Genome Medicine

RESEARCH HIGHLIGHT

Are enrollment sites the key to optimizing participation in genetic studies?

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Abstract

In a time when the challenge of people being over-researched and experiencing research fatigue is increasingly discussed, low participation rates and potential sample biases are a growing concern in genetic research. In a recent study assessing factors relevant to successful recruitment of patients with myocardial infarction to a genetic study, enrollment site was identified as the most important factor associated with patient participation, whereas patient-level factors such as race, gender and education played a limited or no role. These results underline the importance of appropriate recruitment routines at enrollment sites in order to reach high levels of participation in genetic research.

Keywords: Enrollment; ethics; genetic research; myocardial infarction.

Importance of identifying factors that limit participation in genetic studies

For studies involving human research subjects it is, in general, crucial to keep up participation rates in order to reduce the risk of sample bias, that is, the systematic under-representation of certain groups in the study sample, which can potentially bias the research results. So far, genetic research has often faced greater difficulties than non-genetic research in recruiting participants, although participation rates can vary widely [1]. Recent discussions suggest that research subjects can experience 'research fatigue' after being over-researched, making them less prone to consent to further participation, indicating that there might be increasing difficulties in recruiting subjects in the future. This could be especially problematic for genetic studies that are added on to a plethora of existing non-genetic studies. In order to reduce non-participation, which may be due to a variety of factors, it is crucial for researchers to find out why different patient groups, and healthy individuals, choose not to participate in genetic research. While some factors may be strongly tied to specific patient categories, others may be of more general relevance [1].

A study by Lanfear and colleagues [1], published in this issue of *Genome Medicine*, addresses this important issue by examining a large number of factors potentially influencing recruitment to a genetic study of patients with myocardial infarction (MI). This work fills a gap in the literature regarding participation in genetic research among patients with acute illnesses, but the results of Lanfear and colleagues are also of general interest to anyone doing genetic research involving patient material. They identify one factor, the site of enrollment, as particularly important for successful recruitment, while their results indicate that most others are of limited relevance.

Significance of the enrollment site

Taking TRIUMPH (Translational Research Investigating Underlying disparities in recovery from acute Myocardial infarction: Patients' Health status), a prospective multicenter registry of patients with MI, as their starting point, Lanfear *et al*. examined factors associated with participation or non-participation of registered patients with MI in a genetic sub-study [1]. Data for all patients included in the study, enrolled in the 24 hospitals involved in TRIUMPH, were collected. Using trained data collectors at each site, a broad spectrum of information was obtained, including data on health status, medical history, sociodemographic data, socioeconomic status and social support. Standardized sets of questions were used to quantify psychosocial and health status characteristics for each patient.

The overall consent rate to donate genetic material as part of the TRIUMPH sub-study was 80%, but Lanfear *et al*. observed considerable variations between the different enrollment sites. Rates of consent ranged from 100% of the patients enrolled in TRIUMPH to as low as 40%,

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depending on the hospital involved. In fact, the location where the patients with MI were asked to participate in the genetic study was the major identified dividing line between participants and non-participants. Only two patient-level factors (race and body mass index (BMI)) showed statistically significant associations with rates of participation. More specifically, African-American patients showed a lower participation rate compared with white patients, a result that is in line with previous experiences from studies in the USA [2-4]. Lanfear and colleagues take this factor to be of real practical significance and stress the importance of being aware of it in order to counter the risk that African Americans are under-represented in genetic studies. Patients with a BMI ≥25 were associated with a slightly higher participation rate, compared with the others included in the study. Noting that such an association has not previously been reported and seems difficult to explain, Lanfear *et al*. are inclined to interpret this finding as of questionable clinical importance.

Other factors, such as education and gender [3,5], which have been identified as relevant for participation in genetic research in other studies, were not found to be significant. In contrast to the results and interpretations presented in the article by Lanfear and colleagues, personal demographics, health status and sociocultural dimensions are frequently claimed to influence participation in research. These assumptions are supported by a number of studies, although other studies point in the opposite direction [3,6]. The role of enrollment sites is usually not discussed as such, but factors tied to the enrollment situation, such as information provided and communication style, occur in discussions of factors affecting participation rates [3,4,7,8].

Potential for improvement

The results obtained by Lanfear and his colleagues might be viewed with optimism. Although the underlying mechanisms affecting participation rates at the different enrollment centers are not explained in this study, the authors find it likely that differences in recruitment rates depend on differences in the individual study coordinators' motivation to recruit, presentation style, ability to provide patients with satisfactory information, and ability to establish a trusting relationship. If these assumptions are correct, for which there is some support in the literature [4,7,8], then there may be considerable potential for improving participation rates by better training and standardization of enrollment processes. In turn, high-quality enrollment processes could potentially lead to improved quality in genetic association studies.

This view is shared by others who report good recruitment results after having refined their recruitment practices [3,4,7,8]. Open, frequent and personalized communication with potential participants has been identified as one potential success factor [3,7,8]. Reducing a perceived cultural gap and an accompanying lack of trust by, for instance, hiring an African-American nurse to increase recruitment among African Americans is another [7]. Reducing mental and practical barriers by combining recruitment with educational sessions or enrolling at locations closer to underrepresented groups has also appeared to be fruitful, as has the use of targeted recruitment material and engagement of the concerned patient group in discussions on the ethical aspects of the study [4,6,7]. For long-term studies, the importance of participant involvement, keeping participants updated and reliable routines for feeding back clinically relevant results obtained through genetic tests has been stressed [4,8]. However, more systematic research regarding potential 'success factors' is needed. How to optimize communication with potential participants and establish trust might be the core themes to focus on, as suggested by Lanfear *et al*.

Optimal or ethical recruitment - or both?

Success in recruiting participants may, in principle, come at the price of side-stepping ethical requirements for research involving human subjects, such as providing appropriate information about relevant aspects of participation. This means that proven success in recruiting patients to genetic studies does not automatically imply that the recruitment process is to be recommended. Enrollment centers may at times prioritize satisfying the urge of researchers for a large amount of patient material over concern for patient autonomy and privacy. If trust relationships are to be maintained, which seems necessary for success in recruitment in the long run [8], disregarding patient interests would be the wrong way to proceed. The concerns and worries of actual and potential research subjects need to be dealt with thoughtfully. Confidentiality and proper data protection, and respect for privacy and autonomy, are themes that have been pointed out as particularly important by participants in genetic research [9,10].

Lanfear *et al*. touch upon ethical issues in the discussion of their article, where they underline the importance of close collaboration between researchers, coordinators and institutional review boards, among others, in order to guarantee that the interests of research subjects are well protected. Indeed, an underlying idea, shared by others [3,8], seems to be that good research ethics, in the sense of proper and respectful protection of the interests of actual and potential research subjects, is conducive to successful recruitment and thereby to high research quality.

Abbreviations

BMI, body mass index; MI, myocardial infarction.

Competing interests
The author declares that he has no competing interests.

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