy, retinopathy, and foot disorders.

4. Conduct systematic and coordinated randomized controlled trials on the health effects of tai chi, qigong, and yoga in individuals with chronic conditions.

   Rationale: With one exception (osteoarthritis), the evidence for health benefits of tai chi, qigong, and yoga was rated as insufficient by the evidence reviews of this chapter. Although randomized controlled trials of these forms of physical activity were located, often they were few in number, small, and/or of low methodologic quality. Although higher quality randomized controlled trials of these types of physical activity are a priority, it is important that such trials be conducted in a systematic and coordinated fashion. Currently, the types and forms of these physical activity types studied in trials vary substantially, as do reported effects. Public health guidelines need to specify details about physical activity—in this case for each exercise type, to specify the specific movements and minimal dose that are effective in improving health. Such information is not currently available, and systematic and coordinated randomized controlled trials are necessarily to provide this information.

5. Conduct research on whether or not individual characteristics influence the effects of physical activity interventions on health outcomes in individuals with chronic conditions.

Rationale: The evidence reviews of this chapter found little information on whether or not the effects of physical activity vary by individual characteristics, such as age, sex, race/ethnicity, body weight, socioeconomic status, and severity of the chronic condition. The importance of such information is illustrated by findings in type 2 diabetes. The evidence suggested effects of physical activity on hemoglobin A1C were larger in individuals with the highest levels of hemoglobin A1C, thus emphasizing those at higher risk of progression with more severe disease were not less likely to benefit from physical activity. From the standpoint of evidence needed for public health guidelines, this is a lower priority need for research because beneficial effects of physical activity have been demonstrated across a wide variety of populations. However, it is desirable for prevention guidelines be appropriately tailored to individuals. Thus, this topic remains a research priority.

Priority Research Needs on Preventive Effects of Physical Activity in Individuals with a Specific Chronic Condition

Question 1: Cancer Survivors

6. 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 effects of physical activity on recurrence and survival.

   Rationale: Although survival from breast cancer is improving, the risk of mortality continues for 20 years or more, especially for women with hormone receptor positive tumors. Survival from prostate cancer tends to be long-term for most men, but for some, progression occurs in spite of optimal treatment. Furthermore, many men with prostate cancer have increased risk for cardiovascular disease, and the primary cause of death in these patients is cardiovascular disease. Therefore, the effect of physical activity on long-term all-cause mortality in prostate cancer survivors will need to be assessed. Colorectal cancer survival is increased with lower stage at diagnosis, and many individuals survive long-term. However, little is known about effects of physical activity on long-term colorectal cancer survival. Continued follow-up of large cohorts will allow for identification of individuals with less common cancers, who can then be followed to determine associations between physical activity level and survival from these other cancers.

7. Conduct randomized controlled trials and cohort studies of physical activity and cancer survival, recurrence, and second primary cancer, aimed at eliminating effects of possible confounders.

Rationale: Treatment type, adherence, and completion are strong predictors of cancer outcomes and can reduce physical activity levels. Fatigue from the cancer and its treatments can reflect adverse clinical processes, and can also reduce physical activity interest and ability. Therefore, randomized controlled trials to test the effect of physical activity on survival, recurrence, and second primary cancer are needed. In addition, cohort studies with appropriate adjustment for clinical sources of confounding can provide additional information, especially if randomized controlled trials are not feasible.

8. Conduct prospective cohort studies and randomized controlled trials to determine effects of physical activity on cancer survival, recurrence, and second primary cancer in understudied groups, such as survivors from diverse races, ethnicities, and socioeconomic groups; individuals with metastatic cancer; men with breast cancer; individuals with cancers other than breast, colorectal, and prostate cancer; and patients treated with cardiotoxic drugs (such as doxorubicin and trastuzumab), radiotherapy, and hormonal treatments.

   Rationale: Few studies have investigated the effects of physical activity on cancer prognosis and survival within specific race, ethnic, or socioeconomic groups. Some of these groups have high risk for poor survival, and are also less likely to meet recommended levels of physical activity. Therefore, determining whether physical activity can improve survival and reduce recurrence and second primary cancers in specific groups is important. Patients treated with cardiotoxic drugs, radiotherapy, or hormonal therapies may have increased risk for cardiac events; it is not known whether physical activity could be cardioprotective in such patients, or whether some forms of physical activity could increase risk of cardiac events.

Question 2: Osteoarthritis

9. Conduct prospective cohort and longer-term randomized controlled trials on osteoarthritis disease progression, with device-based measures used to quantify physical activity exposures and with molecular and imaging disease status biomarkers as outcomes.

   Rationale: There is great confusion in the field on whether physical activity and exercise causes osteoarthritis in the absence of underlying injury and whether specific physical activity and exercise exposure amounts and intensities lead to disease progression. Studies are needed to address these critical issues. Because it takes years for disease activity to result in structural, detectable

radiographic changes in the joint, sophisticated imaging modalities, such as magnetic resonance imaging, and biological biomarkers of disease activity (circulating systemic or intra-articular) are required to measure the outcomes.

10. Conduct research to clarify how osteoarthritis progression is modified by baseline demographic and disease characteristics**.**

    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 body mass index and osteoarthritis is generally recognized, no studies have investigated through meta-analyses whether body mass index modifies the physical activity-osteoarthritis relationship.

11. Conduct direct head-to-head comparisons of the relative effectiveness of physical activity and analgesics for pain control in individuals with osteoarthritis.

    Rationale: The current review of the literature revealed that the effect sizes of pain control for exercise therapy is very similar to that of analgesics, including narcotic analgesics.[16] If true, this would be a critical observation with profound implications for patient care, especially as the effects of physical activity on osteoarthritis-related pain seem to be durable for up to six months following cessation of an intervention. Determining the comparative effects of physical activity and analgesics on osteoarthritis pain could contribute greatly to effective clinical management of osteoarthritis.

Question 3: Hypertension

12. Conduct research in people with hypertension on the relationships among physical activity and risk of co-morbid conditions, physical function, health-related quality of life, and cardiovascular disease progression and mortality, which compares effects of physical activity in African Americans to effects in other racial/ethnic groups.

    Rationale: Due to the disproportionate burden of hypertension among African Americans, large trials are needed that are sufficiently powered to perform stratified analyses between African Americans and other racial/ethnic groups. Gaining this information will inform public health recommendations about demographic characteristics that influence the relationship between

physical activity and blood pressure, and provide insight into the populations that will experience the greatest cardiovascular health benefits from physical activity.

13. Conduct research that discloses the standard criteria and methods that were used to determine the blood pressure status of the study sample to better isolate samples with hypertension from those with normal blood pressure and prehypertension.

    Rationale: Limited evidence suggests the magnitude of the blood pressure response to physical activity varies by resting blood pressure level, with the greatest blood pressure reductions occurring among adults with hypertension that have the highest resting blood pressure levels. Study sample often include mixed samples of adults with hypertension, prehypertension, and normal blood pressure, and findings are frequently not reported separately by blood pressure classification. Consistent with the law of initial values, this practice underestimates the antihypertensive benefits of physical activity. Reporting findings by blood pressure classification will inform public health recommendations on the magnitude and precision of the blood pressure reductions that result from physical activity among adults with hypertension.

14. Conduct research that discloses and quantifies medication use, particularly antihypertensive medication use among samples with hypertension.

    Rationale: Medication use is poorly reported and is a significant confounder in interpreting the clinical significance of the blood pressure response to physical activity. In addition, evidence is lacking on the interactive effects of physical activity and antihypertensive medication use, another important clinical outcome on that has insufficient evidence. Gaining this information is important to determine whether the influence of physical activity on blood pressure varies by antihypertensive medication use.

Question 4: Type 2 Diabetes

15. Conduct randomized controlled trials comparing the effects of shifting time from sedentary behavior to low-intensity aerobic activity, moderate-intensity aerobic activity, low-intensity muscle-strengthening activity, and moderate-intensity muscle-strengthening activity on indicators of risk of progression of type 2 diabetes.

Rationale: Evidence is growing of the benefits of reducing sedentary behavior, particularly in individuals with chronic conditions affecting metabolic health. Research is needed on whether shifting sedentary time to light-intensity activities affects progression of type 2 diabetes. If light-intensity activities are beneficial, it is important to compare the efficiency and effectiveness of light-intensity versus moderate-intensity activity. Given the well-documented health benefits of shifting time to moderate-intensity aerobic and muscle-strengthening activities, randomized controlled trials are needed that answer questions such as: Does it require shifting, say, 2 to 3 hours from sedentary to light-intensity activity to obtain the same benefits? Or does it take more like 6 to 8 hours?

16. Conduct randomized controlled trials of fall prevention exercise in adults with type 2 diabetes who are at increased risk of falls and fall injuries.

    Rationale: A major finding in the Older Adults chapter (see *Part F. Chapter 9. Older Adults*) is that fall prevention exercise programs can substantially reduce risk of serious fall injuries in the general aging population. However, the risk factor profile for falls in adults with type 2 diabetes may differ substantially from the profile in the general population, due to effects specific to type 2 diabetes-related on fall risk factors (e.g., neuropathy, myopathy, impaired vision, and foot disorders). The search for evidence located one small review of fall prevention programs in type 2 diabetes. Thus, RCTs are needed on effects of fall prevention exercise in individuals with type 2 diabetes at increased fall risk.

Question 5: Multiple Sclerosis

17. Conduct randomized controlled trials to determine the effects of physical activity on basic and instrumental activities of daily living, participation, and community engagement for individuals with multiple sclerosis.

    Rationale: Strong evidence now exists that greater physical activity can improve walking function, strength, and fitness for individuals with multiple sclerosis. This supports a rationale for further research to determine whether this translates into improved basic and instrumental activities of daily living, increased free-living physical activity, and improved safety in mobility.

18. Conduct longitudinal cohort studies to determine the potential for physical activity to serve as a moderator of disease progression and changes in brain health in individuals with multiple sclerosis.

Rationale: Systematic reviews of controlled studies find no evidence that physical activity alters disease progression, in contrast to epidemiological studies that indicate possible disease-modifying effects.[17] However, these controlled studies are limited by relatively brief intervention lengths, small sample sizes, and lack of measures of brain disease activity; factors that multi-site studies of disease-modifying medications show are needed to fully explore the natural history of multiple sclerosis. This discrepancy between epidemiological and controlled studies, and bench neuroscience findings that physical activity can provide neuroprotective effects and stimulate neuroplasticity, including for brain white matter, support a rationale for further research into disease modification.

Question 6: Spinal Cord Injury

19. Conduct randomized controlled trials in children and adolescents with spinal cord injury to determine effects of physical activity on psychosocial and social environmental development and participation.

    Rationale: A knowledge gap exists regarding health benefits in this population, which differs from adults in terms of mechanisms for injury and greater potential for neuroplasticity and recovery. Future research in pediatric spinal cord injury is needed to determine age-appropriate modalities and prescriptions for physical activity to facilitate recovery of mobility, optimize functional recovery and independence in daily activities, prevent or reduce comorbid and secondary complications, and optimize psychosocial and psychological development across the formative childhood and adolescent years.

20. Conduct research in individuals with spinal cord injury to determine effects of physical activity on basic and instrumental activities of daily living, free-living physical activity, social participation and engagement, balance and risk for injurious falls and fractures**.**

    Rationale: The evidence in this report that selected modes of physical activity can produce clinically significant improvements in physical function supports a rationale for randomized studies to determine whether such gains translate into improved daily function, participation, and engagement in activities in the living space and social environment. Systematic analyses of relationships between age, race/ethnicity, socioeconomic status, and weight status need to be built into all such research recommendations. Generally, randomized controlled trials are necessary to address the research need.

Question 7: Intellectual Disabilities

21. Conduct randomized controlled trials to determine the effects of physical activity on cognitive function, neurodevelopmental profiles, instrumental activities of daily living, and adaptive functioning that are related to neuropsychological status in individuals with intellectual disabilities.

    Rationale: Only limited evidence is available on the effects of physical activity on four important outcomes in people with intellectual disabilities: cognitive function, neurodevelopmental profiles, instrumental activities of daily living, and adaptive functioning. Randomized studies are needed to determine whether physical activity can improve cognition for individuals with intellectual disabilities across the age spectrum. Likewise, future research is needed to investigate effects of greater physical activity on neurodevelopment and adaptive functioning. In addition, research should also consider these broader outcomes in an age- and intellectual disability-specific fashion.

22. Conduct randomized controlled trials and cohort studies on effects of physical activity in individuals with a variety of etiologies for intellectual disabilities, and determine whether health effects vary by age, race/ethnicity, socioeconomic status, and weight status.

    Rationale. As the most common genetic cause of intellectual disability in the United States, Down syndrome has received the most research attention. Major gaps exist on the potential health benefits of physical activity in most other conditions, including autism spectrum disorder and autistic traits, Fragile X syndrome, tuberous sclerosis, neurologic sequelae of toxins (e.g., alcohol, lead), maternal and fetal infections, and nutritional deficiencies (e.g., iodine, protein-calorie malnutrition), and neurological sequelae associated with prematurity. Future research is needed to address race/ethnicity, socioeconomic status, and weight status as factors that influence relationships between physical activity and health outcomes for individuals with disabilities.

CHAPTER 11. PROMOTING REGULAR PHYSICAL ACTIVITY

The evidence review in this chapter highlights a number of research needs across the different intervention areas highlighted in the review. It should be noted, however, that given that the evidence review was not comprehensive, a number of other intervention areas were not captured in this evidence review that also undoubtedly merit further research.

In light of some unique aspects of scientific intervention development specific to the Information and Communication Technologies area, the research needs that are broadly applicable to all topic areas contained in this chapter are presented first, followed by an additional set of research needs specific to the fast-growing information and communication technologies intervention arena.

Research Needs that are Broadly Applicable to All Topic Areas Presented in this Chapter

1. Broaden enrollee targets in randomized controlled trials and other research in this area to incorporate 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).

   Rationale: In order to develop interventions that have the potential for having a public health impact at the population level, it is critical to ensure that diverse age, sex, racial/ethnic, cultural, geographic, and income groups are included in the experimental research designs that can most effectively advance the field. Data collected across these various subgroups of the population will inform how to adapt interventions to subgroup needs through formative and iterative intervention design methods, and can help strengthen interventions through ensuring that they are targeted effectively for specific subgroups as well as tailored to individual preferences and requirements.

2 Test physical activity and sedentary behavior interventions over longer time periods (i.e., more than 12 months) to better understand how to sustain their positive effects.

   Rationale: Because many of the positive health effects of regular physical activity and reduced sedentary time can accumulate over time and require regular engagement across time, methods for maintaining regular physical activity and reduced sedentary patterns are critical. Yet, as pointed out in this chapter, relatively few interventions have been systematically tested across time periods lasting several years, and knowledge concerning how best to foster sustained physical activity maintenance in different subgroups over time remains inadequate.

3. Report, in experimental and quasi-experimental investigations of physical activity interventions, intervention-related dose-response relations and adverse events to aid intervention evaluation, translation, and dissemination.

Rationale: Experimental investigations in this area can benefit from consistent inclusion of information related to intervention dose-response (e.g., how does the intensity of the intervention, in terms of the type of communication delivery channel being used (e.g., in-person, mediated), as well as number, length, or schedule of contacts, affect the amount of physical activity change?). In addition, adverse events related to the intervention are important for determining intervention safety and appropriateness for various population subgroups, but are rarely reported in a systematic fashion.

4. Develop efficient methods for collecting cost data on all interventions being tested to inform cost-benefit and cost-effectiveness comparisons across the physical activity intervention field as a whole. For those intervention areas that are further developed, use comparative effectiveness designs to more efficiently advance the study and translation of interventions to promote physical activity and reduce sedentary behavior.

   Rationale: In an increasingly cost-conscious health environment, it is important for the public and decision-makers alike to gain a better understanding of the costs of different interventions relative to their effectiveness to make more informed decisions in relation to intervention choice. In those intervention areas with evidence grades of Moderate or Strong, the use of comparative effectiveness experimental designs, in which interventions that have been shown to have merit are tested "head-to-head," will advance knowledge more rapidly than designs that continue to use weaker controls or comparisons (e.g., minimal or no intervention, wait-list controls). In addition, further systematic evaluation of potentially cost-efficient intervention delivery sources (e.g., peer-led interventions) and delivery channels (e.g., automated behavioral counseling systems, virtual advisors), either as adjuncts to or replacements for more staff-intensive interventions, is warranted.

5. Develop standards in the field for choosing the most appropriate comparator arms with which to compare emerging physical activity interventions when evaluating their efficacy and effectiveness.

   Rationale: Similar to other health behavior fields, advancing the physical activity promotion field along the continuum of science, from discovery of promising interventions through dissemination of interventions that work, will require investigators to employ the most relevant comparator arms to answer the specific questions of interest that are being pursued. Relatively little consensus currently exists, however, concerning the most appropriate comparators to use to answer the various types of

questions reflected across the different levels of impact described in this chapter. The field as a whole would benefit from building general consensus concerning the most appropriate types of comparators, along with design parameters, to be considered, based on the current state of the evidence and the most critical questions emanating from it.

6. For those intervention topic areas receiving a Strong or Moderate evidence grade, develop and systematically test methods for effectively implementing such physical activity promotion and sedentary behavior change approaches in real-world settings.

   Rationale: Although the current evidence review identified a number of physical activity promotion approaches and strategies that are effective in increasing physical activity behavior, few such approaches have been systematically disseminated across the U.S. population. In light of the sizable portion of the population that could benefit from increasing their regular physical activity levels, the development and systematic testing of potentially effective implementation methods and strategies are critical.

7. Develop and systematically test multi-component interventions that span multiple levels of influence to increase intervention impact and potential sustainability of behavior change.

   Rationale: It is clear that health behaviors such as physical activity and sedentary behavior are influenced by an array of individual, sociocultural, community, and environmental factors, yet many of the interventions that have been tested contain elements centered primarily on one level of impact (e.g., personal factors; institutional factors; built environment factors). Increasing the effectiveness and robustness of interventions likely could occur through targeting people within their environmental and social contexts (i.e., person-environment interactions). An example of such multi-level interventions includes combining individual-level behavioral skill-building strategies with neighborhood-level built environmental interventions to promote increased walkability.

8. Test, using experimental methods, strategies for promoting regular physical activity and reduced sedentary behavior across key life-course transitions, when such health behaviors potentially result in deleterious outcomes.

Rationale: Common life-course transitions and the changes in role expectations and social and environmental contexts that often accompany them, can lead to negative impacts on physical activity levels and other health behaviors. Such transitions include changes from school to the workforce; changes in marital status and family roles and configurations; and physical transitions occurring at puberty, menopause, or with the onset of a chronic conditions. Systematic testing of methods and approaches for facilitating regular physical activity and reduced sedentary behavior during and following such common transitions could have significant, population level impacts.

9. Conduct experimental research aimed at testing systematically how best to combine physical activity interventions with other health behavior interventions, such as sedentary behavior, sleep quality, or dietary change interventions, to promote optimal physical activity change within the context of such multi-behavioral interventions.

   Rationale: Given the potential health-related synergies that can accrue when both physical activity and sedentary behavior change, or physical activity and dietary changes are implemented, systematic investigations of how best to combine these important health behaviors in different population subgroups are strongly indicated. Currently, little is known concerning the best approaches for combining health-enhancing physical activity with sedentary behavior change or dietary interventions, regardless of intervention modality, to facilitate sustainable behavior changes in both health behaviors. The few randomized controlled trials in this area are intriguing, however.[18] For example, some evidence exists suggesting that, in some population subgroups, introducing dietary interventions along with physical activity interventions may reduce the amount of physical activity change observed.[19] Further systematic evaluation of potential behavioral compensation effects between physical activity and sedentary behaviors is also warranted to ensure that physical activity increases during one portion of the day do not result in increased sedentary behavior in other portions of the day.

10. Increase the scientific utility of systematic reviews and meta-analyses to inform future research directions in the physical activity promotion and sedentary behavior reduction fields.

Rationale: Although the number of systematic reviews has exploded across virtually all physical activity promotion and sedentary behavior areas, a number of such reviews lack specific types of quantitative information that can be useful in obtaining an accurate summation of a research area upon which future research can be applied. Such information includes the following:

- Inclusion, whenever possible, of quantitative estimates of effect sizes or other magnitude of effect statistics for the articles included in the review, as opposed to simply *P* values;
- Clear descriptions of statistical outcomes for between-arm comparisons for all controlled or comparison arm studies along with specific notations when authors did not report such between-arm comparisons;
- Inclusion in each study, whenever possible, of the net physical activity differences achieved between intervention and control arms (e.g., with respect to mean step increases per day or mean minutes per week of moderate-to-vigorous physical activity achieved) over the specific time period under investigation;
- Inclusion of subgroup analyses based on key sociodemographic characteristics (e.g., sex, socioeconomic status, race/ethnicity, age) to identify which interventions might require specific targeting to be effective in different population subgroups.
- Reporting of adverse events and any unintended consequences of the interventions.

Research Needs Specific to Information and Communication Technologies-Level Evidence

1. Employ additional types of experimental designs and methods that will allow for more rapid testing of information and communication technology interventions.

   Rationale: In light of the rapid evolution of the information and communication technologies interventions discussed in this chapter, traditional 2-arm parallel-arm trial designs may not easily allow researchers to keep up with the technology innovations that are occurring in this area. Further use of more advanced experimental designs, such as fractional or multi-level factorial designs and just-in-time adaptive interventions, is warranted.

2. Further explore methods and pathways for systematically exploiting the vast amounts of commercially available physical activity-relevant data and interventions that already reside in this area.

   Rationale: Millions of people representing a diverse and growing segment of the population are currently using commercial technologies aimed at physical activity behavior. Such databases have vast potential for accelerating our knowledge concerning the most effective ways of promoting physical activity among different population groups, yet remain relatively untouched. Exploring appropriate avenues for using these naturally-occurring databases provides a potentially paradigm-shifting approach to accelerate scientific advances in this area and the attendant public health benefits that can be gained.[20]

REFERENCES

1. Ekelund U, Steene-Johannessen J, Brown WJ. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonized meta-analysis of data from more than 1 million men and women. *Lancet*. 2016;388:1302-1310. doi:10.1016/S0140-6736(16)30370-1.

2. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. November 2017:pii:HYP.0000000000000066. doi:10.1161/HYP.0000000000000066.

3. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42(6):1206-1252.

4. Physical Activity Guidelines Advisory Committee. *Physical Activity Guidelines Advisory Committee Report, 2008*. Washington, DC: U.S. Department of Health and Human Services; 2008. https://health.gov/paguidelines/guidelines/report.aspx. Published 2008. Accessed September 22, 2017.

5. Bennett DA, Du H, Clarke R, et al. Association of physical activity with risk of major cardiovascular diseases in Chinese men and women. *JAMA Cardiol*. 2017;2(12):1349-1358. doi:10.1001/jamacardio.2017.4069.

6. Buchner DM, Rillamas-Sun E, Di C, et al. Accelerometer-measured moderate to vigorous physical activity and incidence rates of falls in older women. *J Am Geriatr Soc*. 2017;65(11):2480-2487. doi:10.1111/jgs.14960.

7. LaMonte MJ, Buchner DM, Rillamas-Sun E, et al. Accelerometer-measured physical activity and mortality in women aged 63 to 99. *J Am Geriatr Soc*. November 2017. doi:10.1111/jgs.15201.

8. LaMonte MJ, Lewis CE, Buchner DM, Evenson KR, Rillamas-Sun E, et al. Both light intensity and moderate-to-vigorous physical activity measured by accelerometry are favorably associated with cardiometabolic risk factors in older women: The Objective Physical Activity and Cardiovascular Health (OPACH) Study. *J Am Heart Assoc*. 2017;6(10). pii:e007064. doi:10.1161/JAHA.117.007064.

9. Lee IM, Shiroma EJ, Evenson KR, Kamada M, LaCroix AZ, Buring JE. Accelerometer-measured physical activity and sedentary behavior in relation to all-cause mortality: the Women's Health Study. *Circulation*. 2018;137(2):203-205. doi:10.1161/CIRCULATIONAHA.117.031300.

10. Merghani A, Maestrini V, Rosmini S, et al. Prevalence of subclinical coronary artery disease in masters endurance athletes with a low atherosclerotic risk profile. *Circulation*. 2017;136(2):126-137. doi:10.1161/CIRCULATIONAHA.116.026964.

11. Aengevaeren VL, Mosterd A, Braber TL, et al. Relationship between lifelong exercise volume and coronary atherosclerosis in athletes. *Circulation*. 2017;136(2):138-148. doi:10.1161/CIRCULATIONAHA.117.027834.

12. U.S. Department of Health and Human Services. *2008 Physical Activity Guidelines for Americans*. Washington, DC: U.S. Department of Health and Human Services; 2008. https://health.gov/paguidelines/guidelines. Published 2008. Accessed September 22, 2017.

13. American College of Obstetricians and Gynecologists (ACOG). Physical activity and exercise during pregnancy and the postpartum period. Committee Opinion No. 650 (Reaffirmed 2017). *Obstet Gynecol*. December 2015;126:e135–e142.

14. Diong J, Allen N, Sherrington C. Structured exercise improves mobility after hip fracture: a meta-analysis with meta-regression. *Br J Sports Med*. 2016;50(6):346-355. doi:10.1136/bjsports-2014-094465.

15. Diong J, Allen N, Sherrington C. Correction: Structured exercise improves mobility after hip fracture: a meta-analysis with meta-regression. *Br J Sports Med*. 2016;50:346–355. doi: 10.1136/bjsports-2014-094465corr.

16. Henriksen M, Hansen JB, Klokker L, Bliddal H, Christensen R. Comparable effects of exercise and analgesics for pain secondary to knee osteoarthritis: a meta-analysis of trials included in Cochrane systematic reviews. *J Comp Eff Res*. 2016;5(4):417–431. doi:10.2217/cer-2016-0007.

17. Dalgas U, Stenager E. Exercise and disease progression in multiple sclerosis: can exercise slow down the progression of multiple sclerosis? *Ther Adv Neurol Disord*. 2012;5(2):81–95. doi:10.1177/1756285611430719.

18. Nigg CR, Long CR. A systematic review of single health behavior change interventions vs. multiple health behavior change interventions among older adults. *Transl Behav Med*. Transl Behav Med. 2012;2(2):163-179. doi:10.1007/s13142-012-0130-y.

19. Campbell MK, Carr C, Devellis B, et al. A randomized trial of tailoring and motivational interviewing to promote fruit and vegetable consumption for cancer prevention and control. *Ann Behav Med*. 2009;38(2):71-85. doi:10.1007/s12160-009-9140-5.

20. Althoff T, Sosic R, Hicks JL, King AC, Delp SL, Leskovec J. Large-scale physical activity data reveal worldwide activity inequality. *Nature*. 2017;547(7663):336–339. doi:10.1038/nature23018.