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Physical activity and physical function: moving and aging

Sheila A. Dugan, MD^{1,2}, Kelley Pettee Gabriel, MS, PhD^{4,5}, Brittney S. Lange-Maia, MPH, PhD^{2,3}, and Carrie Karvonen-Gutierrez, MPH, PhD⁶

¹Rush University Medical Center, Department of Physical Medicine and Rehabilitation; Chicago, IL 60612

²Rush University Medical Center, Department of Preventive Medicine; Chicago, IL 60612

³Rush University Medical Center, Center for Community Health Equity, Chicago, IL 60612

⁴University of Texas Health Science Center at Houston; School of Public Health – Austin Campus; Department of Epidemiology, Human Genetics, and Environmental Sciences; Michael and Susan Dell Center for Healthy Living; Austin, TX 78701

⁵The University of Texas at Austin, Dell Medical School; Department of Women's Health; Austin, TX 78712

⁶University of Michigan, School of Public Health; Department of Epidemiology; Ann Arbor, Michigan 48109-2029

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Introduction

Regular participation in physical activity (PA) has many health benefits, perhaps none more important to midlife women than combatting the decline in physical functioning (PF) accompanying aging. This article reviews the existing literature relevant to PA and PF, including definitions, measurement approaches, and descriptive and intervention studies, drawing on findings from the Study of Women's Health Across the Nation (SWAN) and other relevant studies. Evidence supports the conclusion that the physical disablement process starts earlier than previously thought, with many limitations beginning in midlife rather than old age, when women still have many years to live. Understanding that restrictions in PF begin in the midlife for women is a strong argument for changing one's behavior to include regular PA.

Corresponding author: Sheila A. Dugan, MD, Rush University Medical Center, 1725 W. Harrison Street, Suite 855, Chicago, IL 60612, (P) 312-942-6644; (F) 312-942-2176, Sheila_dugan@rush.edu.

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Physical Activity

Physical activity is defined as a behavior that involves human movement, resulting in physiological attributes including increased energy expenditure and improved physical fitness.¹ Evidence gleaned from several decades of exercise training and public health studies has demonstrated the benefit of PA on a wide-range of health outcomes in adults.² Yet, despite the well-established benefits, the majority of midlife women (defined as ages 45–64 years) are not sufficiently physically active to meet *2008 Physical Activity Guidelines for Americans* (henceforth: *Guidelines*).² Current aerobic *Guidelines* encourage adults to engage in at least 150 minutes per week of moderate intensity (activity types between 3 and 6 metabolic equivalent of task (METs), such as a brisk walk), or at least 75 minutes per week of vigorous intensity (activity types ≥ 6 METs, such as jogging), or an equivalent combination of moderate to vigorous intensity PA. In addition, all adults should incorporate moderate or high intensity muscle strengthening activities that involve all major muscle groups on two or more days of the week. The *Guidelines* also encourage adults to avoid inactivity, and directly state that some PA is better than none. Finally, *Guideline* targets for aerobic and muscle strengthening activities have no specific requirements for:

- (1) activity mode or type,
- (2) minimum duration per session, or
- (3) frequency of sessions per week.

This flexibility in the behavioral targets included in the *Guidelines* may particularly resonate with women who aspire to become more physically active.

Public health surveillance data are particularly useful for monitoring trends in PA behaviors, including examining differences in prevalence estimates by various population sub-groups. This can provide important information on which groups of U.S. adults are in greatest need of targeted health promotion efforts. Based on 2015 Behavioral Risk Factor Surveillance System (BRFSS) data³, 31.1% [standard error (SE) ± 0.47] of women aged 45–54 years met aerobic *Guidelines* only, 7.0% (SE ± 0.25) met muscle strengthening *Guidelines* only, and just 17.4% (SE ± 0.37) met both aerobic and muscle strengthening *Guidelines*. Strikingly, 44.4% (SE ± 0.50) of women aged 45 to 54 years did not meet *Guidelines* for either aerobic or muscle strengthening, which is a higher proportion than similarly aged men [41.2% (SE ± 0.55)]. Among older midlife women (ages 55–64 years), the prevalence estimates for meeting *Guidelines* were similar. More specifically, 33.8% (SE ± 0.44), 6.4% (SE ± 0.22), and 15.9% (SE ± 0.31) met aerobic guidelines only, muscle-strengthening guidelines only, or met both guidelines, respectively. The prevalence of women aged 55–64 years that did not meet *Guidelines* for either the aerobic or muscle strengthening was slightly lower than women aged 45–54 years [43.8% (SE ± 0.46)]. Yet, similar to younger midlife women, this was a slightly higher proportion compared to similarly aged men [41.3% (SE ± 0.51)] (Figure 1).

In the National Health and Nutrition Examination Survey (NHANES), PA levels of a U.S. representative sample were also directly measured via accelerometers.⁴ Because behavioral targets included in the *Guidelines* were established with a body of literature that primarily

utilized participant reported measures, there is some controversy among PA experts about operationalizing accelerometer-derived data using the same intensity-based dose thresholds. Nonetheless, prevalence estimates for meeting *Guidelines* are strikingly lower with accelerometers, compared to those based upon self-report. Using the most current, publically available accelerometer data from the NHANES 2003–06, 26.7% (SE \pm 2.4) and 18.0% (SE \pm 2.6) of midlife women, aged 45–54 and 55–64 years, respectively, met aerobic *Guidelines* (Figure 1).

Yet, data from surveillance systems only provide a snapshot view or point prevalence estimates reflecting meeting or not meeting *Guidelines*. Further, estimates generalize the entire sub-population, with no acknowledgement that there may be different levels of PA within a defined population, and individual-level change in PA with trigger points that correspond to certain life events that characterize various adult life-course transitions. In women, major life events that coincide with midlife that could potentially increase PA levels including change in employment status or family structure.^{5,6} Yet, these events may not always lead to increased PA. A woman may opt to engage in more sedentary pursuits to fill the added discretionary hours of the day due to retirement or may have reduced PA due to changes in health status. However, for some, a recent diagnosis may serve as a prompt for behavioral modification (e.g., joining a fitness club) to manage symptoms or progression of disease or disability. Finally, other life events that are not necessarily rooted in midlife may also result in positive or negative changes to PA behaviors. These include changes in relationship status or changes in residence.

The availability of longitudinal data from cohort studies provides the necessary evidence to characterize patterns of PA change during a period of life, rather than during a single point in time. While the availability of prospective cohort studies focused on midlife women's health is limited, the Australian Longitudinal Study on Women's Health (ALSWH) and the U.S.-based SWAN are two examples of studies that are poised to make significant contributions to improve our understanding of the patterns of PA change across the life-course.

The ALSWH is an ongoing longitudinal survey of over 58,000 women recruited in 1996 and enrolled as part of three age cohorts, including: 18–23, 45–50, or 70–75 years, using a mail-based survey once every three years to assess physical and mental health.⁷ In a 2009 study by Brown et al⁸, the associations between life events and PA change were examined. Based on reported walking and moderate- and vigorous-intensity PA during leisure (or discretionary) time, 33.4% of the midlife cohort were classified as “*active*”, 15.6% as “*low active*”, and 7.0% as “*none*”, consistently over 3 years of follow-up, while 17.6% moved into a lower PA category (*decreasing*) and 26.5% moved into a higher category (*increasing*). Life events associated with a higher odds of “*increasing*” PA in midlife women, after adjustment for area of residence and potential confounders, included retirement, changing conditions at work, major personal achievement, death of a spouse or partner, and decreased income (all $p < 0.05$). Yet, birth of a grandchild had a lower odds of membership in the “*increasing*” PA group. Conversely, after full adjustment, life events associated with a higher odds of “*decreasing*” PA in midlife women (17.6%) included: being pushed, grabbed or shoved and having a family member being arrested or jailed (both $p < 0.05$). Women reporting infidelity

of their spouse/partner or a major personal achievement had a lower odds of being classified in the “*decreasing*” PA group (both $p < 0.05$).

Established at a similar time as the ALSWH, the SWAN study included 3,302 midlife women aged 42 to 52 years who were recruited and enrolled between 1996–97 into one of seven clinical sites across the U.S.⁹ The primary objective of SWAN is to evaluate the impact of reproductive aging on the health outcomes of women during midlife. In SWAN, reported PA data (i.e., moderate- and vigorous-intensity activity during leisure-time) were collected from baseline through the most recent visit in 2015/16. Using latent class growth modeling¹⁰ to examine patterns of PA change, five major patterns of PA emerged from SWAN data including: *maintain low* (26.2%), *increasing* (13.4%), *decreasing* (22.4%), *maintain middle or moderate* (23.9%), and *maintain high* (14.1%) PA.¹¹ Hispanic and black women were more likely to be in the *maintain low PA* group, and white women were least likely. Other characteristics associated with the *maintain low PA* group include income < \$35,000, single/never married, fair/poor overall health status, obesity, current cigarette smoker, severe/very severe bodily pain, reported physical difficulties and osteoarthritis (all $p < 0.01$).

Adherence to PA guidelines in midlife

Since midlife women are not adhering to recommended PA guidelines, there is room for improvement when it comes to health promotion messaging. One strategy is to link more immediate health benefits when one establishes a new PA routine, including favorable relationships to body composition, sleep, pain, and physical functioning. More distal outcomes like chronic disease reduction and changing the trajectory of physical and cognitive functioning decline may also be more relevant when viewed through the lens of midlife but may be perceived as an insufficient or delayed consequence given midlife women’s lack of discretionary hours.

Vasomotor symptoms and PA—While PA is recommended to address vasomotor symptoms of menopause, the impact on menopausal symptoms is not conclusive. A review by Pettee Gabriel et al¹² presents the evidence on the relationship between PA and vasomotor symptoms of menopause, primarily hot flashes and night sweats. While evidence from several cross sectional studies reported a significant association between PA (measured by self-report and accelerometry) and self-reported vasomotor symptoms, more recent prospective cohort studies showed variable results.^{13–15} Randomized controlled trials, including MsFlash, show no association between PA, including both yoga and aerobic exercise, and vasomotor symptoms.^{16,17} Daley et al¹⁸ in the 2014 Cochrane Report conclude there was insufficient evidence to demonstrate that PA is effective in managing vasomotor symptoms. The review noted variability among the observational studies with smaller studies reporting negative or no associations and larger studies reporting positive associations.

Sleep and PA

Given the prevalence of sleep disturbance in midlife¹⁹, informing menopausal women about the conclusive evidence linking PA to improved sleep quality may be an effective behavior

change message. The Dose-response to Exercise in postmenopausal Women (DREW) Study found significant improvements in sleep quality in women randomized to all three exercise groups compared to the control group with a dose-response effect.²⁰ In the MsFlash trial, exercise group participants had greater subjective sleep quality and reduced insomnia but differences were small and no longer statistically significant in adjusted analyses.¹⁷

Body composition and PA

More positively, multiple studies support an inverse association between PA and weight gain. In the Biobehavioral Health in Diverse Midlife Women Study, women in the *increase in PA* group had significantly less weight and waist circumference gain than those in the *decrease PA* group.²¹ An increase in leisure time PA including walking and cycling over six years was inversely associated with weight gain in the Nurses' Health Study II.²² In the Women's Health Initiative, in women aged 50–59, the moderate PA group had significant weight loss compared to the sedentary group while women in the 70–79 age group with higher PA showed attenuation of the expected age-related weight loss from sarcopenia and loss of lean body mass.²³

Mental health and PA

Additionally, PA has an inverse relationship with adverse psychological symptoms including depression and anxiety. The Gabriel et al review noted that a significant positive impact of PA on psychological symptoms was consistently observed across most studies.¹² In SWAN, participants meeting guidelines for moderate intensity exercise had lower odds of clinically significant depressive symptoms, and the finding persisted over ten years.²⁴ Karacan et al reported positive benefits with reduced depressive mood, irritability, anxiety and exhaustion after 3 and 6 months of an intervention that included an aerobic exercise program.²⁵ In a randomized controlled intervention of Finnish women, psychological symptoms were collected twice daily using a mobile phone.²⁶ The prevalence of mood swings, but not irritability or depressive moods, was reduced pre- to post-intervention.

PA and PF

A key message to midlife women is the role of regular PA on PF. In the longitudinal SWAN analyses of PA trajectories, the participants that maintained high or moderate PA demonstrated significantly better PF than those who maintained low PA.¹¹ In a previous longitudinal SWAN analysis, higher baseline PA was independently associated with a 7% higher likelihood of high SF-36 physical role functioning and 10% greater likelihood of low SF-36 bodily pain scores.²⁷ The association between PA and physical role functioning was mediated by level of pain. Women may be motivated by pain to seek medical care, providing a teachable moment to talk about the association between PA and PF.

Physical Functioning—Physical functioning is assessed in a variety of ways, including self-reported and objective, performance-based measures, though the common goal is to measure the degree that one is able to complete tasks related to independent living or tasks that impact quality of life.²⁸ Self-reported measures of PF are an assessment of an individual's *perception* of limitations in functioning given the context of their own

environment.²⁹ Objective measures of PF, such as grip strength or gait speed measures, are less vulnerable to the impact of individual-level factors. As such, self-reported and performance-based assessments of PF measure distinct, yet related domains.^{30,31}

Physical functioning has long been studied in geriatric populations, with functional limitations being highly predictive of future poor outcomes, including disability, hospitalizations, nursing home admission and mortality.^{32,33} Although impairments in PF are most prevalent at older ages, the midlife period is an important life stage with respect to the *onset* of poor functioning, though risk factors for impairments can accumulate across the lifespan. Findings from an analysis conducted from 2000–2008 using data from five national U.S. surveys including NHANES, the National Health Interview Survey (NHIS), the Health and Retirement Study, the Medicare Current Beneficiary Survey, and the National Long Term Care Survey, suggest that the prevalence of limitations in activities of daily living (ADLs) is quite stable among older adults, and even slightly decreasing among those age 85+ years, but that the burden is increasing for midlife adults.³⁴ In NHIS, the number of 50–64 year old individuals reporting difficulty with mobility tasks increased by approximately 10% from the 1997–99 data collection cycle versus the 2005–07 cycle.³⁵ Similarly, among 40–64 year olds in NHIS, the odds of reporting PF limitations or limitations in ADLs increased by 0.9% annually and the increases were independent of increases in obesity.³⁶

Those who have impairments at midlife have a high likelihood of developing further impairments or death within ten years; however, regaining function and maintaining independence is also common.³⁷ SWAN has been instrumental in illustrating the prevalence of impairments during this life stage, and importantly describing the development of functional limitations during the menopause transition. At age 40–55, 81% of women in the SWAN cross-sectional study (N=14,427) reported having no PF limitations, however, 10% reported some limitations, and an additional 9% reported substantial limitations.³⁸ These estimates were in line with those in the NHIS from a similar timeframe (midlife during the mid-1990s) which indicated that 15% of persons aged 45–64 reported having some functional limitations³⁹ and from a British cohort of adults age 43–53 years in which 28% of participants had difficulty walking or stair climbing.⁴⁰ By the fourth SWAN visit when the cohort was between the ages of 45–57 years, 11% reported substantial limitations and approximately 30% reported moderate limitations.⁴¹ At age 56–66 (SWAN visit 12), nearly 50% of women reported having at least some limitations.⁴² The high prevalence of self-reported limitations during midlife was substantiated by findings from performance-based PF obtained from the Southeast Michigan cohort. Thirty-one-percent of women from this cohort (includes 366 women from the Michigan SWAN site and 514 women the Michigan Bone Health and Metabolism Study, which followed the same protocol, mean age 47 years) walked at gait speeds below federal standards set for safely crossing pedestrian intersections (<1.22 m/sec), and an additional 12% walked at speeds indicative of frailty in older adults (<1 m/sec).⁴³

In the U.S. women have a longer life expectancy compared to men, but often live longer with disability.⁴⁴ Women have poorer levels of PF compared to men^{45,46} and experience a more rapid decline in functioning.^{47,48} While the prevalence of PF limitations are positively correlated with age in both men and women, the emergence of declines in functioning often

coincide with the timing of the menopausal transition.⁴⁹ While poorer PF among peri- as compared to premenopausal women can be attributed to health conditions and menopause-related symptoms⁵⁰, the menopause-associated differences among late peri- and postmenopausal women are largely independent of age and other health factors.^{41,49} In SWAN, postmenopausal women and those with surgical menopause were three times more likely to report severe limitations in PF as compared to premenopausal women.⁵¹ Postmenopausal and surgically menopausal women also have poorer performance-based PF and more rapid declines in functioning as compared to pre- or perimenopausal women.⁵¹ Thus, reproductive aging and the associated hormonal and metabolic changes characteristic of the menopausal transition may play a role in this process, independent of chronological aging.

Reproductive aging and PF

Work from SWAN demonstrated that greater reductions in estradiol and testosterone during this time were significantly associated with greater risk of PF limitations.⁵² Further, loss of muscle strength during the menopause^{48,53–55} has been associated with the physiologic declines in estradiol.^{47,55} In some studies, muscle strength has improved following exogenous hormone therapy.^{47,56,57} In SWAN, women with poorer PF were more less likely to initiate use of hormone therapy and the initiation of hormone therapy was associated with poorer subsequent PF.⁵⁸

Body composition changes during midlife and PF

While overall weight gain is primarily a product of chronological aging, changes in body composition, or the relative proportion of fat mass to lean mass, is a function of both chronological and reproductive aging.⁵⁹ Marked changes in body composition occur during the menopausal transition⁶⁰ and greater fat mass and less skeletal muscle mass is associated with poorer performance-based PF measures including gait speed and stair climb.⁴³ Further, in longitudinal analyses, loss of lean mass across the midlife is predictive of slower gait speed and less leg strength.⁶¹

Inflammation changes during midlife and PF

Women experience an exacerbated inflammatory response and alterations in homeostasis due to decreased levels of estrogen and the redistribution of adipose tissue that occurs during the menopausal transition.^{62–64} In a SWAN analysis of black and white women, higher concentrations of C-reactive protein (CRP) and fibrinogen were associated with poorer self-reported PF.⁶⁵ In longitudinal analyses, higher concentrations of the pro-inflammatory biomarker CRP and hemostatic markers plasminogen activator inhibitor-1, tissue plasminogen activator-antigen, and Factor VIIc predicted poorer PF.⁶⁶

One potential mechanism linking changes in body composition and inflammatory changes with PF may be the endocrine activity of adipose tissue through the secretion of adipokines, including leptin and adiponectin. Concentrations of the pro-inflammatory adipokines leptin and adiponectin are positively correlated with insulin resistance, lipid accumulation and decreased oxidation of fatty acids in skeletal muscle.^{67,68} In a longitudinal analysis of black and white SWAN women, higher baseline concentrations of leptin predicted poorer

performance-based measures of PF mobility including stair climb, sit-to-rise, 2-pound lift and forward reach but leptin was not associated with strength measures⁶⁹, findings that persisted after adjustment for CRP. In the same analysis, baseline concentrations of adiponectin predicted quadriceps muscle strength but was not associated with any mobility-based measures of PF.

Midlife mental and physical health and PF

Approximately one-quarter of midlife women experience depressive symptoms^{70,71}. In analyses of black and white women, higher scores (i.e., more depressive symptoms) on the Center for Epidemiologic Studies-Depression scale (CES-D) was significantly associated with poorer performance-based PF including sit-to-stand times and timed walk.⁷² Further, women who had incident depressive symptoms during follow-up experienced subsequent declines in performance-based PF including 2-pound lift and stair climb times.

In terms of physical health conditions, a high prevalence of both peripheral nerve impairment and knee osteoarthritis has been reported among midlife women. Among black and white SWAN women from the Michigan site, the prevalence of peripheral nerve impairment was 14–19%.⁷³ In that same sample, the prevalence of moderate to severe radiographic knee osteoarthritis was 28%.⁷⁴ Women with peripheral nerve impairment had poorer PF performance including stair climb and sit-to-stand.⁷⁵ Further, age-related declines in stair climb time were twice as rapid for women with as compared to women without peripheral nerve impairment. Similarly, the presence of moderate to severe knee osteoarthritis was associated with 20–35% poorer performance in PF including the timed walk and stair climb times.⁷⁶ Associations between mental and physical health measures and PF are likely bidirectional, as maintenance of PA and ability to continue functioning may be protective to long-term health outcomes.

Midlife sociodemographic factors and PF

In addition to an understanding of psychological and physiologic predictors of poor PF, examination of sociodemographic and lifestyle correlates of functioning impairments is needed to help us identify appropriate interventions to support healthy aging and prevent functioning impairments. One of the most notable sociodemographic measures associated with differences in PF is race/ethnicity. In SWAN, black women were more likely to report substantial PF limitations in cross-sectional analyses³⁸ whereas Chinese and Japanese women had the greatest declines in PF over time.⁴²

Modifiable lifestyle factors have shown to be predictive of better midlife PF. In SWAN, better diet quality was associated with less PF limitations.⁷⁷ Greater intake of cholesterol, fat or saturated fat was associated with 40–60% greater odds of having substantial PF limitations and lower fruit, vegetable and fiber intakes were inversely associated with self-reported PF. In SWAN, a healthy lifestyle score based upon self-reported measures of smoking, PA and diet was predictive of better PF including faster timed walk and shorter chair stand times.⁷⁸ When considering each measure individually, the association between healthy lifestyle and PF was largely driven by PA.

Measures of PF are important as markers of healthy aging, and are valuable to our understanding of future poor health outcomes. Poorer PF is associated with unfavorable cardiometabolic biomarkers^{79,80} and worse vascular health indicators.⁸¹ In older women, poor PF may be prognostic for cardiovascular disease.⁸² In SWAN, women with poorer self-reported PF were more likely to experience incident metabolic syndrome in the next 10 years.⁸³

Summary

Functional limitations become more prevalent with age, but PF is a dynamic aspect of health, and recovery from limitations is possible.³⁷ PA interventions have been successful for preventing major mobility disability in older adults⁸⁴, and may be promising for maintaining function at younger ages. Arguably, interventions are needed to help women maintain functional status through midlife and into older ages. The rich longitudinal information in SWAN will continue to allow researchers to further investigate predictors at midlife that influence health well into old age. In addition, as the complete cohort reaches post-menopausal status, researchers can better define the role of reproductive aging on PA and PF.

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Key Points:

- Midlife women do not meet guidelines for physical activity participation for a variety of reasons, missing out on the proven physical and mental health benefits.
- Evidence suggests that the disablement process begins in midlife when women have multiple decades to live.
- Recent studies link physical activity to reduced declines in physical functioning in midlife women.
- Providing messages about the benefits of moving may shift the needle on participation, changing the trajectory not only for disablement but chronic disease.
- Future work should expand on exploring the role of reproductive aging beyond solely chronological aging in midlife.

Synopsis

Evidence supports that the physical disablement process starts earlier than previously thought, in midlife when women still have many years to live. Physical activity participation and interventions have been successful in preventing disability in older adults and may be promising for maintaining function at younger ages. Changing the conversation to more relevant topics in midlife, like positive changes in body composition, sleep and improved mood, may move the dial on participation, as midlife women do not meet guidelines for physical activity. Exploring the role of reproductive aging beyond chronological aging may provide gender-specific insights on both disablement and participation.

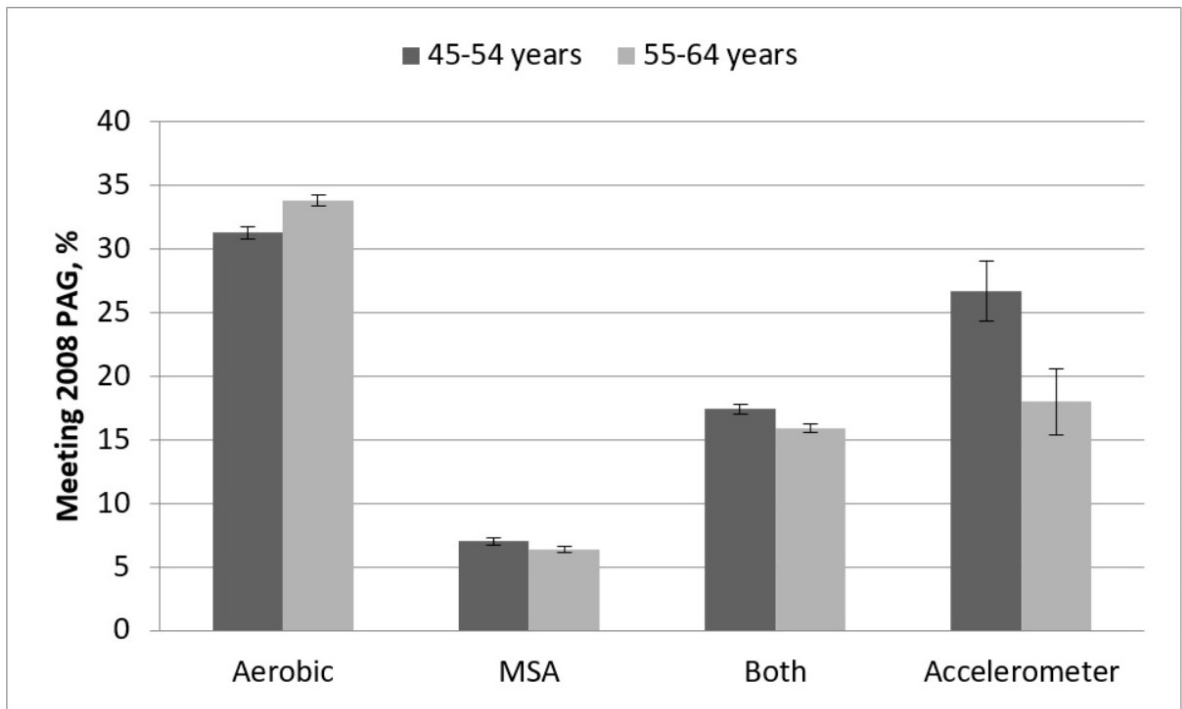


Figure 1: Prevalence of meeting 2008 Physical Activity Guidelines (PAG) for midlife American women (aged 45–54 years and 55–64 years) based on self-reported data from the 2015 Behavioral Risk Factor Surveillance System (i.e., aerobic guidelines, muscle strengthening (MSA) guidelines, and both aerobic and muscle strengthening guidelines) and accelerometer data from 2003–06 National Health and Nutrition Examination Survey (NHANES).