

Expanding Clinical Trials Designs to Extend Equitable Hearing Care

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Abstract: Clinical trials are critically important to translate scientific innovations into clinical practice. Hearing healthcare depends on this translational approach to improve outcomes and quality of life. Across the spectrum of healthcare, there is a lack of diverse participation in clinical trials, a failure to recruit and retain underrepresented and underserved populations, and an absence of rigorous dissemination and implementation of novel research to broader populations. The field of hearing healthcare research would benefit from expanding the types and designs of clinical trials that extend hearing healthcare and novel interventions to diverse populations, as well as emphasizing trials that evaluate factors influencing how that care can be delivered effectively. This article explores the following: (1) the role, value, and design types of clinical trials (randomized controlled, cluster randomized, stepped wedge, and mixed methods) to address health equity; (2) the importance of integrating community and stakeholder involvement; and (3) dissemination and implementation frameworks and designs for clinical trials (hybrid trial designs). By adopting a broader range of clinical trial designs, hearing healthcare researchers may be able to extend scientific discoveries to a more diverse population.

Key words: Disparities, Ear and hearing care, Randomized trials, Underserved.

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INTRODUCTION

An estimated 1.5 billion people worldwide have hearing loss, representing approximately one in five people globally (World Report on Hearing 2021). Those who are affected by hearing loss often have diminished quality of life and encounter challenges across the lifespan, including speech and language delays and poor school performance in childhood, limited employment opportunities in adulthood, and accelerated cognitive decline in older adults (Jung and Bhattacharyya 2012; Lin et al. 2013; Emmett and Francis 2015; World Report on Hearing 2021).

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In addition to human suffering, hearing loss exacts a substantial financial toll, estimated to be upwards of \$980 billion in global macroeconomic losses annually (World Report on Hearing 2021).

Hearing loss disproportionately affects underserved populations. Certain racial and ethnic minorities and underserved populations experience a higher prevalence of childhood hearing loss. This disparity has been demonstrated among rural populations. For example, historical data suggest the prevalence of childhood hearing loss in rural Alaska Native children is 31%, compared to 1.7 to 5% prevalence in the general US population (Reed et al. 1967; Mehra et al. 2009). The majority of hearing loss in Alaska is related to infection, arising from otitis media that is 4 to 5 times more prevalent in rural Alaska Native children than in the general US despite pneumococcal vaccination (Reed et al. 1967; Kaplan et al. 1973; Curns et al. 2002; Singleton et al. 2009; Singleton et al. 2018). Furthermore, children who suffer socioeconomic deprivation have been shown to be at higher risk for otitis media (Smith & Boss 2010). Hearing loss is also more prevalent among adults living in rural communities compared with those in urban settings (Cruikshanks et al. 1998; Merchant et al. 2002). Studies have shown that rural populations are frequently delayed in accessing essential hearing loss treatments such as hearing aids and cochlear implants (Bush et al. 2014; Hixon et al. 2016; Chan et al. 2017). Among older adults in the United States, disparities in hearing care exist by race, ethnicity, and socioeconomic position, where the prevalence of hearing aid use is 2× higher among older White Americans with hearing loss than racial and ethnic minorities (Mamo et al. 2016; Nieman et al. 2016). Although the burden of hearing loss is large and inequitable in the United States, it similarly affects underserved populations around the world. For example, over 80% of people with moderate to severe hearing loss live in low- and middle-income countries, and it is estimated that these countries account for 53% of the associated economic costs of untreated hearing loss (World Report on Hearing 2021).

The 2021 World Report on Hearing highlighted the role of research to improve ear and hearing care (EHC) delivery for disadvantaged groups in both low- and high-resource settings, maintaining that research is needed to inform context-specific interventions, guide policymaking, and strengthen health systems (World Report on Hearing 2021). EHC research pertaining to vulnerable populations has been limited, however, in part because there has been a failure to recruit and retain underrepresented and underserved populations in clinical trials. Populations that may be deemed less accessible by traditional clinic-based research are often overlooked in clinical trials and thus subsequently do not benefit from the delivery and dissemination of evidence-based treatments. In studies pertaining to

hearing loss management in adults that report race/ethnicity, only five studies in the past 30 years included non-White representation greater than 30% of the study population. Likewise, only half of the studies reported greater than 45% female representation (Pittman et al. 2021). There is a dearth of literature including racial and ethnic minorities and disadvantaged groups, and the broader generalizability of results from many existing clinical trials is limited given limitations in patient populations who have traditionally been included in hearing-related research. Even when representative research is published, there has been an absence of rigorous dissemination and implementation of novel research to broader populations.

Clinical research includes both observational and intervention studies, the latter of which are known as clinical trials. Although clinical trials may or may not utilize randomized treatment assignments, this article focuses on clinical trial designs, which include randomization. Randomized clinical trials are important tools used to gauge the efficacy of healthcare treatments and interventions and are essential for translating scientific discoveries into clinical practice. If conducted in real-world settings, these studies can also assess the effectiveness of interventions in broader populations and may detect differences in outcomes based on a variety of variables such as race, ethnicity, income level, location, and sex, among others. However, underserved and underrepresented populations must be included in clinical trials to assess the true effectiveness of interventions within a population (Clark et al. 2019). Historically, this has not been the case. Some explanations for the systematic exclusion of women and racial and ethnic minorities from clinical trials include lack of access to referring physicians, the liability of administering interventions to women who could be pregnant, and mistrust of the medical system (McCarthy 1994). These exclusionary practices are problematic, as clinical trials can serve as valuable tools in translating scientific innovations into clinical practice and promoting health and inclusive care among diverse populations.

There is an opportunity to expand the types of clinical trial designs utilized in EHC research to simultaneously promote the inclusion of underrepresented populations and to increase the scientific rigor of our research. As clinical trials must account for potential barriers including unequal power dynamics between researchers and study communities, limited resources in study communities, and risks to participant health and safety, it is incumbent upon researchers to maximize benefits and minimize harms by selecting the best study design (Prost et al. 2015; Saenz et al. 2018). Researchers should develop a robust understanding of the potential benefits and limitations of each study design and avoid limiting themselves to the subset of clinical trial designs with which they are familiar (Hunt et al. 2019).

In this review, we describe the importance of integrating stakeholder and community involvement as a tool in advancing equity within clinical research. We outline the ability of mixed-methods research to strengthen clinical trial designs, contextualize intervention outcomes, and analyze intervention uptake. Next, we report on the characteristics, role, and value of a subset of clinical trial designs that have been underutilized in EHC research with vulnerable populations, including individual randomized controlled trials (RCTs), cluster RCTs, and stepped wedge RCTs. We then highlight how dissemination and implementation frameworks and hybrid trial designs can be integrated into clinical trials to address health disparities. We urge EHC

researchers to consider adopting these clinical trial designs, as appropriate, to extend access to healthcare, novel interventions, and innovations in care delivery to vulnerable populations.

Equity in Research and the Role in Recruitment and Retention

The issue of equity in research is a growing focus for those conducting research with vulnerable populations (Hedt-Gauthier et al. 2019; Abimbola 2019; Patterson et al. 2021) and these concerns are especially pertinent for RCTs. Globally, RCTs are often funded by external agencies and conducted by nonlocal researchers (Kelaher et al. 2016). This type of research risks excluding the voices of local researchers and prioritizing research questions, study designs, and platforms for dissemination of research findings that are less relevant for the local population.

In this section, we will discuss considerations that may enhance equity within EHC research with regard to the researchers, participants, and host communities. This includes reviews of stakeholder engagement, the incorporation of mixed-methods research, and careful consideration of selecting the control group. We will then present examples of RCT designs (Table 1) and Hybrid-Effectiveness Implementation Trial Designs (Table 2), focusing on attributes that may enhance equity.

Stakeholder and Community Involvement Across Randomized Trial Designs

Stakeholder involvement in the research process, including representation of community members and local researchers as partners, is needed to strengthen research capacity and account for the challenges and needs specific to that community (Farmer 2013; Park et al. 2021). Certain clinical trial designs are well-positioned to integrate community members as co-researchers and can be used to support local research capacity to advance health equity.

Stakeholder involvement in research can take on several forms, including partnership (a long-term, collaborative relationship with a stakeholder group), participation (enrollment as a study participant), and engagement (involvement of community stakeholders throughout the research process—from study initiation to eventual dissemination and implementation) (Staley and INVOLVE 2009). Despite the benefits of including stakeholders and community members in RCTs addressing health disparities, there is limited reporting of stakeholder involvement in the literature, and there has been limited inclusion of stakeholders in EHC research (Ahmed & Palermo 2010; Staniszevska et al. 2017).

To effectively recruit and retain participants from underserved populations, it is imperative for the researcher to recognize the local cultural and historical contexts, including prior abuses and issues surrounding trust in research. This understanding is best developed through authentic, long-term engagement with community partners who can speak to the experiences of community members. Although there are numerous ways to develop these relationships, Community Advisory Boards (CABs) are an excellent starting point. CABs consist of community members who often share history and culture and are well-positioned to serve as an intermediary between the researcher and the community. Well-described in the HIV literature, CAB partnerships can be beneficial when conducting research with other underserved communities (Strauss et al. 2001).

With strong partnerships and knowledge of the local context, the researcher can better understand community characteristics

TABLE 1. Comparison of randomized controlled trial designs

Comparison of Randomized Trial Designs			
Study Design	Individual Randomized Controlled Trial	Cluster Randomized Controlled Trial	Stepped Wedge Randomized Controlled Trial
Unit of Randomization Control	Individuals Group of unexposed individuals	Clusters Unexposed clusters	Clusters Unexposed observation periods of clusters
Effective Sample Size Intervention Timing Considerations	Number of individuals The intervention is typically administered at the start of the trial, though a pre-intervention baseline period may be used.	Number of clusters The intervention is typically administered at the start of the trial, though a pre-intervention baseline period may be used	Number of clusters Intervention implementation requires adhering to a predefined schedule.
Analysis	Must consider participant characteristics	Must consider participant characteristics, cluster characteristics, and cluster size	Must consider participant characteristics, cluster characteristics, cluster size, and crossover time

and refine recruitment approaches to reflect the needs of the community, which will particularly benefit studies that recruit from a community-based setting. In addition, local partnerships allow the researcher to monitor the benefit-to-burden ratio of study participants from the participant’s perspective. Further avenues to improving recruitment include harnessing partnerships to inform cultural tailoring of messaging and diversifying modalities of recruitment, such as hosting community-based information sessions rather than relying exclusively on traditional provider-driven referral models. These efforts and the associated outcomes should be measured and reported proactively to advance the science of diverse recruitment, particularly within EHC research.

Mixed Methods and RCTs • As exemplified by the clinical trials described in this article, qualitative research can be synergistic when employed alongside quantitative RCTs. RCTs are designed to answer the question of whether a causal relationship exists, and this often requires the systematic collection of multiple data points. Qualitative methods can answer highly relevant questions pertaining to the appropriateness and acceptability of the intervention (White 2013). When applied before initiating the quantitative component of an RCT, these data can

inform appropriate trial design, as well as various study aspects, such as questionnaire development, recruitment methods, etc. Incorporation of qualitative methods can also strengthen the sustainability of the intervention and the ability of the RCT to answer the research question. Likewise, qualitative analysis during and after the intervention can describe reasons for intervention success or failure and support post-trial implementation through programs or policy. Despite these potential benefits, the mixed-methods approaches (defined in Table 3) have been underutilized in EHC research.

Selection of Control Groups • Randomized trial designs are specifically used to compare interventions when it is unknown which treatment is best. A control group is typically used for comparison of a new intervention and is carefully selected to maintain similarities between groups while not marginalizing those not receiving the intervention. It is important to take into consideration community preferences when selecting the control treatment to be used as a comparator to ensure that the vulnerable population that is participating receive benefit regardless of randomization. In the study examples later, we have described the thought process that went into the selection of control groups.

TABLE 2. Comparison of hybrid trial designs

Comparison of Hybrid Trial Designs			
Hybrid Trial Design	Hybrid Trial Type 1	Hybrid Trial Type 2	Hybrid Trial Type 3
Use	Used to test the effects of a clinical intervention while observing and collecting information on implementation	Used to simultaneously test clinical and implementation interventions. Requires an explicitly-described implementation strategy that is thought to be feasible in the real world	Used to test an implementation strategy while observing the impact of a clinical intervention
Aims	Primary aim: evaluate effectiveness of a clinical intervention in a new population or setting Secondary aim: explore implementation-related factors such as feasibility, sustainability, and potential barriers and facilitators to implementation	Primary aim: evaluate the effectiveness of a clinical intervention and the adoption and fidelity of an intervention strategy in a new population or setting	Primary aim: evaluate the adoption and fidelity of an implementation strategy in a new population or setting Secondary aim: Observe intervention outcomes
Effectiveness Analysis	Traditional effectiveness trial	Effectiveness trial paired with implementation trial	Analysis of patient-level outcomes
Implementation Analysis	Process evaluation to identify barriers and facilitators to implementation		Traditional implementation trial

TABLE 3. Glossary of terms

Term	
Efficacy	“The performance of an intervention under ideal and controlled circumstances” (Singal et al. 2014).
Effectiveness	“The performance of an intervention under ‘real world’ conditions” (Singal et al. 2014).
Dissemination	“Dissemination is the targeted distribution of information and intervention materials to a specific public health or clinical practice audience. The intent is to spread knowledge and the associated evidence-based interventions” (US Dept of Health and Human Services Program Announcement Number PAR-10-038 n.d.).
Implementation	“Implementation is the use of strategies to adopt and integrate evidence-based health interventions and change practice patterns within specific settings” (US Dept of Health and Human Services Program Announcement Number PAR-10-038 n.d.).
Randomized Controlled Trial	“A study in which the participants are divided by chance into separate groups that compare different treatments or other interventions. Using the chance to divide people into groups means that the groups will be similar and that the effects of the treatments they receive can be compared more fairly. At the time of the trial, it is not known which treatment is best” (Definition of Randomized Clinical Trial—NCI Dictionary of Cancer Terms—National Cancer Institute 2011).
Mixed-Methods Research	“Mixed methods research is the type of research in which a researcher or team of researchers combines elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the broad purposes of breadth and depth of understanding and corroboration” (Johnson et al. 2007).
Hybrid Effectiveness-Implementation Trial Design	“[A study design] that takes a dual focus a priori in assessing clinical effectiveness and implementation” (Curran et al. 2012).

Individual Randomized Controlled Trial

Individual RCTs are the most common RCT study design and rely on the random distribution of participant characteristics. Participants are randomly assigned to one or more study arms for the duration of the study. Each study arm is administered a different intervention, and there is often a placebo group that is used as a control. When possible, researchers and participants should be blinded to the assignments (Evans 2010). Like the other clinical trial designs discussed here, the ethics of individual RCTs rely on clinical equipoise, which is present if there is “genuine uncertainty within the expert medical community—not necessarily on the part of the individual investigator—about the preferred treatment” (Freedman 1987).

With regard assessing the effect of an intervention, RCTs are often referred to as the “gold standard.” This is primarily due to the random allocation of participants, which is intended to limit the influence of confounding factors (e.g., socioeconomic position and comorbidities) on study results. The blinding process prevents knowledge of treatment assignment from influencing the study team’s care, treatment of participants, or analysis of results. Likewise, this prevents treatment assignment from affecting the participant perspective of the intervention (Crisp 2015). Pertinent to research with underserved populations, individual RCTs require the recruitment of individual participants, which presents the opportunity to partner with communities to achieve representative study populations and improve study retention.

There are several limitations of individual RCTs. Due to within- and between-subject variation, they may require large sample sizes, which can result in logistical challenges and high costs (Evans 2010). Furthermore, individual RCTs may not be appropriate for studies that employ community-level interventions or other units of analysis. In addition, given the focus on the individual participant, individual RCTs risk inadequately integrating perspectives of the local community (Hunt et al. 2019).

Baltimore HEARS Study • The Baltimore HEARS (Hearing Health Equity through Accessible Research & Solutions) study,

led by author CN, is an ongoing individual RCT that aims to evaluate the efficacy of the HEARS intervention (Fig. 1) (Johns Hopkins University 2020). HEARS is a theory-driven hearing care intervention designed to be delivered through a community health worker model that incorporates provision and orientation to an over-the-counter listening device and basic aural rehabilitation (Nieman et al. 2017). The study randomized over 150 participants and is being conducted in partnership with local aging service providers (e.g., affordable senior housing and senior centers). The primary endpoint is a 3-month change in communication function, as measured by Hearing Handicap Inventory for the Elderly (HHIE-S) scores between the intervention arm and a 3-month waitlist control arm. Secondary endpoints include changes in self-reported loneliness and depression.

Several unique characteristics of the Baltimore HEARS RCT enhance its relevance to the local underserved population. The Baltimore HEARS RCT is a community-engaged RCT, guided by both a long-standing community and scientific advisory boards, along with an embedded human-centered design practitioner within the research team. These efforts aim to ensure a focus on the end-user and the community needs throughout each phase of a clinical trial, including the design of the study to recruitment and retention efforts and dissemination plans. Development of the HEARS intervention also relied on community engagement through a series of focus groups with community representatives with hearing loss, including low-income and racial and ethnic minority older adults, primarily African American older adults (Nieman et al. 2017; Suen et al. 2021). This community engagement has remained central to implementation, and the study has benefitted from an embedded human-centered design practitioner, who has contributed to the development of the HEARS training program as well as the execution of the RCT (Suen et al. 2021). The human-centered design practitioner serves as an expert consultant in human-centered design methodology as well as translating these efforts into tangible products, such as tailored recruitment strategies and dissemination plans responsive to community priorities.

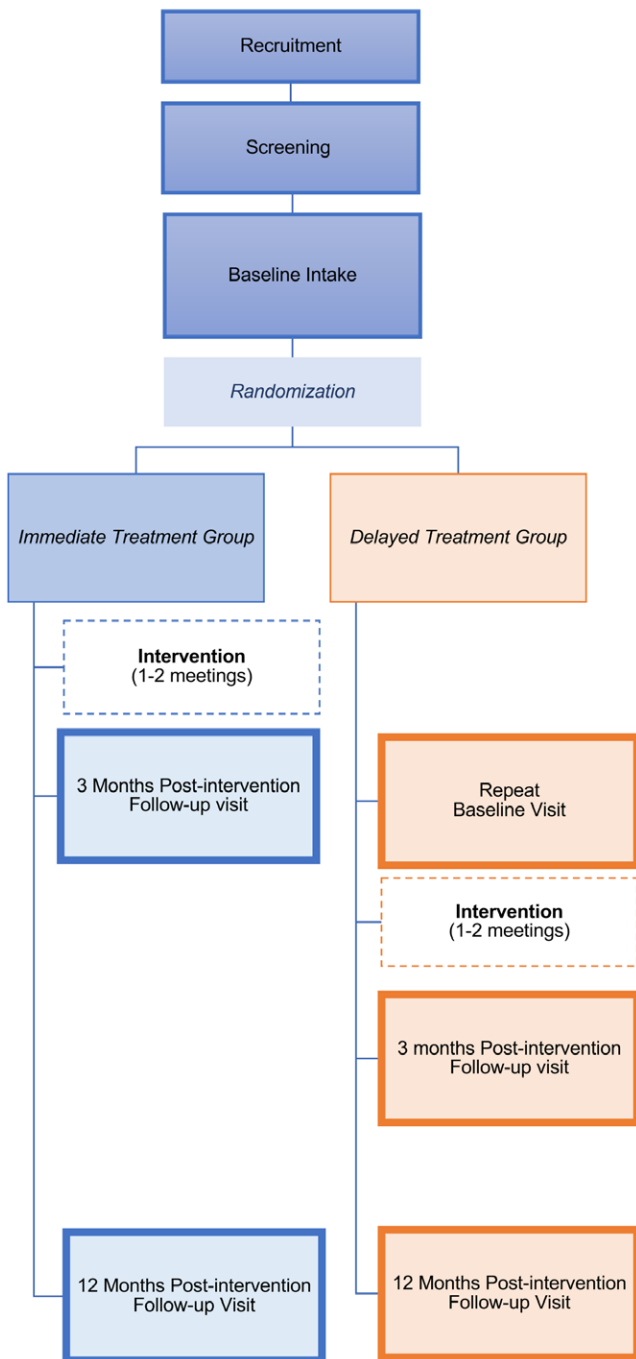


Fig. 1. Participant study flow diagram for the Baltimore Hearing Health Equity through Accessible Research & Solutions Study.

An early example of an outcome of this type of engagement is the inclusion of a waitlist control group in response to community partners' mandate that all participants receive access to the intervention. The waitlist control group receives the intervention after the active treatment group, meaning that all study participants will receive the potential benefits of the intervention. As an entirely community-delivered trial, representatives from community partner organizations, such as service coordinators, who are known and trusted leaders within the community sites, have been critical to participant recruitment and retention. Recruitment strategies have been developed and implemented

collaboratively with community representatives and the CAB. Strategies include cosponsored community events, pop-up recruitment tables and hearing screenings, participation in local health fairs, targeted referrals through community leaders, and inclusion in community newsletters and bulletin boards.

Finally, this study is relevant to underserved populations in Baltimore as it is one of the largest trial-based cohorts of African American older adults with hearing loss to date. Although the trial aims to include a strong representation of racial and ethnic minority older adults as well as low-income older adults, sampling was not stratified by race, ethnicity, or income, and quotas were not applied. Race and ethnicity are self-identified by participants and utilized categories employed within the National Health and Nutrition Examination Survey. Accrual numbers are monitored by race and ethnicity and inform recruitment strategies and selection of community sites, which was ultimately guided in concert with the CAB. Community sites were identified based on potential unmet hearing care needs, such as consideration of the percentage of subsidized housing in a particular affordable senior housing complex. Although the Baltimore HEARS RCT is not designed to be representative of one community, stakeholder engagement throughout all aspects of the RCT inform the design and execution of the trial to maximize the participation of racial and ethnic minority older adults as well as low-income older adults, who have been underrepresented in hearing-related research.

Cluster Randomized Controlled Trial

The cluster RCT uses clusters of people as the unit of analysis. The characteristics of clusters vary between studies and are selected based on the intervention and target population. For example, the definition of a cluster may range from an entire village or town to a subset of patients or providers at a health-care facility. Once selected, the clusters (rather than individuals) are randomized to an intervention or control arm, and all members of a cluster receive the same intervention at parallel time points (Hemming et al. 2017).

There are several benefits inherent to using a cluster RCT design. First, this study design facilitates the analysis of intervention effects on populations rather than individuals. Accordingly, this approach often better aligns with public health interventions that target groups, institutions, or systems. This design also enables researchers to account for the risk of "contamination," which can occur when an individual receives an intervention that can impact community members (e.g., vaccinations inducing herd immunity) (Osirin et al. 2009).

The cluster RCT design offers additional potential benefits when applied to underserved populations. As these studies are undertaken with communities or groups of people, community partnership and feedback can optimize the trial for local participants. For example, the study community may express that it is unacceptable for a control arm to receive only the standard of care and no intervention (WHO Ethics Working Group Meeting 2014). Randomization by cluster can confer further benefits, including improved study efficiency and compliance, as entire communities or facilities are receiving the intervention (WHO Ethics Working Group Meeting 2014; Mtande et al. 2019). This community focus requires researchers to seek high-level buy-in from community leaders and partners during the initial stages, which often improves trial design and may also facilitate

post-trial adoption of the intervention (Osrin et al. 2009; Robler et al. 2020). The continued access to the intervention after study completion is particularly important for vulnerable populations (World Health Organization and Council for International Organizations of Medical Sciences 2017).

There are limitations of the cluster RCT that must be considered. Depending on the intervention being studied, it may not be possible to select well-defined communities. Clusters may not self-identify as a cohesive group, and this presents challenges to engendering buy-in, partnership, and feedback. As study power is affected more by the number of clusters than the number of individuals within a cluster, achieving adequate power could require increasing the number of clusters, which can be expensive and logistically burdensome (Hemming et al. 2017). In addition, randomizing by cluster means that cluster RCTs generally have fewer randomized units than individual RCTs and therefore carry a greater risk of imbalanced study arms (Weijer et al. 2012).

Hearing Norton Sound Study • The Hearing Norton Sound trial, led by authors SDE and SKR, is a recently completed cluster RCT that evaluated a telemedicine referral intervention for school hearing screening in rural Alaska (Emmett et al. 2019a,b). This study randomized 15 Alaska Native communities in the Bering Strait region of northwest Alaska, including a total of 1481 participants from kindergarten through 12th grade, to receive either the telemedicine specialty referral pathway intervention or the standard primary care referral pathway. The primary outcome measure was time to follow-up, and secondary outcome measures were change in the prevalence of hearing loss, hearing-related quality of life, and school performance (Emmett et al. 2019a). Inclusion was promoted in this trial by encouraging participation of all children in all grades across an entire school district in rural northwest Alaska where the population is primarily Alaska Native.

With the overarching goal of this study to identify culturally relevant solutions to address undiagnosed childhood hearing loss in rural Alaska, stakeholder and community engagement played

central roles in study conception and design, as well as interpretation of findings and plans for dissemination. In addition, an Alaska Stakeholder Team, including Co-PI SKR, partnered with the scientific team to oversee the entirety of the study, from grant preparation through dissemination. The cluster RCT was paired with qualitative components to elicit community input and perspectives. The mixed-methods design incorporated both pre- and post-trial focus groups and community events, as well as over 100 semi-structured interviews with Alaskan stakeholders, including, teachers, parents, principals, healthcare workers, elders, and children (Fig. 2). Stakeholders and community members guided fundamental elements of the study design, including the decision to not randomize the screening protocols so that all children received enhanced screening and selection of cluster randomization to ensure that all children from a community received the same referral pathway (Robler et al. 2020). These design selections were made based on stakeholder and community input that emphasized the importance of all participating children receiving benefit, including those randomized to control communities. Semi-structured interviews with stakeholders contextualized RCT findings, providing insight into individual and community experiences with the telemedicine referral pathway and refinement of the intervention for stakeholder-driven post-trial implementation (Emmett et al. 2019a).

The Cultural Council assembled for the study guided presentations and translation of preliminary results to community members in post-trial focus groups and community events, where a community-guided dissemination plan was developed. As part of these community-guided dissemination efforts, documentary narratives were developed using audio, video, and photographic media so that community members could present findings through storytelling in their own voice, in keeping with the oral tradition of participating Alaska Native communities.

Stepped Wedge Randomized Controlled Trial

Compared to a parallel design, cluster randomized trial, a stepped wedge RCT design randomizes research participants,

Exploratory Sequential

Explanatory Sequential

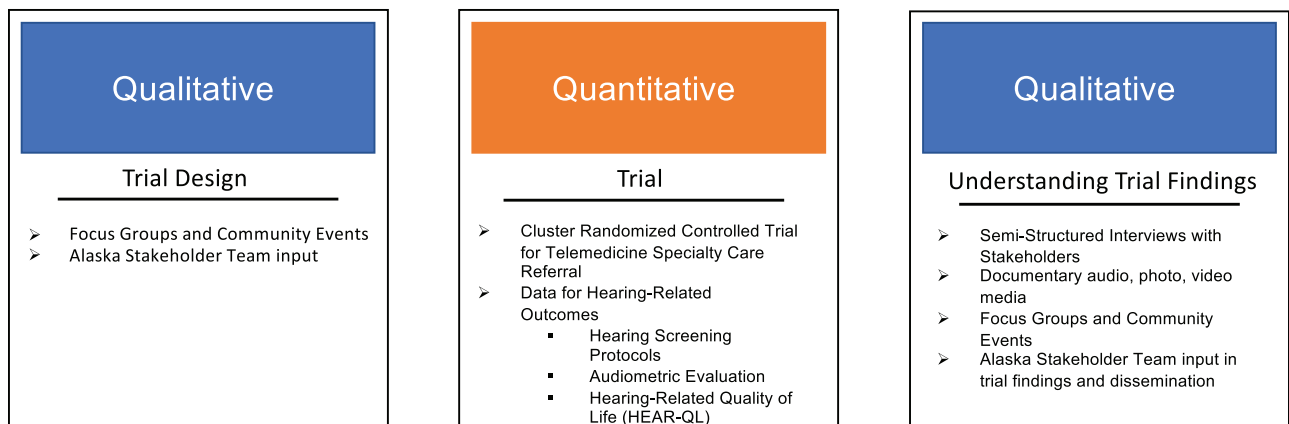


Fig. 2. Mixed-methods design of the Hearing Norton Sound cluster randomized controlled trial.

clusters of participants, or groups of clusters to receive the intervention at varying time points (Joag et al. 2019). Historically, this design has been referred to as a waitlist design. Typically, this design has a period of time at the start of the trial in which none of the participants or clusters receive the intervention, and thus this period can provide valuable control condition data (Hemming et al. 2015). During the course of the trial, participants or clusters cross over into the intervention condition at regular intervals known as steps. The sequence of when each cluster crosses over is randomized. At the end of the trial, all participants or clusters are in the intervention condition. The length of time before a participant or cluster crosses over to receive the intervention is defined as the “step length,” which informs both the trial duration and the total number of participants or clusters. Unique to the stepped wedge RCT, all groups eventually receive the intervention during the study period (Copas et al. 2015). At the conclusion of the study, all clusters have both control and intervention condition data, and this unique pragmatic trial design can facilitate both between cluster and within-cluster analyses of intervention efficacy or effectiveness. In a traditional cluster RCT, the intervention is only available to a select number of clusters; however, in the stepped wedge RCT study design all clusters receive the intervention. The stepped wedge design is appropriate in situations where withholding the intervention could have unfavorable political or ethical effects on the communities in which the study is implemented (Hemming et al. 2015).

The stepped wedge RCT design offers several unique benefits in addition to many overlapping benefits with the cluster RCT. As opposed to simultaneously launching the intervention into a large number of clusters at once, the stepped implementation of the intervention in this design over the course of months or years may allow the research team to logistically plan and prepare for intervention launch in each of the clusters increasing the feasibility of the study (Joag et al. 2019). If the population within the clusters differs significantly (i.e., size of the community, racial/ethnic diversity, socioeconomic status), the stepped wedge design is superior to a cluster design since within-cluster analysis is possible. Furthermore, in the setting of a pending policy decision regarding the implementation of

a particular intervention, this study design provides a way to analyze the effect of the intervention across a broader population and may be more informative than a before-and-after study (Prost et al. 2015).

Relevant to underserved populations, the stepped wedge RCT ensures the availability of the intervention to all participating groups. This design also allows researchers to assess the effect of the intervention in clusters that may differ significantly, such as comparing the effectiveness of an intervention in a rural cluster compared with an urban cluster. This has the benefits of improving acceptability in communities that want control groups to receive the intervention and providing access to a potentially beneficial healthcare intervention (WHO Ethics Working Group Meeting 2014; Prost et al. 2015). Finally, compared with those leading individual RCTs, researchers conducting a stepped wedge RCT are likely to be better positioned to feasibly ensure intervention roll-out to the clusters (Prost et al. 2015).

This study design is associated with several limitations, including one limitation with high relevance to underserved populations. It must be acknowledged that some groups will be delayed in receiving the intervention - an important consideration in communities that have high disease burden and limited access to healthcare resources (Joag et al. 2019). Another important consideration is that some of the clusters will not receive the intervention until near the end of the trial, and there may be changes that occur within the overall population health, developing policy, healthcare practices, or access to care, resulting in “confounding with any underlying temporal trend” (Hemming et al. 2015). This requires vigilance on the part of the research team to monitor for such changes and to attempt to control for and/or account for temporal trends in the analyses of the data at the conclusion of the study.

CHIRRP Study • The Communities Helping the Hearing of Infants by Reaching Parents trial (Bush 2020) led by author M.B., utilizes a stepped wedge RCT design to evaluate the effectiveness of a patient navigator intervention to decrease the nonadherence rate of infants who are referred on newborn hearing screening to obtain an outpatient definitive diagnostic hearing evaluation (Fig. 3). The study is designed to launch the

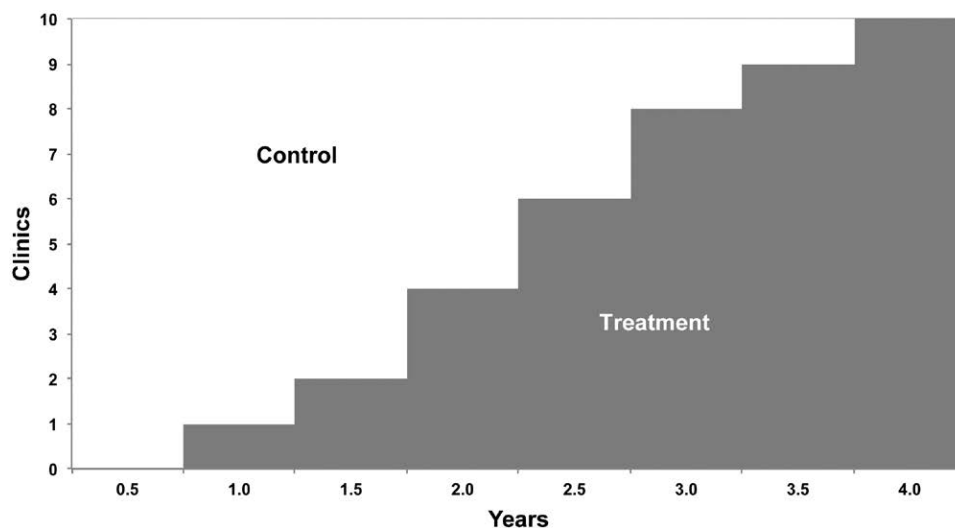


Fig. 3. Communities Helping the Hearing of Infants by Reaching Parents trial stepped wedge randomized controlled trial design.

intervention in a total of 10 state-funded clinics across the state of Kentucky over the course of 4.5 years. At the onset of the study, all clinics (which represent a cluster and the unit of randomization) are in a control condition without the intervention, and the nonadherence rate for each clinic for follow-up diagnostic audiology appointments after a referred newborn hearing screen was assessed as the primary outcome. A randomization scheme was developed before the initiation of the study to determine the order in which the clinics would “step” into receiving the intervention during the study. The step duration is 6 months, and each step involves either one or two clusters converting from the control condition to the intervention condition. For those clinics that are in the intervention phase, all families referred for diagnostic hearing testing after a referred newborn hearing screening test are potentially eligible, and attempts are made to recruit those participants. The effectiveness of patient navigation is assessed by comparing the nonadherence rates of referred newborns to obtain diagnostic audiological testing by 3 months after birth before and after patient navigation. Intervention effectiveness can be assessed within a cluster (within one clinic before and after intervention launch) and between clusters (comparing nonadherence rates across different clinics before and after intervention launch) (Bush 2020).

This trial design was selected due to the number of benefits previously outlined. On the basis of the preliminary work and prior individual RCT efficacy study (Bush et al. 2017), there was a strong preference of community members and key stakeholders to provide the intervention to all clinics/clusters over the course of the study. In addition, this design had higher feasibility than an individual RCT, which would add significant complexity and challenges in randomization at the individual level and launching the intervention simultaneously to all 10 clinics/clusters. Furthermore, since these clusters are quite heterogeneous based on geographic locations and sociodemographic composition, this design allows rigorous assessment of the effectiveness of the intervention across a diverse population. This design facilitates the overarching goal of improving healthcare access and utilization by enabling equitable enrollment without compromising scientific rigor.

The Role of Dissemination and Implementation Research Methodology to Promote Equity

Translation of novel research findings into diverse populations has been surprisingly inefficient. The goal of the research is to enhance human health, yet most discoveries are translated slowly or never fulfill this promise. The challenge of moving health research findings from discovery to real-world settings is complex and multifaceted. Although evidence-based interventions are intended to affect the health of large populations, the lack of dissemination and implementation of scientific discovery into practice results in less than 5% of the eligible population actually receiving benefits from evidence-based therapies (Glasgow et al. 2012).

Dissemination and implementation science is an evolving field that seeks to address this issue by using the rigorous and validated methodology to investigate barriers and facilitators to translation of research into diverse contexts. Dissemination is defined as an “active approach of spreading evidence-based interventions to target audience via determined channels using planned strategies;” however, implementation science involves the “process of putting to use or integrating evidence-based interventions within a setting” (Glossary n.d.). Dissemination

and implementation science focuses on investigating and understanding the processes involved in the adoption, implementation, and sustainability of evidence-based interventions. A commonly used framework is the Consolidated Framework for Implementation Research (CFIR), which provides guidance to systematically assess barriers and facilitators across five domains to prepare for implementation of an intervention using theory-based constructs (Damschroder et al. 2009; Keith et al. 2017). CFIR domains include intervention characteristics, outer setting of intervention delivery, inner setting of intervention delivery, characteristics of individuals, and processes of intervention delivery. A variety of validated instruments are used to measure outcomes among these domains (Keith et al. 2017). Furthermore, this field depends heavily on mixed methodology to gain robust and diverse perspectives.

Since dissemination and implementation research focuses on moving research evidence into more diverse populations, it is critical for hearing healthcare researchers to consider how dissemination and implementation methodology could be combined with traditional clinical trial designs to expedite and expand the translation of their work. It is an accepted practice to design hybrid trials which combine dissemination and implementation research methodology with traditional clinical trial designs to promote rapid translation of research while gaining an understanding of factors influencing equity.

Hybrid Effectiveness-Implementation Trial Designs • Hybrid effectiveness-implementation design type 1 is focused on the effectiveness of a clinical intervention in a new population or setting. The secondary focus is to explore implementation-related factors, such as feasibility, adaptation, and appropriateness. This may involve a traditional effectiveness study and a “process evaluation.” The effectiveness study is intended to evaluate performance in a “real world” setting and provide increased external validity compared with traditional clinical trials. For example, ultrasound sensitivity for detecting early-stage hepatocellular carcinoma was 63% in prospective efficacy studies but only 32% in an effectiveness study due to the operator-dependent nature and low utilization of ultrasound (Singal et al. 2014). The process evaluation component is used to describe the implementation experience (i.e., what worked or did not work), identify how the intervention needs to be adapted for the setting, and/or determine what is needed to support the people and place implementing the intervention (Landes et al. 2019). This design identifies barriers and facilitators to implementation, and data can be collected through mixed methods. A hybrid type 1 design should be utilized when the clinical effectiveness evidence is scarce. This type of effectiveness study also offers an ideal opportunity to explore implementation barriers and help plan implementation strategies for the next stage (Landes et al. 2019).

Hybrid effectiveness-implementation design type 2 has a dual focus on the clinical intervention and implementation-related factors. This requires an explicitly-described implementation strategy that is thought to be feasible in the real world. This is distinct from a type 1 design and always includes measurement of implementation outcomes. This type of hybrid trial could involve an effectiveness trial paired with an implementation trial (Landes et al. 2019).

Hybrid effectiveness-implementation design type 3 has a primary focus on implementation outcomes, such as adoption, fidelity, and sustainability. The secondary focus is to observe or collect data on the intervention outcomes and evaluate the level of adoption

and fidelity produced by the implementation strategies. This trial includes an implementation trial plus an evaluation of patient-level outcomes. These designs primarily compare implementation strategies, and if studied in healthcare settings, the strategies typically focus on provider, clinic, and/or system levels and their impact on implementation outcomes. In some cases, implementation strategies may also target patients. When randomization is used in hybrid type 3 studies in healthcare settings, it commonly occurs at the provider, clinic, or system level (Landes et al. 2019).

Overall, hybrid designs will either (1) test the effects of a clinical intervention while observing and collecting information on implementation; (2) simultaneously test clinical and implementation interventions/strategies; or (3) test an implementation strategy while observing and collecting information on the clinical intervention's impact (Curran et al. 2012). These trial designs can give the researcher insight into the efficient and effective delivery of novel evidence-based interventions across broader practices, populations, and policies.

CONCLUSIONS

Clinical trials are essential to evaluating EHC innovations and translating them into clinical practice to improve outcomes and quality of life. Among clinical trials in EHC, there is often a lack of key stakeholder and community involvement, a failure to recruit and retain underrepresented and underserved populations, and an absence of rigorous dissemination and implementation of novel research to broader populations. As EHC researchers, we must expand our repertoire of clinical trials designs and prioritize partnerships with communities to best serve the patients who are most in need of care.

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