

# Constructing a South Asian cardiovascular disease: a qualitative analysis on how researchers study cardiovascular disease in South Asians

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## ABSTRACT

**Background** Debates on the use of race in biomedical research have typically overlooked immigrant groups outside of the black-white racial dichotomy. Recent biomedical research on South Asians and cardiovascular disease provides an opportunity to understand how scientists define race and interpret racial health disparities from an underexamined perspective.

**Purpose** To examine how researchers in the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study defined a South Asian population, and then compared health differences between South Asians and other populations.

**Methods** Qualitative content analysis was performed on eleven articles from August 2013 to January 2021 that directly compared the South Asian cohort in MASALA to four other groups. The MASALA study design article was also included in this analysis. Articles were analysed for how South Asians were defined, and for how health differences between South Asians and other populations were studied and discussed.

**Results** Researchers in MASALA were neither clear nor precise in defining South Asians as either an ancestral group or ethnic group. Their studies also prioritised investigating genetic and molecular causes of the cardiovascular health disparity between South Asians and other populations and failed to examine possible social factors.

**Conclusions** These findings reflect a broader trend in biomedical research in which race and racial health disparities are poorly defined and studied, limiting scientists' understanding of the relationship between race and health. I propose methodologies to help researchers define populations and design studies without relying on biologically reductive assumptions.

## INTRODUCTION

### South Asians and cardiovascular disease

Racialised groups within the USA suffer health disparities associated with social disadvantages tied to their racial identities.<sup>1</sup> However, debates on the use of race in biomedical research to study factors contributing these disparities have typically focused on a black-white racial dichotomy, thereby overlooking other immigrant groups whose presence complicates these debates. For instance, bioethicists have largely ignored a growing area of racial health disparities research: cardiovascular disease among South Asians. Both in their native countries and as immigrants, South Asians experience a higher prevalence of cardiovascular disease compared with other racial or ethnic groups despite lacking traditional risk factors such as obesity and smoking.<sup>2</sup> I

will refer to this health disparity as the South Asian cardiovascular health disparity.

To contribute to the growing literature, the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study aims to provide longitudinal data on the aetiology of and risk factors for subclinical atherosclerosis among South Asians in the USA. Researchers recruited a prospective cohort of South Asians without a cardiovascular disease diagnosis to follow for ten years. Researchers plan to study the progression of cardiovascular disease and its risk factors in South Asians and compare these findings to other ethnic groups.<sup>3</sup> To do so, researchers in MASALA used the same methodology as an earlier study on subclinical atherosclerosis: the Multi-Ethnic Study of Atherosclerosis (MESA). MESA studied the aetiology and risk factors of subclinical atherosclerosis among white, black, Chinese-American and Hispanic participants.<sup>4</sup> By using the same methodology, researchers can make direct comparisons between South Asians in MASALA and ethnic groups in MESA.

MASALA provides an opportunity to understand how scientists define race and interpret racial health disparities outside a black-white dichotomy. Unfortunately, previous studies found that most biomedical, genetic, and health services researchers provided vague definitions of race or ethnicity and failed to explain why race or ethnicity matter to health outcomes.<sup>5–9</sup> Lee argues that the 'undertheorised and unspecified use of race or ethnicity and the biological conclusions drawn about health and difference have the potential to reify 'race' and to limit our thinking about what these biomedical differences suggest about health disparities and inequalities in general.'<sup>8</sup> Thus, scientists can overemphasise or prioritise genetic and molecular explanations of racial health disparities while downplaying social factors, including systemic racism and structural inequities. To add to the literature, I examine how researchers in MASALA define a South Asian population, and then compare health differences between South Asians and other populations. The way researchers defined South Asians determined what research questions were relevant, how they should present and discuss their findings, and how others should interpret findings on the MASALA cohort. I conclude by proposing some methodologies to help researchers define populations and design studies without relying on biologically reductive assumptions.

### Defining race, ancestry and ethnicity

Scientists and philosophers critical about the use of race in biomedical research typically define race according to a social constructionist definition like



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Haslanger's: 'A group is racialised (in context C) if and only if (by definition) its members are (or would be) socially positioned as subordinate or privileged along some dimension (economic, political, legal, social, etc) (in C), and the group is 'marked' as a target for this treatment by observed or imagined bodily features presumed to be evidence of ancestral links to a certain geographical region.'<sup>10</sup> If Haslanger is correct, then assuming these races are biologically different in medically important ways can lead to false or problematic beliefs about individuals of those races. It can also lead scientists to design studies that fail to elucidate the complex relationship between race and health by reducing their association to biological differences. Thus, if biomedical scientists want to study health disparities, they should not use categories that reify race as a real, biological division between humans.

Scientists and philosophers who find race objectionable may consider ancestry a preferable population concept. The concept of ancestry that has attracted most scientists' attention is genetic ancestry. DNA sequencing and statistical programmes allow scientists to group individuals into populations based on shared DNA sequences likely inherited from ancestral populations. Some scientists consider genetic ancestry a better predictor of one's genetics, and thus of one's genetic risk factors, than race precisely because these groups are based on objective genetic differences, not phenotypic differences presumed to indicate genetic differences.<sup>11</sup> Furthermore, the development of these genetic ancestry populations is not born out of the desire to subjugate or privilege some arbitrary group of people; these populations are simply descriptive of human evolution and migration.

However, scientists need to differentiate genetic ancestry from geographic origin. Geographical origin groups individuals whose ancestors come from a particular region irrespective of any shared genetics. Although this does not mean that geographical origin is scientifically invalid for all studies, Deborah Bolnick highlights several issues when scientists use geographical origin as an alternative to race.<sup>12</sup> First, scientists do not always explain why they chose a certain region to determine a person's geographical origin. This is often complicated by the fact that scientists often define geographical origins as continental populations that align with race categories in the USA (eg, African ancestry aligns with the Black racial group). Second, scientists do not always explain which ancestors (eg, parents, grandparents, great-grandparents and how many of each) are pertinent to establishing a person's geographic origin, despite this explanation being important to answering their hypotheses.

Scientists and philosophers may also turn to ethnicity instead of race. Ethnicity groups people according to shared cultural qualities, including 'language, diet, religion, dress, customs, kinship systems or historical or territorial identity.'<sup>13</sup> Some social scientists believe ethnicities are achieved statuses because they are group-defined and voluntary, rather than ascribed statuses of hypothetical common biology or genetics like races.<sup>8</sup> Additionally, some epidemiologists prefer conceptualising racial differences as ethnic or cultural differences. To them, ethnic and cultural differences are empirically measurable and verifiable, resonant with the goals of health promotion and risk reduction, and useful for organising community members to address public health issues.<sup>14</sup>

However, these claims overstate the distinction between ethnicity and race. First, ethnicity can be an ascribed status like race, which can be equally problematic if an ethnic group is defined according to unwarranted assumptions about shared history, culture or kinship.<sup>13</sup> Second, ethnic groups are often defined by shared ancestry and kinship, implicating a biological

or genetic linkage between ethnic group members that may distinguish them from members of other ethnic groups.<sup>13</sup> Therefore, ethnicity does not avoid implicating biological differences between ethnic groups. Finally, some officially recognised racial identities are defined like ethnicities. For instance, the US Census uses kinship and political identity to define the 'American Indian or Alaska Native' racial category as persons 'having origins in any of the original peoples of North and South America (including Central America) and who maintains tribal affiliation or community attachment,' much like an ethnicity.<sup>15</sup>

## METHODS

This study was done through the Duke University School of Medicine Third Year programme. Qualitative content analysis was conducted on all eleven articles publicly available on the MASALA study's website that were published from August 2013 to January 2021 and compared South Asians in MASALA to the four ethnic groups in MESA.<sup>16</sup> The MASALA study design article was also included in this analysis, which detailed the participant eligibility criteria and recruitment strategies for the MASALA cohort. Each article was read full-length and analysed for how South Asians were defined in relation to other populations, and how health differences between South Asians and other populations were studied and discussed. Content analysis was performed by the student researcher, who recorded notes on each article regarding the two research questions. Notes were then discussed with research mentors to review findings and refine analysis strategies. No human subjects or protected health information were collected or used in this study.

## FINDINGS

### How do researchers define South Asian identity in MASALA?

In the MASALA study design paper, researchers define South Asians as people living in the United States from India, Pakistan, Nepal, Bangladesh and Sri Lanka.<sup>3</sup> They cited the US Census's definition of South Asians and previous studies on cardiovascular disease among South Asians to support selecting these countries as the ancestral origins of their South Asian study population. Additionally, the researchers' exclusion criteria required participants to have at least three grandparents born in India, Pakistan, Nepal, Bangladesh or Sri Lanka in order to be included in MASALA. Thus, researchers used a concept of ancestry to construct a South Asian group.

However, the researchers did not define their South Asian group according to genetic ancestry, but rather geographical origin. Importantly, the researchers did not cite any prior studies demonstrating a genetic cluster that aligns with this geographically defined population. Rather, they have chosen geographic boundaries consistent with previous studies on South Asians and the US Census's definition of South Asia. As I discussed in section II, using geographic origin is not inherently an invalid population concept, but researchers did not explain why India, Pakistan, Bangladesh, Sri Lanka and Nepal are the appropriate geographical boundaries to define their study population. They simply deferred to the USA's bureaucratic definition and previous studies' definitions of South Asians to define the study population's geographical origin.

Furthermore, some researchers use this geographic linkage as a stand-in for biological or genetic heritage. When reviewing limitations to their study of the MASALA cohort, Garg *et al* state, 'given that 98% of MASALA participants were immigrants to the United States, mixed race/ethnicity is much less likely.'<sup>17</sup> Setting

**Table 1** Terms used to describe white, black, Hispanic and Chinese-Americans (from MESA) in MASALA papers

	'Races' or 'racial groups'	'Ethnicities' or 'ethnic groups'	'Races/ethnicities' or 'racial/ethnic groups'
No of articles	0	9	12
MASALA, Mediators of Atherosclerosis in South Asians Living in America; MESA, Multi-Ethnic Study of Atherosclerosis.			

aside the problematic (and possibly false) assumption that immigrants are less likely to be racially or ethnically admixed, this group's concern about 'mixed race/ethnicity' only makes sense if they hypothesised that there were biological differences between South Asians and other groups. If they included too many admixed participants, they could miss these biological differences. However, researchers never established any biological or genetic linkage between these South Asian individuals, such as genetic ancestry. Instead, researchers used a sociopolitical definition of South Asians (based on the US Census and previous studies) to define this population according to geographic origin. Furthermore, these sociopolitical definitions are historically novel as they do not necessarily align with established populations; where the Punjabi people live, for instance, does not align with the aforementioned national borders. Researchers should have made this incongruity explicit as a potential limitation to their study to express caution to other scientists and doctors when drawing conclusions about South Asians' genetics or physiology as a group.

Additionally, while researchers refer to South Asians as an ethnic group, they conflate race with ethnicity by using both terms interchangeably to refer to white, black, Chinese American and Hispanic groups from MESA (see table 1).

Researchers complicate this conflation by providing no definition for race or ethnicity to explain the distinction between the terms. Thus, it is unclear how readers should interpret what distinguishes these study populations from one another or makes them appropriate groups for comparison.

Despite these issues, researchers relied on the concept of ethnicity to recruit South Asians for MASALA. Researchers used commercial mailing list companies, such as InfoUSA, to identify individuals with South Asian surnames in the San Francisco Bay Area and Chicago. InfoUSA uses a culture coding algorithm to identify ethnicities, ethnic groups, countries of origin, language preferences and religious affiliations to classify first and last names as South Asian.<sup>3</sup> This algorithm aligns with scientists' conception of ethnicity, which defines ethnicity according to shared culture, customs, kinship, territorial identities, language and religion.<sup>13</sup>

However, calling South Asians an ethnic group raises the same conceptual confusions between race and ethnicity discussed in section II. First, the South Asian ethnicity imposes a unified group identity on Pakistanis and Indians, Punjabi and Pashtun people, and Sikhs and Muslims, even if none of these groups would consider themselves an ethnic group on the basis of shared culture, customs, language, religion, territory or kinship. Second, because the researchers designing MASALA defined their South Asian group according to ancestry, they implicated a hypothetical biological or genetic linkage between South Asians. Therefore, calling South Asians an ethnic group relies on cultural assumptions about South Asians and retains potentially unwarranted biological or genetic assumptions.

### How do researchers study and discuss health differences in MASALA?

Ambiguities in researchers' definition of a South Asian population also lead us to question the interpretation of data from the

MASALA cohort. In this section, I will refer to South Asian, white, black, Hispanic and Chinese American groups as ethnic groups. This is how researchers using the MASALA and MESA cohorts typically refer to these groups and doing so will keep my analysis consistent with these researchers' language. Researchers largely used data from the MASALA cohort to investigate biological differences, specifically physiological or cellular differences, between South Asians and each of the ethnic groups from the MESA cohort. From August 2013 to January 2021, 9 of the 11 MASALA papers comparing South Asians to the ethnic groups from MESA investigated biological differences between ethnic groups, and their associations with cardiovascular and metabolic disease prevalence or progression. For example, Kanaya *et al* compared prevalence of diabetes with beta cell function and insulin resistance across ethnic groups.<sup>18</sup> Conversely, Rodriguez *et al* compared a non-biological difference across all ethnic groups: diet quality.<sup>19</sup>

Closer examination of some papers' discussions revealed peculiar findings. For example, Kanaya *et al* found that South Asians in the MASALA cohort had a significantly higher prevalence of diabetes, higher insulin resistance, and lower beta cell function than each ethnic group in the MESA cohort.<sup>18</sup> However, they could not determine whether their findings were the result of genetic factors, environmental factors (which would include social factors), or a combination of both; they could not even determine if dietary differences explained their findings. Despite recognising these limitations, they concluded that the 'biological and genetic mechanisms underlying these differences deserve further study,' notably omitting environmental and, by extension, social factors. This omission could be a clerical error or a casualty of concision, but the omission ultimately privileges biological and genetic differences over environmental and social factors to explain this health disparity.

Another team, Makshood *et al* also made unusual claims in their paper. A prior study on the MESA cohort showed that elevated lipoprotein(a) (Lp(a)) levels were significantly associated with an increased prevalence of aortic valve calcium among black and white subjects.<sup>20</sup> However, Makshood *et al* did not find any significant association between elevated Lp(a) and aortic valve calcification among South Asians in the MASALA cohort. Instead, Makshood *et al* found that while South Asians from MASALA had lower Lp(a) levels than Black subjects from MESA, those Black subjects had a lower prevalence of aortic valve calcification. Additionally, while South Asians from MASALA had higher Lp(a) levels than White subjects from MESA, both groups had a similar prevalence of aortic valve calcification.<sup>21</sup> Therefore, they believed the relationship between Lp(a) and aortic valve calcification is 'likely multifactorial.' Specifically, they hypothesised that 'race specific factors' might explain their findings, such as 'racial/ethnic differences in the composition of Lp(a) particles or in Lp(a) associated factors.' Their assumptions regarding 'race-specific factors' are highly speculative and may even be irresponsible if they further entrench beliefs about innate genetic or molecular features among South Asians compared with other populations.

### DISCUSSION

In this study, I found that researchers in MASALA were neither precise nor clear in defining South Asians living in the USA.

Specifically, researchers used sociopolitical definitions of South Asians to establish a geographic origin but retained unwarranted biological assumptions about this group. They also conceptualised South Asians as an ethnic group, relying on cultural assumptions about South Asian identities to recruit participants. Furthermore, researchers prioritised investigating genetic and molecular causes of the South Asian cardiovascular health disparity over social factors. In doing so, researchers reified a socially constructed South Asian identity as a biological group.

Although this is a small study performed by a single reader with limited generalisability beyond the MASALA study, the research practices identified fit within a larger trend in biomedical research in which race and racial health disparities are poorly defined and studied.<sup>5–9</sup> Therefore, I argue that scientists should adopt two practices when studying health disparities: (1) clearly defining their populations, such as South Asians and (2) designing health disparities studies that do not rely on unwarranted, biologically reductive assumptions. In this section, I want to propose potential methodologies that may support such efforts.

First, scientists need to define a South Asian group in a rational and clear way. How scientists define South Asians guides their research questions and interpretations of their findings. Confusion over populations and terminology can break down communication between scientists. Unfortunately, if scientists think South Asians are a racial group, they may not be able to defer to any widely accepted concept of race. Quayshawn Spencer has convincingly argued that there is no one dominant meaning of race in the USA.<sup>22</sup> A previous study found adults in the USA use a variety of criteria (ancestry, visible physical features, ancestry and even the one-drop rule) to categorise individuals by race, not a single, dominant criterion.<sup>23</sup> This would suggest that Americans do not have a single, broadly accepted, colloquial definition for race, but instead several competing definitions depending on the context in which they consider race. Spencer argues, then, that different definitions of race may be valid and useful in different contexts.<sup>22</sup> Therefore, scientists cannot simply rely on a dominant meaning of race to define a South Asian group.

Scientists should also notice that simply defining South Asians as an ancestral or ethnic group does not resolve these issues. As discussed in section II, scientists face several difficulties when conceptualising a population as an ancestral or ethnic group. Researchers in MASALA did not address these difficulties when defining South Asians by ancestry or ethnicity. Furthermore, scientists may also be less aware that they are conducting biologically reductionist research if they assume that ancestry and ethnicity are less epistemically and ethically fraught population concepts than race. Defining South Asians as an ancestral or ethnic group did not prevent researchers in MASALA from framing the South Asian cardiovascular health disparity in a biologically reductionist way.

To address these complications, I argue that scientists should use Haslanger's ameliorative analysis to conceptualise a South Asian population. An ameliorative approach requires scientists to determine their legitimate purposes for defining a group of people as South Asian and then determine if their definition for South Asian achieves those legitimate purposes.<sup>24</sup> Legitimate purposes could include investigating risk factors (including genetic, physiological, environmental or social) that lead to a higher prevalence of cardiovascular disease among South Asians compared with other populations. However, scientists using an ameliorative analysis must question whether geographical origin or ethnicity are the best way to identify South Asians for the purpose of studying physiological or genetic risk factors. They must also question how they define these

'other populations' they are comparing to South Asians, and whether these 'other populations' are appropriate comparison groups. These are discussions and limitations that researchers should bring to the attention of other scientists when presenting their findings on health disparities.

Insights from an ameliorative analysis of the South Asian population concept also demonstrate that researchers need to consider how a variety of factors (genetic, social or otherwise) may be associated with the South Asian cardiovascular health disparity. This connects with the second important point to address when studying racial health disparities: design racial health disparities studies that are not biologically reductive. Masi and Olopade, for example, propose a 'multilevel perspective' to understand racial health disparities in breast cancer. Specifically, they identify societal (eg, occupational exposures, insurance status), individual (eg, reproductive history, past hormonal therapy) and cellular factors (eg, genetic mutations, oestrogen metabolism) that influence breast cancer outcomes, and argue that systematic perturbations in societal and individual factors varying by race result in racial health disparities.<sup>25</sup> Cardiovascular disease, like breast cancer, also has a complex aetiology, with a variety of societal, individual, and cellular factors contributing to health outcomes. Researchers should design studies that can assess whether there are systematic perturbations in societal and individual factors between South Asians and other populations. Biomedical researchers might also consider including social scientists to design studies on racial health disparities. Biomedical scientists may not be trained to study how societal and individual factors vary between South Asians and other populations. Social scientists, on the other hand, can provide the expertise to design studies that evaluate societal and individual factors.

Ultimately, resolving issues identified in this study may require institutional changes in research funding and editorial guidelines. For instance, while the National Institutes of Health (NIH) inclusion mandate has led to greater interest in studying health disparities affecting minorities, scientists may need to amend this mandate to clarify what minority status means, who counts as a minority, and how studies concerning their health should be conducted or discussed. I do not have space to explore specific guidelines, rules or laws to regulate racial health disparities studies. However, the methodologies I proposed could guide the crafting of specific policies that aim to improve biomedical research on racial health disparities.

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