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Six dimensions of research trial acceptability: how much, what, when, in what circumstances, to whom and why?

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ABSTRACT

Ethics guidelines emphasise that research should be acceptable to the people invited to take part. However, acceptability is subjective and dependent on context, complicating its assessment and use as an ethical standard.

This paper examines the concept of acceptability in relation to parents' perspectives on a paediatric vaccine trial in Malawi. We examined decisions on participation and experiences of the trial through interviews with parents in 41 households invited to enrol their children and participant observation of trial processes. Fieldwork took place in Chikwawa, Southern Malawi from February–October 2016.

Parents were not neatly split between those who saw the trial as acceptable and those who did not; instead there were mixed and changing feelings among parents who enrolled their children, and among those who withdrew or did not take part. Some parents agreed to participate but had concerns about the trial, while others expressed satisfaction with the trial but still did not take part.

These experiences indicate substantial variation in the nature of acceptance. We describe these variations in relation to six dimensions of acceptability: how acceptable the trial is, what aspects are acceptable, changes over time, circumstances affecting acceptability, variations between people, and reasons for participation or non-participation.

The findings illustrate the difficulty of determining whether a trial is sufficiently acceptable to potential participants. We suggest that clarifying definitions of acceptability and examining how acceptability varies in degree, between trial components, over time, and between people and contexts may help researchers generate more nuanced descriptions of acceptability that support responsive and ethical trial design.

1. Background

The acceptability of research to invited participants is essential for ethical practice. WHO identifies "acceptability to participants" as a key ethical issue in study design (WHO, 2014, p. 6), and the UK Health Research Authority suggests that defining "what is acceptable to participants" helps "make research ethical" (Involve, 2016, p. 1). Understanding and enhancing acceptability among the people invited to participate is an important function of community engagement (CIOMS, 2016; Nuffield Council on Bioethics, 2015): community input helps "in ensuring that protocol designs and procedures are […] acceptable to the trial population", in turn "improving recruitment, retention, adherence, and other trial outcomes" (UNAIDS/AVAC, 2011, pp. 44, 20). As such, as well as holding ethical significance, acceptability affects study feasibility: adequate recruitment is unlikely if potential participants see procedures as unacceptable (Feeley et al., 2009).

While the importance of acceptability seems clear, its meaning is more ambiguous; indeed, the idea of acceptability among people affected by research has been criticised as "extremely vague" (Macdonald, 2017, p. 32). Dictionary definitions include both positive and negative situations: acceptable is defined as both "welcome, pleasing" and "barely satisfactory or adequate" (Merriam-Webster, 2017a), while accept can mean "receive willingly" or "endure without protest" (Merriam-Webster, 2017b). Discussions about the acceptability of research to invited participants often lack explicit definitions (Feeley et al., 2009). Some analyses equate acceptance with participation,

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contrasting this with refusal to participate, as in "deciding whether to accept or decline the research" (Mfutso-Bengo et al., 2008, p. 58; other examples include Gysels et al., 2008; Fayter et al., 2007; Moynihan et al., 2012). However, these categories of participating and refusing can hide substantial variation in views on study procedures (Fairhead et al., 2004). Further, researchers often discuss promoting "acceptance" when they mean ensuring "tolerance" or "avoiding organised opposition" (Lavery, 2017). To accommodate this variation in meaning, we adopt a working definition of acceptability as a perception among invited participants that the research design is, to varying extents, "favourab[le]" (Feeley et al., 2009, p. 86), "agreeable, palatable, or satisfactory" (Proctor et al., 2010, p. 67). This definition reflects our focus on acceptability of study designs to participants as ethically significant.

As well as ambiguity regarding its meaning, assessment of acceptability is complicated by subjectivity, variability and dependence on context. Acceptability is not a fixed property of a trial or particular research procedure, but rather determined by individual perceptions, and shaped by personal and social contexts. This influence of context is discussed explicitly in some accounts of views on research among participant communities (Fairhead et al., 2004; Kingori, 2015), and suggested by studies on willingness to participate (Cunningham et al., 2018; Gamble et al., 2012; Otwombe et al., 2011; Trauth et al., 2000) and reasons for participation or refusal (Gysels et al., 2008; Strömmer et al., 2018) that describe varied perspectives among target participants. However, the significance of contextual variability is explored more extensively in literature on acceptability of health interventions. As this literature suggests, different individual, household or group circumstances and priorities generate varied perceptions of acceptability (Heise, 1997; Montgomery et al., 2010). Research on health interventions also shows that acceptability can change over time, for example shifting through social interactions (Cohn, 2016) or with experience (Dyer et al., 2016). Acceptability is also relative, such that views of a particular health intervention depend on the perceived suitability of any alternative interventions (Heise, 1997; Hyder and Morrow, 2006; Mcintyre et al., 2009). Finally, the degree of acceptability varies, ranging from high demand to ambivalence (SAGE Working Group on Vaccine Hesitancy, 2014).

Although existing literature points to these variations in acceptability, the concept of acceptability has not been a specific focus in discussions about research participation. We lack frameworks for examining acceptability among invited participants, and reviews of research on trial participation and acceptability call for more in-depth analysis and understanding of individual variation (O'Cathain et al., 2014; Ross et al., 1999). Some approaches to assessing acceptability may miss important variations in and reasons behind invited participants' perceptions. For example, assessing acceptability based on consent to enrol or using single timepoint questionnaires (e.g. Richards et al., 2014; Stead et al., 2005; Wallace et al., 2018) may overlook different degrees of acceptability, changes over time, or contexts affecting decisions on enrolment. Qualitative reports may also neglect underlying contexts or describe only limited areas of variation, for example, between individuals rather than over time (e.g. Crawley et al., 2013; Gafos et al., 2017). Given the ethical importance of acceptability and its ambiguity, further work to clarify this concept may support more nuanced investigation of participant perceptions to inform responsive trial design.

Our research examines acceptability in the context of a paediatric influenza vaccine trial in Malawi. We explore parents' decisions about enrolling their children and reasons behind these decisions, perceptions of the trial, and variation in acceptability between trial procedures, over time and between contexts and people. Our aim is to deepen understanding of the acceptability of research to potential participants, and to suggest directions for future assessment of acceptable trial design.

The vaccine trial examined whether malaria infection affects immune response to influenza vaccine in children (the FLUVAC trial, details in Peterson, 2016). The trial took place in Chikwawa, a rural district in Southern Malawi where under 5 mortality is 62 per 1000 live births and the poverty rate is 82% (compared to 73 per 1000 and 51% for Malawi overall, Government of Malawi, 2012; National Statistical Office, 2017). Approximately 1300 children aged 6–59 months were recruited. Participation involved three main appointments, spaced one month apart. Children received the influenza vaccine at the first two appointments, and had samples taken at all three appointments, including a venous blood sample to measure influenza serology, a finger prick blood sample to test for the malaria parasite (not in real time), and stool samples from a subset of children. A point of care rapid diagnostic test for malaria was administered to febrile children to guide treatment. Trial teams rotated between 28 villages, spending approximately two weeks at a time in each village and returning one month later for follow-up visits.

Given the age of child participants, enrolment was decided by parents. Fieldworkers and community volunteers approached parents in their homes and invited them to visit a study tent assembled in each village, where further information was provided. Trial staff gave parents an information sheet describing procedures, risks (potential side effects and discomfort from the vaccine and blood samples) and benefits (reduced risk from influenza, malaria treatment if tested positive, and the population health benefit of additional evidence on influenza vaccination) (see supplementary file 1). Procedures, risks and benefits were also explained verbally, with time for questions. Although parents were not vaccinated, they were required to participate actively in the trial by answering questionnaires on household circumstances and their own health status, completing an adverse event diary, and accompanying their child during study appointments. The trial protocol referred to parents as participants, and consent forms completed by parents indicated their agreement "to take part in the above study". Parents also described themselves as participating or withdrawing during interviews. Given this role, we consider parents as participants or non-participants, not just as enrolling their children.

2. Methods

We used qualitative research to examine parents' experiences and decisions about trial participation. We conducted interviews with parents in 41 households invited to enrol their children, including parents who enrolled their child (21), who withdrew (9), and who did not participate (11). Most interviews involved the main carer (usually the mother), but in some cases a wife and husband were interviewed together because both wanted to be interviewed. With these joint interviews, we took care to encourage responses from both parents. Interviews were divided between nine villages where the trial took place, selected to cover variations in circumstances such as proximity to health centres, time points during the trial, and levels of uptake as reported by trial staff. Some parents were interviewed a few days after the first appointment, others midway through participation, and others after completion or withdrawal, providing a range of experiences. Repeat interviews were conducted with three parents who were initially interviewed shortly after their first trial appointment, including one who withdrew and two who remained in the trial, to understand any changes in their experiences over time. Topic guides covered experience of the trial, decisions regarding participation, information about the trial purpose and procedures, perceived benefits and drawbacks, and issues that might affect engagement such as previous research experience (see Supplementary file 2). Interviews lasted approximately one hour and were conducted in Chichewa by an experienced qualitative researcher (MP). Audio recordings were transcribed verbatim and translated into English.

We also conducted participant observation of trial processes. This involved accompanying fieldworkers as they approached parents, observing informed consent procedures, attending community meetings about the trial, and holding informal discussions with trial staff and