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The Challenges of Enrolling Older Adults into Intervention Studies

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Adults aged 65 years or older have been routinely and systematically excluded from research. With the number of older adults at a record high and growing faster than any other age group, there must be an increased priority on meeting the enrollment challenges so intervention studies are relevant to this population. The challenge centers around the complexity and heterogeneity of older adults, leaving a gap between older adults who participate in studies and those who exist in the real world. Barriers to enrollment stem from both the researcher and participant side. Eight barriers from the research perspective and six from the participant perspective are identified and discussed. Solutions to these barriers can be approached from a three-tier framework. The lowest tier is direct solutions to problems, the middle involves support from funders and journals, and the top tier considers a comprehensive view of sampling and design decisions.

There are more people over the age of 65 alive today than at any other time in history, a situation that will persist and grow. By 2030, the number of people who will be at least 65 years old in America is expected to more than double to 71.5 million, growing faster than any other age group [1]. This growth among the aging is also a global phenomenon, with China and India graying at an even faster pace than America [2]. Given this rapid growth, there must be an increased priority to have research studies targeting this population. This means enrolling people over the age of 65 and those with comorbidities into intervention studies. This population has largely been excluded from clinical trials, yet the need for appropriate interventions for older adults will only continue to increase. The purpose of this paper is to review the challenges as-

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sociated with recruitment and enrollment of older adults, along with the state of the science and proposed solutions to barriers.

DEFINING THE CHALLENGE

Many older adults have medical problems. In 2003, 53 percent of Medicare beneficiaries, people 65 years or older, had at least one chronic condition [3]. In 2008, two-thirds of beneficiaries had two or more chronic conditions, and 12 percent had six or more chronic conditions [4,5]. The number of comorbidities also increases with age. Sixty-two percent of those between the ages of 65 and 74 had two or more chronic conditions, compared to 76 percent of those between 75 and 84 years and 81 percent of those aged 85 years or older [4].

Given the medical complexity often associated with advancing age, older adults tend to be excluded from intervention studies. For example, despite 63 percent of people with cancer being older adults, only 25 percent of participants included in cancer treatment trials have been within this age group [6]. Use of upper age limits in cholesterol-lowering trials has been widespread [2]. In a systematic review of clinical trials addressing the five leading U.S. health-risk behaviors, it was found that 53 percent of the 198 identified trials excluded people over the age of 65 [7].

The difficulty in enrolling older adults is not new, and articles have cited this problem since the 1970s [8,9]. Despite attention to the topic, the problem persists, with changes being relatively small, such as increasing the age limit from 65 to 75 years. Many studies still enroll people with minimal comorbidities, on few medications, independent with activities of daily living, and still driving [10]. This leads to a large gap between real-world older adults and those who participate in intervention studies. With the baby boomer bulge aging, this will undoubtedly emphasize the need for a change.

While it may be possible to extrapolate results from studies using younger adults or healthy older adults, this approach may lead to erroneous conclusions. Assuming successful interventions in younger, healthier patients will translate to success in older adults with comorbidities, lower physical functioning, and higher consumption of medications may potentially lead to harmful outcomes. Reports of such problems have emerged from drug trials, such as with spironolactone. A large, randomized trial of the drug revealed significantly positive outcomes in heart failure patients, but after publication of the results, there was an increase in spironolactone prescriptions and a subsequent increase in hospitalizations and mortality from hyperkalemia. Those adversely affected were older with a higher prevalence of diabetes and renal failure than study participants [11].

Although the majority of the literature on this topic focuses on drug trials, the relevance to nursing and behavioral intervention trials should not be overlooked [7]. Clinical trials aimed at assessing an intervention's efficacy in older adults should not exclude the exact population the intervention is meant to target. Efforts need to be taken to recruit, enroll, and retain older adults who have comorbidities and may be frail [12].

In addition, there are 8.8 million low-income older adults, and 20 percent of those enrolled in Medicare enrollment are also eligible for Medicaid, referred to as dual-eligibles [3]. By 2050, racial and ethnic minorities will become the largest proportion of the older population. Both low-income and racial/ethnic minorities are known to suffer more health problems and health care disparities [13]. These subgroups experience even greater underrepresentation in studies, despite being in greater need of the study outcomes, and specific attention to such subgroups should also be carefully thought out when enrolling older adults.

ANALYSIS OF THE SCIENCE

Researcher's Perspective

A simplified approach to looking at the lack of research involving adults over the age 65 and with comorbidities can be done by dividing it into two main categories. The first and more common reason is from the

Table 1. Barriers to enrollment of older adults in research studies.

Barriers	
Research perspective	Exclusion criteria
	To avoid attrition (mortality, relocation, health decompensation)
	To avoid longer recruitment phase
	To avoid lengthier study process
	To avoid increased costs
	Wanting to minimize adverse events and confounding variables associated with a comorbid conditions
	Belief older adults less inclined to participate
Participant perspective	Long/complex documents
	Gatekeepers/proxies
	Distrust of research/researchers
	Problems with transportation/access
	Lack of understanding of study protocol/ participant requirements
	Concern over excessive intrusiveness

researchers' perspective. As seen in Table 1, there are at least eight identifiable barriers from the researchers' perspective. It is common for researchers to institute exclusion criteria that minimize variability. Researchers may intentionally screen older and more frail potential participants out of studies to create a more homogeneous sample that can ensure treatment effects are not attenuated and avoid risking non-significant results. Older adults are a notoriously heterogeneous group. They are complex with many different characteristics and circumstances, which become confounding variables in a study and another barrier [14]. If the purpose of the research is to conduct a strict efficacy trial, these efforts for homogeneity may then be justifiable, but this is not true for effectiveness studies.

There are other barriers from the researchers' perspective. A researchers' concern over attrition exists for any study, but is particularly legitimate in this population. Older adults have an increased likelihood of becoming too sick to continue the study, dropping out due to hospitalization or institutionalization, or dying [10]. Yet some barriers are more a matter of perspective. Researchers tend to hold the belief that older adults are not as inclined to participate in research. Studies have shown that they are willing to participate, particularly if the study relates to their own health issues [15]. Moreover, they often report participation as a positive experience, even if the outcomes of the research study are not positive [13].

It has also been reported that recruiting older adults takes more time than for younger ones, with subject recruitment failure often around 50 percent [15]. Older adults live in a variety of locations, each with their own advantages and disadvantages. While locating potential participants in nursing homes and hospitals may be easy, there is the issue of gaining entry and having a sample primarily of institutionalized older adults that will surely not represent the community. On the other hand, finding and enrolling community-dwellers has its own difficulties [14]. Moreover, the time investment over the entire study takes longer for consenting, explaining, follow-up appointments, involving gatekeepers or proxies, and addressing special needs. Research involving older and sicker patients is likely to require additional resources to recruit or retain them in the study, such as addressing transportation considerations. With the increase in time and resources, higher costs associated with studying the older adult can be expected, which is a common limitation in any research [10].

Participants' Perspective

The second reason for the poorer involvement of this population in intervention

Table 2. Hierarchy of solutions to older adult study enrollment.

Solutions	
Top Tier: Scientific Community at Large	Earlier transition to effectiveness trials Open discussion within scientific community of enrollment difficulties Enroll older adults even in efficacy studies
Middle Tier: Funding Bodies and Journals	Grant reviews need an understanding of the challenges in older adult research Requiring researchers to justify why older adults would be excluded May also request researchers to justify why comorbid older adults would be excluded Increasing reporting of age stratification
Bottom Tier: Research Groups	**Transportation:** Offer free transportation Taxi voucher Follow-up at the participant's residence Use of participant's support system **Good communication:** Thorough, straightforward explanations Simple language Avoid health care jargon Explain purpose of participant's signature Include gatekeepers **Simplify the consent form:** Large font Language at 2nd – 5th grade level Short version Audio-visual supplements

studies comes from the participants themselves. Older adults may refuse to participate for a range of reasons, and six identified barriers are listed in Table 1. Because older adults have been around longer, they have seen and heard of ethical violations that have occurred in science and health research over the years, which may make them distrustful of the researchers or the study itself [14]. There may be lack of understanding of the study protocols, which can be expressed as a fear of the participation requirements and expectations [15].

There are other reasons older adults might be reluctant to participate. Difficulties with the consent process itself, which often involves long and complex documents, is a commonly identified barrier [13,15]. One of the main concerns reported by older adults is a lack of transportation and/or access to research sites [10]. Another limitation to enrollment is that some older adults perceive research to be excessively intrusive through probing interviews or collection of biological samples [10,14], as well as the fact that gatekeepers often play a big role in the older adult's decision to participate [15]. Family members can be very protective of their relatives, and their own lack of understanding of the study's purpose and requirements can negatively impact their influence on the potential participant's decision.

SOLUTIONS

Solving the challenges of enrolling older adults in research can be thought of as a three-tier method. Table 2 demonstrates the three-tiered approach that may serve as a framework to address the problem. Each level will be discussed. The bottom tier is the most specific, prescriptive, and focused

at a more individual level, and the top tier addresses the issues from the larger scientific community level. To address specific barriers to enrolling older adults, lower-tiered solutions may actually increase costs, which underscores the importance of higher-tier solutions.

Bottom Tier: Research Groups

As seen in Table 2, the lowest level is directly addressing the specific problems identified. This level is primarily managed by the researchers themselves. For example, there are a variety of ways to resolve the barrier of transportation. Options include offering a financial incentive to cover transportation costs, providing a taxi voucher, conducting follow-up at the participant's residence, or an inexpensive alternative of enlisting the help of the participant's support system such as friends, relatives, or community groups [10,15]. A way to overcome the barrier of using complex documents is to modify them, such as simplifying the consent form. This modification could include printing it in large font, making the language at second- to fifth-grade reading level, and creating a short version that includes only the essential information. It might also be helpful to have audio-visual supplements handy in case of hearing or visually impairment [13].

Good communication throughout the process, starting at recruitment, can assuage many of the participant-sided barriers. A thorough but straightforward explanation of the study, intervention, and participant requirements can be a key approach to managing their concerns, with half of the identified participant barriers listed in Table 1 potentially resolvable through communication. Language should be simple and avoid health care jargon. Providing an explanation about the purpose for requesting the participant's signature on the consent form may also be advantageous, since some older adults have concerns over signing apparent legally binding documents for fear of losing control [15]. Because of the key role gatekeepers often play in the older adult's decision to participate, it can be useful to include them in the conversations, the consent process, and answer any of their questions as well [16].

Using proxy-derived information has been suggested as a possible solution for gathering data in the event that the participant becomes unable to provide accurate and reliable data [10]. This approach would only really be applicable if data collection is through self-report, and the proxy would need to be in a position to accurately step in for those data. Because proxy report might differ substantially from the participant's report, proxy data would realistically need to be collected from the start of the study so that these differences could be identified, quantified, and accounted for in the analysis.

Middle Tier: Funding Bodies and Journals

While ground level solutions are necessary to combat definable barriers, support for research involving older adults must also occur at higher levels. Since this difficulty is not new, yet persists despite acknowledgments of the problem, there is an apparent need for systems changes as well. Taking a bigger picture can help provide the researchers studying the older population with adequate support to carry it out. While the onus begins with the researchers to justify their financial needs, reviewing bodies need an understanding of the unique barriers in older adult research. Grant reviewers need to recognize the additional resource needs of studies recruiting and enrolling older adults and offer funding consistent with these needs. If funding is limited because grant funders don't understand how extra costs exist, enrollment of older adults will likely still be a problem, even if researchers appropriately plan and take measures to overcome barriers [17].

A shift in thinking needs to occur when it comes to research involving older adults. The mentality that one needs to explain why a research study is enrolling older adults needs to change to justifying why older adults are excluded. For research that will have outcomes likely to target the older adult population, it may also be reasonable

to request justification for the exclusion of adults with comorbidities. Grant reviewers and journal editors should also institute criteria for accurate reporting research with older adults. They may tend to require authors to report age by strata to help readers better understand the study's age distribution [13].

Top Tier: Scientific Community at Large

A final way to look at the problem can be considered the highest level approach to this problem. This involves thinking about sampling and study design. Although these are considerations the research team needs to make, therefore appearing to be within the low-tier approach, it needs to become a conversation within the scientific community, at least in the short term while the challenges of involving older adults in research begins to be corrected. It will continue to be the job of the researchers to establish the sampling method and design; however, these questions need to be considered and discussed at-large, to help future researchers understand the specific difficulties in making study decisions in this population.

Early efficacy studies may still need to begin with subjects free from comorbid conditions in order to establish evidence that the intervention is effective without potential alternative explanations or threats to internal validity. This approach would still tend to be most applicable to drug trials, although could be applied to a proof of concept of a behavioral intervention [12]. Nonetheless, these early studies should still make efforts to enroll adults at least 65 years old, if the ultimate intent is for the older adult to receive the intervention. Even if the intervention is not explicitly intended for the older adult, but the vast majority of recipients are likely to be over the age of 65 years, this should also be grounds for specifically recruiting and enrolling older adults. For example, if a symptom-management intervention is targeting patients with cancer, excluding older adults would not be appropriate since more than three out of five people diagnosed with cancer are over the age of 65 [18]. Likewise, a study evaluating the efficacy of a falls prevention program should not exclude older adults, since falls are the leading cause of hospitalization and injury deaths in this population [19]. Appropriate sampling and exclusion criteria should be carefully reviewed, with particular thought to why a healthy older adult should not be included in even the earliest of intervention studies.

However, the majority of older adults do have comorbidities, and the quest for a homogeneous sample has little practical relevance to the older adult population. The transition to effectiveness trials might need to occur sooner than traditionally accepted. Not only does excluding the older adult with comorbidities limit evidence-based practice, but there are ethical considerations as well. A particular population is essentially prohibited from participating, even if willing, while the burden of early research is consistently placed on younger, healthier subjects. Although there has been some argument that randomized controlled trial might not be reasonable in older, comorbid adults [10], it has been shown that this design is still possible by incorporating measures of comorbidity and frailty and using the index score in analyses [12]. Further research on the use of cognitive and functional scales in randomized controlled trials of older adults should be done and may settle the debate of the best design in this aging population.

CONCLUSION

Adults aged 65 years or older and with comorbidities are often excluded from intervention studies. Age alone should not be a limitation for participation in clinical trials, and the enrolled sample should reflect the population that will receive the intervention. Barriers to older adult enrollment stems from both the researchers' and the participants' perspective. Solutions to this enrollment challenge can be approached from a three-tiered method. While direct solutions are necessary, researchers need financial and systems support for it to be successful. Funding should reflect a priority on gerontological research. Design and sampling issues need to be considered at both the

researcher and scientific community level. If now is not the time to increase the enrollment of older adults in research, when the population over age 65 is at a record high, then when is?

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