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 currently using or who may use wheeled mobility devices in the future, specifically individuals with multiple sclerosis, cerebral palsy, and spinal cord injury who are at increased likelihood for use of a wheeled mobility device. On December 1-3, 2020, the National Institutes of Health convened the Pathways to Prevention 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 currently using or who may use wheeled mobility devices in the future, with the aim of developing recommendations to fill gaps in the evidence base. 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 the National Institutes of Health, attended the workshop; convened to develop recommendations on the basis of the systematic review, presentations, and public comments received during the workshop; and revised recommendations based on public comments received. 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 currently using or who may use wheeled mobility devices in the future.

KEYWORDS
Exercise; Physical activity; Rehabilitation; Wheelchairs

List of abbreviations: AE, adverse event; CP, cerebral palsy; CDE, common data element; MS, multiple sclerosis; NIH, National Institutes of Health; RCT, randomized controlled trial; SCI, spinal cord injury.

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Approximately 65 million people worldwide require the use of wheeled mobility devices as a result of a disabling injury or illness. The World Health Organization and the Centers for Disease Control and Prevention have released guidance encouraging regular physical activity (defined as any bodily movement produced by skeletal muscles that requires energy expenditure) for children, adolescents, and adults living with a disability.\textsuperscript{1,2} Yet, these recommendations are based on limited evidence on the effect of physical activity on health for people currently using or who may use wheeled mobility devices in the future.\textsuperscript{3}

On December 1-3, 2020, the National Institutes of Health (NIH) convened the Pathways to Prevention 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 currently using or who may use wheeled mobility devices in the future, with the aim of developing recommendations to fill gaps in the evidence base. The Pacific Northwest Evidence-based Practice Center prepared a systematic evidence review (unpublished observations),\textsuperscript{4} which was presented at the workshop. Because the population of people currently using or who may use wheeled mobility devices in the future is diverse, encompassing individuals with a wide range of conditions, the review focused on 3 diverse conditions commonly associated with wheelchair use representing different populations, etiologies, and pathophysiologies: multiple sclerosis (MS), cerebral palsy (CP), and spinal cord injury (SCI). The systematic review included 141 randomized controlled trials (RCTs), 7 cohort studies that addressed the benefits and harms of physical activity among MS, CP, and SCI participants. Review findings were organized by the following intervention categories: aerobic exercise (eg, aquatics), postural control (eg, balance exercises), as well as strength exercises and multimodal exercise with strength as a major component. Although the systematic review included RCTs, the heterogeneity and methodological weaknesses of those studies challenged our ability to generate robust conclusions. The workshop 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. The workshop included 27 presentations and received 48 public comments during discussion periods of the workshop, through an online comment feature of the web-based conference tool. The panel’s impressions relating to the systematic review and workshop presentations as well as specific recommendations for new research and methods development are summarized below according to key question. In addition, the panel identified 3 cross-cutting themes and associated recommendations. These themes are essential considerations for achieving the goal of generating useful, high-quality evidence to provide guidance to people currently using or who may use wheeled mobility devices in the future, health care providers, and the public health community.

**Methods**

The online workshop, cosponsored by the NIH Office of Disease Prevention, the National Center for Medical Rehabilitation Research of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and the National Institute of Neurological Disorders and Stroke, was planned and implemented by a multidisciplinary team of content experts from academia, government, and the private sector. A federal working group developed the 4 key questions, coordinated the initial planning, and nominated panelists and workshop presenters.

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 and convened virtually via WebEx 5 times to discuss and revise the draft report. Using a consensus-driven approach facilitated by the chair, panel members synthesized findings from the systematic review, presentations, and public comments received during the workshop and subsequently developed recommendations. The draft report was posted for 4 weeks on the NIH Office of Disease Prevention Pathways to Prevention website and received public comments from 9 respondents. The panel reconvened virtually and reached consensus on incorporating revisions based on the public comments received.

**Findings**

The systematic review included 141 randomized controlled trials (RCTs), 15 quasi-experimental nonrandomized trials, and 7 cohort studies that addressed the benefits and harms of physical activity among MS, CP, and SCI participants. Review findings were organized by the following intervention categories: aerobic exercise (eg, aquatics), postural control (eg, balance exercises), as well as strength exercises and multimodal exercise with strength as a major component. Although the systematic review included RCTs, the heterogeneity and methodological weaknesses of those studies challenged our ability to generate robust conclusions. The workshop 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. The workshop included 27 presentations and received 48 public comments during discussion periods of the workshop, through an online comment feature of the web-based conference tool. The panel’s impressions relating to the systematic review and workshop presentations as well as specific recommendations for new research and methods development are summarized below according to key question. In addition, the panel identified 3 cross-cutting themes and associated recommendations. These themes are essential considerations for achieving the goal of generating useful, high-quality evidence to provide guidance to people currently using or who may use wheeled mobility devices in the future, health care providers, and the public health community.
Our recommendations call for enhanced efforts to include users of wheeled mobility devices in population-based, prospective observational studies; the conduct of large, longitudinal observational studies specifically focused on people currently using or who may use wheeled mobility devices in the future; and preemptively planning for extended periods of follow-up for longer term outcomes in RCTs. Such efforts will facilitate the development of evidence-informed physical activity guidelines specific to people currently using or who may use wheeled mobility devices in the future (Table 1).

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?

**Table 1** Summary of workshop panel recommendations for future research according to the key questions to address physical activity for people currently using or who may use wheeled mobility devices in the future

| Key Questions | 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? | 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 (eg, cardiovascular disease, diabetes, and obesity) over time among people currently using or who may use wheeled mobility devices in the future.  
3. Extend research timelines to examine longer-term outcomes of physical activity, including effects on chronic conditions.  
4. With evidence from RCTs and longitudinal observational studies, develop evidence-informed physical activity guidelines specific to people currently using or who may use wheeled mobility devices in the future. |
| 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. Incorporate symptom burden (eg, pain and fatigue), functional decline, and health-related quality of life measures in longitudinal observational studies. Quantify burden of disease measures (eg, healthy life expectancy, years of life lost, years lived with disability, disability adjusted life years) as part of the health outcomes assessed.  
2. Diversify the outcomes examined to include the mental health benefit.  
3. Compile more comprehensive information on AEs, applying validated definitions that allow for data harmonization across studies. Information on AEs should include type, severity, timing, duration, and assessment of causality. |
| 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? | 1. Consider the role of age, sex, gender, race, economic status, and their intersectionality in developing a research agenda on the benefits and harms of physical activity interventions for people currently using or who may use wheeled mobility devices in the future.  
2. Promote studies that span all levels of functional status and disease severity. Studies that focus on Gross Motor Function Classification System (IV-V) populations and patients with more severe MS, CP, and SCI are especially needed.  
3. Use community-based participatory research approaches to engage a more representative population to produce generalizable research findings. |
| 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? | 1. Achieve consensus for defining and measuring physical activity for people currently using or who may use wheeled mobility devices in the future.  
2. Include key stakeholders (eg, users of wheeled mobility devices) in all phases of the research design and implementation process.  
3. Employ CDEs across studies of physical activity for users of wheeled mobility devices.  
4. Standardize reporting of study sample descriptive data and intervention description (including setting and key components of the intervention). |

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?

Because regular physical activity is known to favorably lower risk for chronic medical conditions, these benefits may be particularly relevant to people currently using or who may use wheeled mobility devices in the future. However, among those with MS, CP, or SCI, the systematic review did not identify any studies that provided evidence on the effect of physical activity on cardiovascular conditions (eg, 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 under key question 2.
While the systematic review found insufficient evidence related to the effect 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 (eg, peak oxygen uptake) in RCTs that enrolled participants with CP. Though 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 (eg, Xbox, Wii). 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 currently using or who may use wheeled mobility devices in the future. They described positive effects on metabolism, cardiovascular health, strength, cognition, energy, independence, social connections and integration, employment, and mental health (eg, 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% 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 of certain AEs. For example, users of manually operated wheelchairs are prone to shoulder injuries from overuse, which may be mitigated with targeted shoulder exercises.11 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 approach to coding AEs to capture type, severity, timing, causality, and duration for systematic analytical efforts.

We recommend incorporating a more expansive range of outcomes in clinical studies relating the benefits and harms of physical activity interventions for people who are at risk for or currently using a wheeled mobility device including pain and fatigue, functional decline, health-related quality

| Cross-Cutting Theme       | Primary Recommendations                                                                 |
|----------------------------|----------------------------------------------------------------------------------------|
| Theme 1: “What matters most” | 1. Focus research on the outcomes that matter most to users of wheeled mobility devices. |
|                            | 2. Consider perspectives across multiple stakeholder groups (including patients, families, providers, etc). |
|                            | 3. Include individuals across all stages of the disability spectrum (especially those with the most disabling conditions) to maximize the generalizability of the research. |
| Theme 2: Translation of research into practice | 1. Utilize scalable, pragmatic trial designs—trial designs focused on testing the effectiveness of interventions under real-world conditions. |
|                            | 2. Consider the foundational elements of implementation at the start of study design to increase the likelihood that successful trials can my integrated within existing health care and community settings. |
|                            | 3. Ensure sample diversity (functional severity, age, gender, race/ethnicity, and geographic location) including those individuals from underrepresented groups. |
|                            | 4. Integrate design elements (eg, virtual or tele-health options) into interventions to expand their potential reach and long-term sustainability. |
| Theme 3: Research infrastructure | 1. Develop a national data repository for physical activity data that is specific to users of wheeled mobility devices to capture important CDEs that should allow for broader examination of both within and across diseases. |
|                            | 2. Promote funding opportunities that allow for large-scale, multicenter, multidisciplinary trials. |
|                            | 3. Train the next generation of researchers. |
Physical activity for wheelchair users

of life, and mental health. We also recommend systematic efforts to ascertain information on AEs and applying validated definitions that allow for data harmonization across studies (table 1).

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 such as age, sex, gender, or race/ethnicity limit the effect of physical activity interventions on benefits and harms for people currently using or who may use wheeled mobility devices in the future. 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 participants 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.

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 participants’ 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 do/may affect patients’ abilities 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 an individual’s ability to participate in and benefit from physical activity interventions. Though the presenters offered plausible causal pathways as to why these factors are important, there are no studies that have systematically investigated these factors.

We recommend that age, sex, gender, race, social determinants of health (economic stability, education, and health care access), and their intersectionality receive consideration among 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. We also encourage the design and implementation of studies that include participants with all levels of functional status and disease severity. Finally, we endorse the use of community-based participatory research approaches to engage more representative populations to produce generalizable research findings (table 1).

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 (eg, 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 (eg, users of wheeled mobility devices) 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 (ie, “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, including those available through the Patient-Reported Outcomes Measurement System, a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children. 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, whereas 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 around dosing and frequency/intensity of physical activity), AEs, and complete information regarding the use of assistive devices (eg, manual vs powered wheelchairs and whether the device is optimal for the user).

CDEs should be developed with the input of people currently using or who may use wheeled mobility devices in the future. 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, because 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 (eg, only 3 studies reported more 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 (eg, studies of CP are often
on those who are younger and higher functioning). 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, a study design that randomizes participants into different sequences of intervention options based on decision rules about when to adjust a participant’s treatment, could balance the need for sample heterogeneity with the need for scientific rigor.

Our recommendations highlight the need for consensus in defining and measuring physical activity for people currently using or who may use wheeled mobility devices in the future and the involvement of key stakeholders (including users of wheeled mobility devices) in all phases of the research design and study implementation process. We strongly recommend the use of CDEs across studies and standardized reporting of study sample descriptive data and the intervention description including setting and key components of the intervention (table 1).

Cross-cutting themes and recommendations

Over the course of the workshop, discussions, and public comments, the panelists identified 3 cross-cutting, intersecting themes with relevance to physical activity for people currently using or who may use wheeled mobility devices in the future 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 (table 2).

Theme 1: What matters most

Research efforts to date have been narrow in focus and effect, failing to capture what matters most to people currently using or who may use wheeled mobility devices in the future (eg, maintaining independence, addressing pain, or simply “being a good dad,” as stated by 1 presenter). The panelists challenge researchers to consider outcomes that are more meaningful to these individuals. Researchers should consider outcomes that enhance patients’ abilities 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 people currently using or who may use wheeled mobility devices in the future 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 effect 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 owing 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 effect and generalizability of the research.

Theme 2: Translation of research into practice

The current evidence-based physical activity interventions for users of wheeled mobility devices 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 currently using or who may use wheeled mobility devices in the future, 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 incorporation into practice, the panel recommends that researchers consider the foundational concepts of implementation science (ie, diffusion, dissemination, implementation, adoption, and sustainability) at the earliest stages of research planning.

As emphasized under cross-cutting 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 and those with more severe limitations and/or at earlier stages of readiness (ie, “pre-intenders”). Finally, the potential for scale-up, spread, and long-term sustainability 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 (eg, virtual or tele-health options) and address barriers faced by individuals who use wheelchairs (eg, environmental or social) 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 currently using or who may use wheeled mobility devices in the future. 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 currently using or who
may use wheeled mobility devices in the future. Such a repository would help mitigate the existing limitations of current research that is hampered by small sample sizes by allowing for researchers to pool data. We call upon federal and private funders to create the infrastructure for the repository and promote its use to address the key questions listed above through targeted funding opportunities.

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 effect 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 mentoring by established investigators 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 currently using or who may use wheeled mobility devices in the future, the existing evidence is limited. This presents challenges in creating physical activity guidelines for such individuals and their health care providers that, if followed, are both effective and safe. Lessons learned from the systematic review and workshop emphasize the need for a call to action for 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 have been traditionally measured by researchers. Further, we strongly endorse the need for a coordinated, national research agenda focused on the effects of physical activity on people currently using or who may use wheeled mobility devices in the future. 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.

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