Ethnically representative, comparable and inclusive samples in biomedical research: when are they necessary, possible and effective?

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Abstract: Ethnic disparities in health and health care utilisation have encouraged policy makers and researchers to press for ethnically inclusive sampling frames that are both: (i) representative (so that their findings are generalisable and applicable to the population as a whole); and (ii) comparative (so that any ethnic disparities can be exposed, examined, understood and addressed). This paper explores the potential consequences of policies that have sought to impose ethnically inclusive sampling frames that are both representative and comparative. Since the statistical requirements of representative and comparative samples are very different, the conflation of these two sampling frames under the aegis of inclusivity often leads to inadequately powered comparative analyses, particularly those involving the smaller samples of minority ethnic groups. Likewise, since the denominators required to assess the ethnic inclusivity of research samples are usually provided by statutory agencies, and since these agencies increasingly use socially-constructed and context-specific ethnic categories based on self-reported identity, researchers are obliged to use the very same categories when calculating their studies' enumerators. In the process these categories become standardised within scientific practice, and used therein as (if they were) reliable, valid, discrete and generalisable markers of wholesale and fundamental difference. Thus, when the types of samples and data required to address and assess ethnic inclusivity are subsequently used in comparative analyses, these are predisposed towards the production of statistically underpowered, analytically flawed, aetiologically imprecise and potentially misleading findings. This paper argues that the analytical and aetiological requirements of representative and comparative research designs are often incompatible, and that different research questions might benefit from: representative, exclusive and/or boosted sampling frames; and from statutory and/or bespoke ethnic categories. It seems unlikely that the sampling frames required for research that is both representative and comparative are possible, necessary or cost-effective given their requirement for inclusive and boosted sample sizes and disproportionate levels of participation amongst minority ethnic groups.

Abbreviations: DH, United Kingdom Department of Health; NIH, United States National Institutes of Health; OMB, United States Office of Management and Budget; ONS, United Kingdom Offi ce for National Statistics

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Transatlantic variation in attitudes towards ethnic inclusivity in biomedical research

There are three key reasons why ethnic inclusivity might be warranted in policy-relevant research: (i) to ensure that research findings are applicable and generalisable to multi-ethnic referent/target

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populations; (ii) to support comparative analyses of any differences between people identified as belonging to different ethnic groups; and (iii) to prevent the unnecessary and potentially unethical exclusion of participants from particular ethnic groups [1]. A number of recent studies (including that published by Sheikh et al. [2]) have made important contributions to ongoing debates surrounding ethnic inclusivity in biomedical research. By exploring the views and experiences of asthma researchers in the UK and US, and of community leaders from the UK's largest minority ethnic group ('South Asians'), Sheikh et al.'s [2] study highlighted a number of important differences between the UK and US contexts, including those relating to the: size and sociocultural characteristics of each country's minority ethnic populations; financing and availability of healthcare; and regulation of funding for biomedical research. However, in *both* contexts their study found extensive (initial) reluctance on the part of biomedical researchers to address the issue of ethnic inclusivity on socio-political, scientific and practical grounds. In particular there was: resistance to what some viewed as political interference in their work; some skepticism about the perceived merits of focusing on ethnicity (rather than on a broader range of biomedically relevant sociodemographic and clinical factors); and widespread apprehension about the additional time, effort and cost required to achieve ethnic inclusivity in research.

Yet despite their initial reluctance, the US-based researchers acknowledged that the inclusivity policies introduced by the National Institutes of Health (NIH) [3] had succeeded in facilitating the inclusion of minorities in biomedical research. They also acknowledged that an important benefit of these policies was that they could generate samples capable of supporting potentially insightful comparative analyses. While there was little evidence that the UK-based researchers actively excluded ethnic minorities from their research, they appeared to pay little attention to ethnicity during recruitment and did not design their recruitment practices to facilitate participation by ethnic minorities or to capitalise on the potential for comparative analyses of study participants identified as belonging to different ethnic groups. Interviews with UK-based South Asian community leaders revealed that they were concerned that biomedical research did not adequately consider ethnicity. These leaders were keen to facilitate greater participation by members of their communities but were largely unaware of opportunities to engage in biomedical research and identified a number of likely barriers to participation (as well as potential solutions for addressing these).

Unresolved concerns about the potential utility of ethnic categories in biomedical research

The principal strengths of Sheikh et al.'s [2] study are its qualitative approach and comparative design. These ensure that their findings can help us understand the differential participation rates of minority ethnic groups in biomedical research within the US and UK from the perspectives of those involved in designing and conducting these studies. Indeed, notwithstanding the very different experiences, attitudes and views of US- and UK-based researchers, their study also found substantial consensus concerning: the additional time, effort and cost required to achieve ethnic inclusivity; and the likely role that funding policies might play in facilitating and promoting ethnic inclusivity in biomedical research. However, many of the studies exploring the merits of ethnic inclusivity, including Sheikh et al. [2], tend to overlook a number of concerns regarding the use of ethnic categories in biomedical research. Instead, these focus on the potential role that ethnic inclusivity might play in supporting comparative analyses of biomedical differences amongst ethnic groups (rather than on the role that inclusivity might play in generating generalisable evidence or non-exclusionary research practices).

The longstanding debate over the questionable utility of ethnic categories in biomedical research (including their use to achieve and monitor inclusivity) shows no signs of dissipating [4]. Substantial concerns remain over what these terms and concepts mean, how they should be operationalised, and when (and in what form) they might offer analytically useful markers of associated socio-political, cultural and/or genealogical characteristics [6]. It is also unclear how researchers might minimise the potential for reification, essentialisation, stereotyping and stigmatisation that can accompany the routine use of socially-constructed and context-specific ethnic categories as if these were always scientifically robust (i.e. discrete, reliable, valid and generalisable) markers of wholesale and fundamental difference [1,7] (as Sheikh et al [2] reveal).

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Statutory statistical agencies – such as the US Office of Management and Budget [8], the UK Office of National Statistics [9]) and the biomedical agencies these support (including the US NIH [3] and the UK National Health Service [10]) – have essentially side-stepped many of these conceptual and methodological issues by developing ethnic classifications and related categories that are socially sensitive and salient markers of self-assigned identity rather than scientifically robust markers of associated socio-political, cultural and/or genealogical characteristics [10, 11]. This may seem a pragmatic if not expedient compromise given the lack of consensus on what ethnicity means and the different measurement techniques required to operationalise the different definitions favoured within different analytical and applied contexts [5]. However, their focus on what constitutes a more 'global' measure of 'identity' has important consequences when these categories are imported into and used within biomedical research settings – not least when they are used to generate the data required to assess whether study samples are representative/inclusive of multi-ethnic referent/target populations [see, for example, 10]. Since the denominators required for these assessments are likely to be provided by statutory agencies using the (sensitive, salient yet expedient) classifications and categories they prefer, biomedical researchers will be obliged to use the very same categories when calculating their study's enumerator [10]. And unless biomedical researchers collect additional data on ethnicity using alternative (i.e. bespoke) categories with greater relevance to the intra-group heterogeneity of the associated (socio-political, cultural and/or genealogical) characteristics their studies set out to explore, any comparative analyses will be based on (and will tend to reify) statutory categories as robust markers of these characteristics or as discrete entities in their own right.

Biomedical differences between ethnic groups: practical challenges and analytical opportunities

Notwithstanding these unresolved concerns many researchers and commentators argue that ethnic differences in disease susceptibility, and in the efficacy of diagnostic and therapeutic interventions, are sufficiently widespread and fundamental amongst these sociodemographic groups to present both practical challenges *and* analytical opportunities for biomedical researchers. The practical challenges include designing studies to support analyses that are not subject to potential confounding from any biomedically relevant differences between participants identified as belonging to different ethnic groups [e.g. 13]. However, inclusive studies adopting comparative designs also provide analytical opportunities for generating and testing important aetiological and/or clinical hypotheses concerning genuine biomedical differences between different ethnic groups (whether these arise from associated socio-political, cultural and/or genealogical characteristics) [5, 14].

To address the challenge of potential confounding from any biomedically relevant differences between groups of people identified as belonging to different ethnic groups, researchers must: (i) ensure that their samples are truly representative of the population as a whole; (ii) statistically adjust for ethnicity in any analyses of non-representative samples; or (iii) recruit participants from just one ethnic group (i.e. exclude all others). Because adjusting for ethnicity requires data from adequate numbers of participants from all of the ethnic groups concerned (and even then appears statistically questionable [15]), many researchers appear to believe that the best way to avoid the need to recruit additional participants from each and every potential ethnic group is by limiting the number of ethnic groups for which sufficient numbers of participants need to be recruited or by excluding participants from all but one ethnic group [16]. Whenever important biomedical differences exist between groups of people identified as belonging to different ethnic groups, including participants from a limited number (or just one) of the potential group(s) available inevitably limits the generalisability of any evidence such studies produce. Moreover, given the racialised nature of contemporary societies, evidence generated from limited or mono-ethnic samples of multi-ethnic populations is unlikely to be perceived as applicable across all ethnic groups (even when it is [17].

Non-inclusive/non-representative study samples are also contentious on ethical grounds because the potential benefits (and costs) of participation in such research are unevenly distributed amongst participants from different ethnic groups. Likewise, when researchers focus on mono-ethnic study samples the research questions they pose are unlikely to address those issues felt to

be most pertinent to the experiences of other ethnic groups. For these reasons, and to generate research evidence that can meet the needs of contemporary multi-ethnic societies, there has been growing pressure to encourage researchers to recruit study participants from different ethnic groups. In the US, as Sheikh et al [2] describe, NIH policies [3] emanating from the 1993 NIH Revitalisation Act oblige researchers to "ensure that… members of minorities and their subpopulations are included" in research funded by the NIH and, for Phase III clinical trials, to ensure that sufficient numbers are included "such that valid analyses of differences in intervention effect can be accomplished". In the UK, the Department of Health's 'Research Governance Framework for Health and Social Care' [18] recommends that "Whenever relevant, it [research] should take account of… race, culture and religion in its design, undertaking and reporting…" and that "The body of research evidence available to policy makers should reflect the diversity of the population."

Priorities for future research

Most biomedical researchers and clinicians would agree that study samples should aim to reflect the diversity of society at large (or at least the diversity of the specified referent/target populations to which the results of their studies are intended to apply). Indeed, this is likely to be considered particularly important for any sociodemographic or clinical characteristics that are relevant, or causally related, to the disease or intervention concerned [6, 7]. However, it is unclear whether many biomedical researchers and clinicians recognise that routine comparative analyses of ethnic groups – such as those required by the US NIH [2] for Phase III trials and those encouraged by the UK DH's [18] 'Research Governance Framework' – are predicated on (and thereby reify) the somewhat contested view that wholesale and fundamental differences exist between different ethnic groups. Nor do many biomedical researchers demonstrate in their published research designs that comprehensive comparative analyses require the use of adequately powered samples of participants from *all* ethnic groups, classified using categories that are equivalent in content and heterogeneity [7]. Thus, despite official support for study populations that are representative/inclusive of the ethnic groups prevalent in society at large [3, 18], and despite Sheikh et al.'s [2] encouraging findings regarding the likely impact of funding policies like those introduced by the NIH [3], it remains unclear:: precisely when ethnic inclusivity is necessary; in what forms inclusive research practices are sufficient; and if the disadvantages of focusing on ethnic inclusivity (not least at the expense of other important sociodemographic and clinical characteristics) might outweigh any potential benefits.

If, even as part of a well-intentioned inclusivity agenda, ethnic categories are routinely operationalised in biomedical research as if these are always scientifically robust markers of wholesale and fundamental differences, there is a risk of generating spurious findings, and of exaggerating and reifying the nature and extent of genuine biomedical differences between ethnic groups [5, 6, 7]. Given these risks, and the analytical limitations of statutory and bespoke categories, the ongoing proliferation of ethnic identities, and the finite constraints on research funding, it is important to consider when: ethnicity is a relevant, important and therefore necessary characteristic on which inclusivity should be based; it is possible (or practicable) to achieve comparable inclusivity for *all* ethnic groups within contemporary multi-ethnic societies; and spending a greater proportion of available research funds on (fewer) studies with greater ethnic inclusivity actually generates a larger volume of the aetiological and/or clinical evidence required to address inequity in health? Given that Sheikh et al [2] found funding policies (such as those introduced by the NIH [3]) are likely to increase ethnic inclusivity in biomedical research, it would certainly be prudent to seek answers for each of these questions to establish when such policies might do more harm than good.

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