Title: National Institutes of Health Pathways to Prevention Workshop: Physical Activity and Health for Wheelchair Users

Running Title: Physical Activity and Health for Wheelchair Users

Authors: Jerry H. Gurwitz, M.D., Noelle Carlozzi, Ph.D., Kirsten K. Davison, Ph.D., Kelly R. Evenson, Ph.D., Darrell J. Gaskin, Ph.D., M.S., Boris Lushniak, M.D., M.P.H.

Corresponding Author: Jerry H. Gurwitz, M.D., Meyers Primary Care Institute, 385 Grove Street, Worcester, Massachusetts 01605 Email: jerry.gurwitz@umassmed.edu.

Jerry H. Gurwitz, MD, Meyers Primary Care Institute, a joint endeavor of University of Massachusetts Medical School, Reliant Medical Group, and Fallon Health
Noelle Carlozzi, Ph.D., University of Michigan Department of Physical Medicine and Rehabilitation
Kirsten K. Davison, Ph.D., Boston College School of Social Work
Kelly R. Evenson, Ph.D., University of North Carolina, Chapel Hill Gillings School of Global Public Health
Darrell J. Gaskin, Ph.D., M.S., Johns Hopkins Bloomberg School of Public Health
Boris Lushniak, M.D., M.P.H., University of Maryland School of Public Health

Authors have no financial disclosures.

(Abstract word count: 261; Manuscript word count: 3,329)
Abstract

Health benefits of physical activity are well recognized in the general population for reducing the risk of chronic health conditions. Less is known about the effects of physical activity on people at risk for or currently using wheeled mobility devices. On 1–3 December 2020, the National Institutes of Health (NIH) convened the Pathways to Prevention (P2P) Workshop: “Can Physical Activity Improve the Health of Wheelchair Users?” to consider the available scientific evidence on the clinical benefits and harms of physical activity for people who are at risk for or currently using a wheeled mobility device, with the aim of developing recommendations to fill gaps in the evidence base. The online workshop was cosponsored by the NIH Office of Disease Prevention (ODP), the National Center for Medical Rehabilitation Research of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), and the National Institute of Neurological Disorders and Stroke (NINDS). A multidisciplinary team of content area experts developed the agenda, and an Evidence-based Practice Center prepared the evidence report. An independent panel, selected by NIH, attended the workshop; convened to develop recommendations on the basis of the systematic review, presentations, and public comments received during the workshop; and prepared a draft report that was posted for public comment. This final report summarizes the panel's findings and identifies current gaps in knowledge. The panel made recommendations for new research efforts, including novel methods and new research infrastructure to improve the evidence base about the effects of physical activity on people at risk for or currently using wheeled mobility devices.
Approximately 65 million people worldwide require the use of wheeled mobility devices as a result of a disabling injury or illness. Physical activity, defined as any bodily movement produced by skeletal muscles that results in energy expenditure, is recommended to improve physical fitness, function, and health-related quality of life (1). Health benefits of physical activity, including associated reductions in chronic health conditions, are well recognized in the general population. A 2018 scientific report from the U.S. Physical Activity Guidelines Advisory Committee concluded that regular moderate to vigorous physical activity reduced the risk of death and many common diseases or conditions, including cardiovascular disease, stroke, hypertension, type 2 diabetes mellitus, dementia, depression, postpartum depression, excessive weight gain, and certain types of cancer (1). However, much less is known about the effects of physical activity on people at risk for or currently using wheelchairs to inform the development of evidence-based guidelines specifically relevant to these populations.

Although the population of people who are at risk for or currently using a wheeled mobility device is diverse encompassing individuals with a wide range of conditions, those with multiple sclerosis (MS), cerebral palsy (CP), or spinal cord injury (SCI) represent groups at special risk for wheelchair use and chronic health conditions. MS is a chronic inflammatory and neurodegenerative disease affecting over 700,000 people in the United States (2) and 2.1 million people worldwide (3). Worldwide prevalence estimates of CP range from 1.5 to more than 4 per 1,000 live births (4). A recent estimate suggested that the annual incidence of SCI is approximately 54 per one million people in the United States, or 17,810 new SCI cases each year (5).

On 1–3 December 2020, the National Institutes of Health (NIH) convened the Pathways to Prevention (P2P) Workshop: “Can Physical Activity Improve the Health of Wheelchair
Users?" to consider the available scientific evidence on the clinical benefits and harms of physical activity for people who are at risk for or currently using a wheeled mobility device (e.g., manual wheelchairs, motorized wheelchairs, and motorized scooters; broadly encompassed in the term ‘wheelchair’ in this report), with the aim of developing recommendations to fill gaps in the evidence base. This report synthesizes the workshop findings and presents recommendations for a variety of stakeholders (summarized in Table 1) organized around four key questions, which guided both the systematic review and workshop proceedings, and three additional cross-cutting themes.

Methods

The online workshop, cosponsored by the NIH Office of Disease Prevention (ODP), the National Center for Medical Rehabilitation Research of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), and the National Institute of Neurological Disorders and Stroke (NINDS), was planned and implemented by a multidisciplinary team of content area experts from academia, government, and the private sector. A Federal Working Group developed the four key questions, coordinated the initial planning, and nominated panelists and workshop presenters.

The Pacific Northwest Evidence-based Practice Center prepared a systematic evidence review (6), which was presented at the workshop. Six panel members (authors of this article) were selected by NIH as experienced researchers in the areas of public health, geriatrics, internal medicine, and health disparities, with no relevant conflicts of interest. They attended the workshop; convened to synthesize findings from the systematic review, presentations, and public
comments received during the workshop; and subsequently developed recommendations. The recommendations will be posted for four weeks and revised based on public comments received.

Findings

The systematic review included 141 randomized controlled trials (RCTs), 15 quasi-experimental nonrandomized trials, and seven cohort studies that addressed the benefits and harms of physical activity among MS, CP, and SCI participants. The workshop included 27 presentations and received 48 public comments during discussion periods during the workshop, through an online comment feature of the web-based conference tool. Although the systematic review included RCTs, the methodological weaknesses of those studies challenged our ability to generate robust conclusions. The presentations expanded the review to include studies that did not meet the inclusion criteria for the systematic review because the studies lacked a control group, focused on more diverse outcome measures, or did not meet the minimum 10 supervised physical activity sessions. Our findings and recommendations are summarized below by key question.

Key Questions and Recommendations

Key Question 1: What is the evidence base on physical activity interventions to prevent obesity, diabetes, and cardiovascular conditions in people who are at risk for or currently using a wheeled mobility device?

Since regular physical activity is known to favorably lower risk for chronic medical conditions (1), these benefits may be particularly relevant to people who are at risk for or
currently using wheeled mobility devices. However, among those with MS, CP, or SCI, the systematic review did not identify any studies that provided evidence on the impact of physical activity on cardiovascular conditions (e.g., myocardial infarction, stroke, development of hypertension) or the development of diabetes or obesity. Considering that the short duration of most studies challenged the ability to assess effects on chronic disease outcomes, more proximal outcomes were commonly assessed as detailed below (Key Question 2).

**Key Question 2: What are the benefits and harms of physical activity interventions for people who are at risk for or currently using a wheeled mobility device?**

While the systematic review found insufficient evidence related to the impact of physical activity on chronic health conditions, other health benefits were identified for individuals with MS, CP, and SCI. The systematic review found that physical activity improved walking ability, function, balance, sleep, activities of daily living, female sexual function, and depression in participants with MS. Physical activity also improved balance, function, and measures of cardiorespiratory fitness (e.g., peak oxygen uptake) in RCTs that enrolled participants with CP. While the evidence was sparse, some studies suggested that physical activity improved activities of daily living, function, and aerobic capacity in participants with SCI.

The systematic review also delineated the effects of specific types of physical activity, although the majority of this evidence was characterized as low strength. In participants with MS, walking ability may be improved with treadmill training and multimodal exercise regimens that include strength training. Function may be improved with treadmill training, balance exercises, and motion gaming. Balance is likely improved with postural control exercises (that may also reduce risk of falls) and may be improved with aquatic exercises, robot-assisted gait training, treadmill training, motion gaming, and multimodal exercises. Additionally, aquatic
therapy may improve activities of daily living and female sexual function, and aerobic exercise may improve sleep. In participants with CP, balance may be improved with hippotherapy and motion gaming, and function may be improved with cycling, treadmill training, and hippotherapy. In participants with SCI, some evidence suggests that activities of daily living may be improved with robot-assisted gait training.

Workshop presenters, including elite athletes involved in adaptive sports, provided anecdotes testifying to the benefits of physical activity in improving the health of people who are at risk for or currently using a wheeled mobility device. They described positive effects on metabolism, cardiovascular health, strength, cognition, energy, independence, social connections and integration, employment, and mental health (e.g., improved life satisfaction, reduced anxiety and depression).

The systematic review did not identify any studies focused on the harms of physical activity. Thus, knowledge of possible harms was limited to the reporting of adverse events (AEs), which were reported by less than 30 percent of studies. Of the studies reporting AEs, falls and joint pain were the most common—additional reported AEs included muscle strain, stress fracture, exacerbation of existing injuries and disease symptomology, gastric problems, urinary tract infections, blisters, and bruising.

Other possible harms mentioned by workshop presenters included overheating, autonomic dysreflexia, and fatigue. Users of wheeled mobility devices may be at special risk for certain AEs. For example, users of manually-operated wheelchairs are prone to shoulder injuries from overusing that muscle group. Presenters emphasized that risk for AEs must be weighed against the benefits of exercise in this population and that the majority of AEs identified were minor. Both the systematic review and presentations highlighted the lack of a standardized
Key Question 3: What are the patient factors that may affect the benefits and harms of physical activity in patients who are at risk for or currently using a wheeled mobility device?

There is little to no evidence that person-level factors moderate the effect of physical activity interventions on benefits and harms for those who are at risk for or currently using a wheeled mobility device. For most outcomes across the different types of interventions, there was no variation in the effects by participant condition. The systematic review suggested that participants with MS who were less ambulatory improved with core stability training, and that patients with incomplete SCI who were less impaired improved with aerobic interventions. However, beyond limited information on condition-specific effects, the systematic review found no studies that provided findings on the benefits or harms of physical activity interventions according to person-level factors such as age, sex, gender, or race/ethnicity.

Presenters offered some suggestions of patient factors that could moderate the effects of physical activity interventions on those with MS, CP, and SCI. These moderators extend beyond basic sociodemographic data and would require a more detailed understanding of patients’ health conditions and social context. One presenter observed that individuals with less severe injuries, more recent injuries, and/or better functional status may derive greater benefit from physical activity interventions compared with those who have more severe injuries, older injuries, or poorer functional status. Presenters suggested that bone health, muscle structure, functional status, and prior treatments are factors that could influence the relative success of any physical activity intervention. The presence of comorbid conditions such as seizures, cardiovascular disease, chronic kidney disease, obesity, mental health problems, cognitive/brain health, and
respiratory diseases may impact patients’ ability to participate in and benefit from physical activity. Transportation, access to equipment, the quality and fitting of the equipment, social support, sex/gender intersectionality, and other social and personal factors may also influence patients’ ability to participate in and benefit from physical activity interventions. While the presenters offered plausible causal pathways as to why these patient factors are important, there are no studies that have systematically investigated them.

Key Question 4: What are methodological weaknesses or gaps that exist in the evidence to determine benefits and harms of physical activity in patients who are at risk for or currently using a wheeled mobility device?

There are substantial methodological gaps and weaknesses in the existing literature. Of critical importance is the absence of clear consensus for defining and measuring physical activity in users of wheeled mobility devices (e.g., intensity, frequency, duration, and mode). In regard to outcomes, few studies evaluated key aspects of health, such as mental health, social health/participation, cognitive function, and/or health-related quality of life. Workshop presenters highlighted that the exclusion of key stakeholders (e.g., wheelchair users) from the research design and implementation process resulted in a failure to adequately consider a full range of outcomes that were most relevant to users of wheeled mobility devices (i.e., “what matters most to me”).

Furthermore, published studies—both represented within the systematic review and discussed during the workshop—lacked common data elements (CDEs), such as those found within the NIH CDE Repository (7). CDEs can be used across studies with different research designs and study populations, and as a result, permit comparisons over time and between groups with different conditions. The use of CDEs could facilitate the conduct of future meta-analyses.
and provide insights into why some users of wheeled mobility devices respond to an intervention, while others do not. Currently, there is no standardization of the minimal data elements that should be reported in clinical trials. Studies often lack information describing: the study sample (including little to no description of the control group); the intervention setting; key components of the intervention (especially information about dosing and frequency/intensity of physical activity); AEs; and complete information regarding the use of assistive devices (e.g., manual versus powered wheelchairs and whether the device is optimal for the user).

CDEs should be developed with the input of people who are at risk for or currently using a wheeled mobility device. Many of the data elements in current trials were not developed for users of wheeled mobility devices, and thus, may lack evidence for reliability and/or validity to support their use. For example, measures derived from most traditional, wearable physical activity trackers do not provide data relevant to users of wheeled mobility devices, as accelerometry algorithms are based primarily on step count rather than wheelchair propulsion. Even in cases where wheelchair-specific metrics are available, there is an absence of information on reliability and validity to support their use in clinical research.

There are also several study design limitations that lessen the ability to draw strong conclusions from current evidence. Studies captured in the systematic review employed small sample sizes (e.g., only three studies reported greater than 100 participants) that were extremely homogenous in terms of their sex/gender, age, and race/ethnicity composition, as well as their level of disability (e.g., studies of CP often include younger and higher functioning participants). Many trials failed to include control groups and, even when present, control groups were often inadequately described, which hampered assessment of the quality of the evidence. Studies that
employ longitudinal designs are critical to capture variability and assess longer-term health outcomes.

In addition, the systematic review was striking in the absence of more innovative study designs, which could accelerate the pace of understanding while maintaining methodologic rigor. For example, employing a Sequential Multiple Assignment Randomized Trial (SMART) design (8) to develop an adaptive intervention could balance the need for sample heterogeneity with the need for scientific rigor.

Cross-Cutting Themes and Recommendations

Over the course of the workshop, discussions, and public comments, the panelists identified three cross-cutting, intersecting themes with relevance to physical activity for people at risk for or currently using a wheeled mobility device that were not specifically captured in the systematic review or in any single presentation: “What Matters Most” to users of wheeled mobility devices; Translation of Research into Practice; and Research Infrastructure.

Theme 1: “What Matters Most”

Research efforts to date have been narrow in focus and impact, failing to capture what matters most to patients who are at risk for or using wheeled mobility devices, and their families, caregivers, and health care providers (e.g., maintaining independence, addressing pain, or simply “being a good dad”). The panelists challenge researchers to consider outcomes that are more meaningful to these individuals. Researchers should consider outcomes that enhance patients’ ability to participate in physical activity in their homes and local community. Patients value their independence and ability to interact with others. Thus, researchers need to approach the health and social needs of patients who are at risk for or currently using a wheeled mobility device with
a broader lens. It is also important to consider the perspectives of other stakeholders including spouses, children, other family members, caregivers, and health care providers. The impact of interventions on patients and these stakeholders will influence whether they are adopted and incorporated into the lifestyles of patients. There was a consensus among the panelists that individuals who currently use a wheeled mobility device need “a seat at the table” when decisions are being made about prioritization of research questions and research design, including the intervention to be tested, in whom it will be tested, how it will be implemented, and the types of outcomes assessed.

It is also apparent that persons most severely ill or with more advanced disability are often excluded from studies. This is in part due to the types of interventions studied and the outcomes that researchers are aiming to achieve, which restricts study samples to healthier patients. However, this limits the potential impact and generalizability of the research.

**Theme 2: Translation of Research into Practice**

The current evidence-based physical activity interventions for wheelchair users cannot be readily scaled-up and implemented in real-world settings. Factors that limit the translation of evidence-based interventions include highly select groups of study participants who do not reflect populations at risk for or currently using a wheeled mobility device; tightly controlled interventions tested in lab-based settings; specialized equipment not readily available outside of the research context; and the lack of consideration of real-world issues such as insurance coverage and reimbursement challenges. To increase the translational potential of interventions and accelerate the timeline from research to its incorporation into practice, the panel recommends that researchers consider the foundational concepts of implementation science (i.e.,
diffusion, dissemination, implementation, adoption, and sustainability) (9) at the earliest stages
of research planning.

As emphasized under Theme 1, meaningful engagement of stakeholders in the
intervention design process, including patients, providers and caregivers, will facilitate the
development of interventions that are feasible and acceptable to a broader range of individuals
and in a wider range of settings. Consistent with an implementation science perspective, it is
critical to increase the diversity of study participants. Research has typically focused on
homogeneous samples with low severity of disease and functional impairment, and high levels of
readiness for change, leading to challenges in generalizing study findings to underrepresented
populations including those with more severe limitations and/or at earlier stages of readiness
(i.e., “pre-intenders”). Finally, the potential for scale-up must be considered at all key decision
points in the research process. Intervention components that are cumbersome and resource
intensive should be avoided—those with the potential to expand intervention reach (e.g., virtual
or tele-health options) should be prioritized.

Theme 3: Research Infrastructure

One of the overarching themes from the workshop was a call for a more robust national
research infrastructure to support studies of physical activity for people at risk for or currently
using a wheeled mobility device. There are a number of important ways to achieve this goal.
The panel calls for standardized outcome measures to allow for harmonization of data across
studies. The panel recommends the development of a national data repository that would foster
the collection of CDEs from all physical activity research studies focused primarily on people
who are at risk for or currently using a wheeled mobility device. Such a repository would help
mitigate the existing limitations of current research that focuses primarily on small sample sizes
by allowing for researchers to pool data. Funding opportunities are also needed to promote research that spans agencies and institutes in order to foster multisite and multidisciplinary collaboration. Such synergistic efforts are needed to support larger studies to capture the long-term impact of physical activity on the health of users of wheeled mobility devices. Finally, an investment is needed in the training of the next generation of researchers. Standardized curricula and accessibility to mentorships will help ensure that the next generation of scientist-practitioners is prepared to pursue research that will meet the needs and maximize health outcomes for users of wheeled mobility devices.

Conclusions

Although some efforts have been made to expand the evidence base regarding the effects of physical activity for people at risk for or currently using wheeled mobility devices, the existing evidence is limited. This presents challenges in creating physical activity guidelines that, if followed, are both effective and safe. Lessons learned from the systematic review and workshop indicate that further progress will require larger, more ambitious, and more inclusive research efforts, including RCTs and observational studies to assess short-term as well as long-term outcomes. We encourage a greater emphasis on outcomes that “matter most” to users of wheeled mobility devices, in contrast to those that seem most easily measured by researchers. Further, we strongly endorse the need for a coordinated, national research agenda focused on the effects of physical activity for people at risk for or currently using wheeled mobility devices. This will require an adequately funded research infrastructure to foster multisite and multidisciplinary studies employing novel methods and including underrepresented populations as
study participants. Only through such concerted and sustained efforts will genuine progress be achieved.
Table 1: Summary of workshop panel recommendations for future research according to the key questions to address physical activity for people who are at risk for or currently using a wheeled mobility device

<table>
<thead>
<tr>
<th>Key Questions</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| Key Question 1: What is the evidence base on physical activity interventions to prevent obesity, diabetes, and cardiovascular conditions in people who are at risk for or currently using a wheeled mobility device? | 1. Include users of wheeled mobility devices in population-based, prospective observational studies with measures of physical activity and health outcomes.  
2. Conduct longitudinal observational studies examining the risk of developing chronic conditions (e.g., cardiovascular disease, diabetes, and obesity) over time among those who are at risk for or currently using a wheeled mobility device.  
3. Incorporate symptom burden (e.g., pain and fatigue), functional decline, and health-related quality of life measures in longitudinal observational studies. Quantify burden of disease measures (e.g., healthy life expectancy, years of life lost, years lived with disability, disability adjusted life years) as part of the health outcomes assessed (10).  
4. With evidence from RCTs and longitudinal observational studies, develop evidence-informed physical activity guidelines specific to patients who are at risk for or currently using a wheeled mobility device. |
| Key Question 2: What are the benefits and harms of physical activity interventions for people who are at risk for or currently using a wheeled mobility device? | 1. Quantify the benefits and harms of physical activity on long-term health outcomes among patients who are at risk for or currently using a wheeled mobility device.  
2. Assess the importance of equipment and technology, including muscle stimulation therapies.  
3. Diversify outcomes to assess how factors such as cognition, mental health, and negative experiences (e.g., injury, perceived burden) are linked with study participation.  
4. Examine the role of health literacy for the effectiveness of interventions.  
5. Include individual and family/caregiver-level outcomes.  
6. Compile more comprehensive information on adverse events (AEs), applying validated definitions that allow for data harmonization across studies. Information on AEs should include type, severity, timing, duration, and assessment of causality. |
<p>| Key Question 3: What are the patient factors that may affect the benefits and harms of physical activity in | 1. Consider the role of age, sex, gender, and intersectionality in developing a research agenda on the benefits and harms of physical activity interventions for patients who are at risk for or currently using a wheeled mobility device. |</p>
<table>
<thead>
<tr>
<th>patients who are at risk for or currently using a wheeled mobility device?</th>
<th>Use community-based participatory research approaches to engage a more representative population to produce generalizable research findings that can lead to meaningful health benefits.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Promote studies that span all levels of functional status and disease severity. Studies that focus on Gross Motor Function Classification System (GMFCS IV-V) populations and patients with more severe MS, CP, and SCI are especially needed.</td>
</tr>
<tr>
<td></td>
<td>Conduct studies to assess the impact of physical activity on “universal health outcomes” (11) including symptom burden (e.g., pain and fatigue), functional decline, and health-related quality of life in patients who are at risk for or currently using a wheeled mobility device—overall and according to patient-level factors.</td>
</tr>
<tr>
<td></td>
<td>Include samples that capture the full spectrum of users of wheeled mobility devices, including those with the highest-level injuries.</td>
</tr>
<tr>
<td></td>
<td>Consider sedentary behavior, which may modify the impact of physical activity, such that wheelchair users with co-occurring high physical activity and high sedentary behavior may be at greater risk for adverse health outcomes than those with high physical activity and low sedentary behavior.</td>
</tr>
<tr>
<td></td>
<td>Conduct studies that ensure inclusion across the lifespan.</td>
</tr>
<tr>
<td></td>
<td>Develop tele-studies to ensure greater access to the full spectrum of users of wheeled mobility devices.</td>
</tr>
</tbody>
</table>

**Key Question 4: What are methodological weaknesses or gaps that exist in the evidence to determine benefits and harms of physical activity in patients who are at risk for or currently using a wheeled mobility device?**

| | Develop valid and reliable measures to assess physical activity among diverse samples of users of wheeled mobility devices. |
| | Promote study designs that evaluate dosing and intensity of physical activity for people who are at risk for or currently using a wheeled mobility device. |
| | Employ common data elements (CDEs) across studies of physical activity for users of wheeled mobility devices. |
| | Focus on adapting/developing consumer grade devices that can reliably capture physical activity for users of wheeled mobility devices, especially with regard to capturing the duration and intensity of physical activity. |
| | Assess longer interventions and/or longer maintenance periods following interventions. Scrutinize whether an inactive control group is ethical. Consider alternative control conditions to provide benefit to enrolled participants. |
| | Assess mechanisms of effect (e.g., fitness, depression, sleep, pain, fatigue, blood pressure). |
| | Conduct clinical trials based on impairments and functional deficits rather than just underlying diagnosis and pathology. |
8. Identify and measure mediators, moderators, and process measures, as well as behavioral change techniques in interventions and incorporate behavioral change theory into interventions.
9. Consider rigorous study designs to assess adaptive interventions (12) (e.g., SMART).
10. Lengthen the typical intervention period of 6–12 weeks as indicated by the systematic review and track outcomes beyond the immediate intervention period in order to capture variability and assess longer-term health outcomes.
11. Design larger studies with more diverse, multisite enrollment to enhance generalizability of the research.
References


