

## Medical News &amp; Perspectives

# MASALA Study Probes Why People With South Asian Ancestry Have Increased Cardiovascular Disease Risks

Jennifer Abbasi

Studies dating back to the late 1950s have shown that people with South Asian ancestry have higher cardiovascular disease risk than people of other racial and ethnic groups, and the heightened risks have been observed in the US over the past 2 decades. To better understand why, in 2010 two Indian American internists, Alka Kanaya, MD, and Namratha Kandula, MD, MPH, launched the Mediators of Atherosclerosis in South Asians Living in America, or MASALA, prospective cohort study.

For the first decade, the study mainly included people of Indian ancestry, the largest South Asian group in the US. A new round of federal funding in 2021 has allowed the investigators to add hundreds of participants of Bangladeshi and Pakistani origin, the other largest US South Asian groups. By 2024, the cohort will include around 2300 participants in California, Illinois, and New York whose health will be tracked over the next several decades.

The word *masala* roughly translates to “a mixture of spices” in several South Asian languages. “We like our foods with a lot of *masala*—a lot of spices—and hence the name of the study,” Kanaya, a professor of medicine, epidemiology, and biostatistics at the University of California, San Francisco, said in an interview. (In fact, sodium-laden commercial South Asian spice blends are one culturally specific dietary factor that could increase cardiovascular risk, according to the MASALA investigators.)

Kandula, a professor of medicine and preventive medicine at Northwestern University, is also leading 2 lifestyle intervention trials in the Chicago, Illinois, area: the South Asian Healthy Lifestyle Initiative (SAHELI, or “friend”) and the South Asian Active Together (SAATH, or “together”) Study. She and Kanaya recently spoke with *JAMA* about cardiovascular health and risk



Alka Kanaya, MD (left), and Namratha Kandula, MD, MPH (right).  
Left: Marco Sanchez/UCSF; Right: Teresa Crawford/Northwestern University



Multimedia



Medical News website

of participants of Bangladeshi and Pakistani origin, the other largest

US South Asian groups. By 2024,

factors among people with South Asian ancestry—and the importance of recognizing that the risk factors can vary in different South Asian groups. The following is an edited version of the conversation.

**JAMA:** What led you to launch the MASALA study in 2010?

**DR KANAYA:** I think it was the recognition that there were no real prospective cohort data for this very large global population of South Asians that comprise 23% of the world’s population. There are many, many cross-sectional studies that show that South Asians have higher risk of myocardial infarction, or heart attacks, and strokes, but no one really understands why. We were both trying to understand this in a deeper way looking at many different factors.

The goal is to understand multilevel risk factors that are important in predicting who develops cardiovascular disease over time. We’re looking not only at individual factors but at interpersonal, societal, and structural factors.

**DR KANDULA:** As a primary care physician, I would see young South Asians com-

ing in who’d had a heart attack. They didn’t necessarily fit the traditional risk factor profile. I think that’s something that many of us [South Asians] grew up with: seeing people having heart attacks at young ages and wondering, “Why is this happening?” There were really no studies to answer that question.

**JAMA:** Last year a large study in the UK found that people with South Asian ancestry had double the risk of atherosclerotic cardiovascular disease than people with European ancestry. Was this finding surprising to you?

**DR KANDULA:** No. This is something that has been documented over the past 30 or 40 years. It does appear that individuals of South Asian background who migrate to European countries or to North America seem to have an elevated risk for atherosclerotic cardiovascular disease compared to White populations of European background.

But what was important about the UK Biobank study is that it was a very large electronic health record study that included Bangladeshis, Pakistanis, and Indians.

It was able to show that this risk for cardiovascular disease is not homogenous among South Asians—there may actually be differences between different South Asian groups. I think this is an important contribution and something we're very interested in understanding more.

The UK Biobank study showed that individuals who had their origins from Bangladesh or Pakistan were actually at higher risk for cardiovascular disease than individuals of Indian background, and it wasn't quite clear what explained their higher risk. It does appear that they had more risk factors such as high blood pressure and a higher prevalence of diabetes, but we don't fully understand this. Some people have hypothesized that maybe there are genetic differences among South Asians, but I think it's important to consider that there may be social and structural factors that are actually contributing to these differences rather than any kind of genetic underpinning or genetic difference.

**JAMA:** Can we talk a little bit more about some of the risk factors that South Asian groups have for cardiovascular disease? What factors have you identified in the MASALA study? What factors have other researchers identified?

**DR KANAYA:** Some individual risk factors to think about: there are important places where South Asian people seem to deposit extra fat in their bodies. Most people deposit fat under their skin, but South Asian people seem to have more fat deposited in organs like the liver, inside muscle tissue, and around the abdominal visceral organs. That seems to be out of proportion to other populations when we compare our MASALA data, for example, with other US racial and ethnic groups in the MESA [Multiethnic Study of Atherosclerosis] study.

Another really important risk factor is diet. We have found that there are 3 major types of dietary patterns that our MASALA participants are consuming. One is a Western diet with more animal fats and proteins—a lot more meat—and alcohol, as well. A second dietary pattern has fried foods and high-fat dairy types of dishes. That's a more traditional South Asian diet. And the third diet is a more prudent diet with whole grains and fruits and vegetables. Of these 3 dietary patterns, 2 of the patterns were higher risk—

the Western diet and that traditional South Asian diet with the fried foods and high-fat dairy products.

**JAMA:** How has the MASALA study evolved over time?

**DR KANAYA:** We are currently in the third wave of in-person data collection. The first cohort comprised 906 participants from 2 sites, UC San Francisco and Northwestern University in Chicago. We used a population-based sampling method to enroll anyone who had ancestry from any of the South Asian countries. We were able to add another 250 people to the cohort in 2017 and 2018. Currently, we are adding another 1150 participants from Pakistani and Bangladeshi backgrounds. In total, by the end of 2024, we anticipate having about 2300 people in the cohort who we hope to follow forward over the next few decades.

**JAMA:** Does adding more people with Pakistani and Bangladeshi backgrounds get to what we were talking about earlier—the potential differences in cultural or social factors between the different groups and the idea that “South Asians” are not 1 homogenous group?

**DR KANDULA:** It's been really interesting to think about the South Asian diaspora in the United States and who are South Asians. We've had a lot of discussions with people to think this through, and I would say that the way we are conceptualizing is that these are individuals who trace their cultural, their historical roots back to the region of South Asia. But it's a really diverse group of people with a unique context for what country they might have originated from, where they may have lived along the way before they came to the United States, the reasons that they immigrated. And, once people immigrate, what that experience is like for them, as well as the fact that in South Asia, you have tremendous religious, cultural, and dietary variation across the region. So how do we capture this heterogeneity and this richness of what it means to be South Asian?

And yes, absolutely, that's the reason that we wanted to enrich our cohort with people who identify as Bangladeshi or Pakistani, because we really want to understand the full spectrum of the South Asian phenotype, as well as identify individuals who might be at higher risk so that we can

appropriately target our prevention and treatment efforts.

**JAMA:** One of the interesting things about the UK Biobank study was that, in addition to looking at the prevalence of cardiovascular disease in the cohort, the researchers also checked to see if their increased risk was captured in the risk calculators that are used clinically in the United States and the UK. They found that the increased risk among South Asian people was not apparent. What does that mean clinically?

**DR KANAYA:** Clinically, it tells me that we're missing something and that we can't really apply these calculators to help in prognosticating. Are we doing our patients who are of South Asian origin a disservice by using calculators that really don't apply to them? Maybe it's falsely reassuring. We're missing the boat, and that's really worrisome. That is one of the long-term goals of MASALA—to develop a better risk calculator to help prognosticate the people at highest risk of cardiovascular disease. What are those missing factors that we really need to add to these risk calculators?

**JAMA:** What are some of the factors that you think are missing from the calculators?

**DR KANDULA:** An interesting paper that came out within the past 18 months looked at different [diabetes subtypes](#) in the MASALA participants and the participants from MESA. It showed that there are different subtypes of diabetes and that in South Asian people, there seems to be both an insulin-deficient and an insulin-resistant type. Most risk calculators can't capture those types of nuances related to insulin resistance or insulin sensitivity, which is something that may be able to help us understand who is at higher risk for cardiovascular disease.

A lot of risk calculators also don't incorporate any social determinants of health. And that may be something that's very important. What is the environment that an individual is living in?

**JAMA:** Can you explain the insulin deficiency that researchers have observed with South Asian people?

**DR KANAYA:** Type 2 diabetes comes in different subtypes. The most common of these 5 subtypes that South Asian people have, at least from the data from MASALA, is this insulin-deficient subtype.

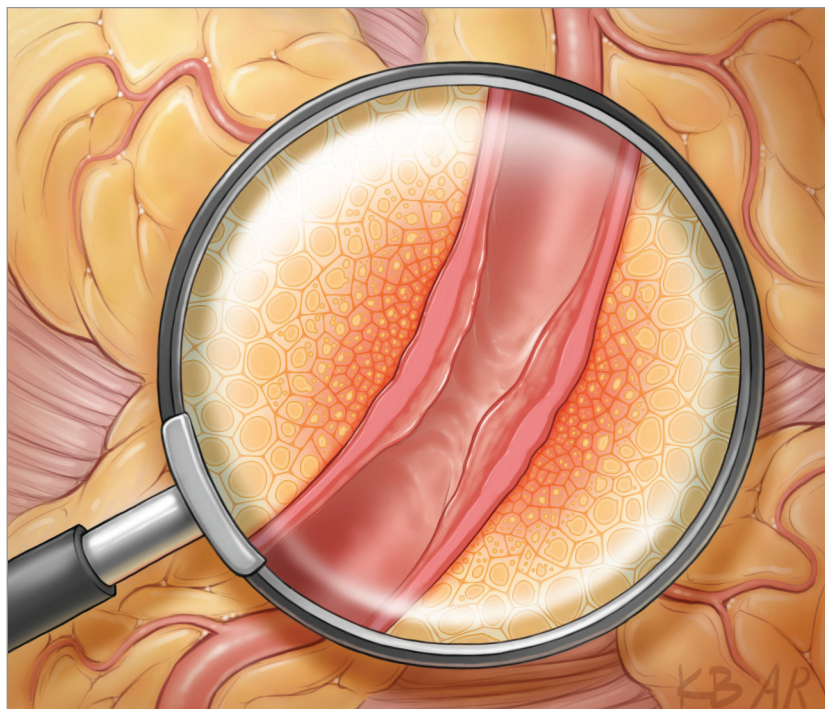
That's really important to understand because here we are trying to figure out ways to prevent diabetes, thinking that diabetes is a major driver of cardiovascular disease. And if we are promoting healthy lifestyle and healthy behaviors, but they really don't do anything to prevent beta cell loss, and if there are other ways to intervene early to prevent beta cell loss, that is important to know because that's fundamentally going to change the main drivers of cardiovascular disease.

**DR KANDULA:** Another factor that the risk calculators don't capture is the **adiposity that might be in different organs in South Asian people** compared with other groups. We traditionally think of people who are overweight or obese based on body mass index [BMI] as at risk for cardiovascular disease. And what we see is that a lot of South Asian people—up to a third—even at a body mass index of 23 will have cardiovascular risk factors like high blood pressure, abnormal blood glucose, abnormal cholesterol. BMI is not a good way to capture who might be at risk. And so, is there a way to incorporate other measures of adiposity?

**JAMA:** In 2018, the American Heart Association and the American College of Cardiology added South Asian ancestry as a risk-enhancing factor in its **cholesterol management guidelines** for people who have intermediate atherosclerotic cardiovascular disease risk. How did that come about?

**DR KANAYA:** I think that came about from a lot of vocal people who made it clear that there is this higher risk among South Asian people that isn't being captured well by the current risk-prediction equations that we have, the calculators. We know for a fact that statins do help in preventing cardiovascular disease. And it is important to get people who are at highest risk on medications like statins to lower this risk. The thinking was to basically use that higher intrinsic risk to help physicians identify people who would benefit from earlier lipid-lowering therapies, maybe not only directed toward lowering cholesterol, but to the other effects that statins can have in stabilizing plaque and decreasing inflammation around any kind of atherosclerosis.

**DR KANDULA:** I do think there is increasing awareness, but we have a lot of work to do to help physicians understand how to have those culturally appropriate conversa-



tions with patients from South Asian backgrounds. And then what do you do with that information?

**JAMA:** How can physicians appropriately ask, "Are you South Asian?" Is that a question they should be asking?

**DR KANAYA:** I'm a practicing primary care doctor, and I think it's very relevant to ask people about their own ethnic identity. It's important to know where people come from and their family history and risk factors that run in families no matter what background they're from. I do think it's important to be open-ended in these questions and to ask broad questions like, "How do you define your ethnic identity?" or "What is your ancestral background?"

In terms of asking specific questions, I do think that you have to be very specific when asking questions about diet. In our study, 40% of our participants were lifelong vegetarians. When I was talking about the dietary patterns that people consume and that traditional South Asian diet, half of our participants were vegetarian on that diet that had high risk. The quality of the diet as we've learned matters so much more than just eating a vegetarian diet.

**JAMA:** Are there any other pieces of dietary advice? We haven't talked much about meat. I think there is often an assumption

that if a person is South Asian, they are vegetarian and that's not necessarily true.

**DR KANDULA:** Yes. The SAHELI study is focused on heart disease prevention and improving people's diet, physical activity, and stress management. We have the individual participants build their own food plate based on what it looks like at home. It's very interesting to see the differences between somebody who is very vegetarian or families where there's more meat consumption.

The message that we really try to work with to promote behavior change is that there's a lot of things in the traditional South Asian diets or what you're doing at home that are really good. Let's build on that and incorporate some small changes, like reducing red meats and thinking about how to prepare them differently, yet also honoring traditions and the importance of these foods. We have participants try to brainstorm those ideas and think about, if they're consuming a lot of red meat as part of their diet, how can they move toward healthier meats or fish or other types of proteins like lentils and legumes.

**JAMA:** Can you talk about exercise and how it affects the South Asian community?

**DR KANAYA:** That's really important because when we compared our study participants' exercise levels with the 4 different



groups represented in the Multiethnic Study of Atherosclerosis, we found that South Asian people had the lowest amount of exercise per week and a more sedentary lifestyle.

I think that this is an important thing to talk about because a lot of people in the MASALA study have told us that they didn't grow up with parents who exercised. They weren't raised with exercise being a normal part of their routine, their lifestyle, and it's very hard to adopt something like that in later life. We found that the adult children of our participants were the most influential in them making healthy lifestyle changes to become more active and eat more fruits and vegetables. I think that our younger generations have a lot to offer in terms of motivating their parents.

**JAMA:** I'd love to talk about the SAHELI and SAATH studies.

**DR KANDULA:** The SAHELI study is a trial for adults of South Asian origin who have cardiovascular risk factors. They are randomized into our culturally adapted lifestyle intervention or into a group that

receives traditional health education materials. Our intervention is a 16-week, group-based, lifestyle intervention that is focused on how South Asians can eat a more healthy diet, get more exercise, and also stress management. We developed it with a lot of community input, and one of the things that we heard was that immigration and the cultural changes that people are undergoing cause a lot of stress and affect their healthy behaviors. We've really tried to incorporate those experiences, those lived experiences in understanding how lifestyle interventions can be more effective for people from immigrant backgrounds.

The SAATH study is a mother-daughter intervention study for South Asian moms and their girls because we've identified that South Asian girls and women are really at high risk for not doing exercise. As girls get into adolescence and teenage years, their exercise levels really drop off. We have this intervention where moms and daughters are encouraged to exercise together as well as improve their communication with each other around health issues and as a family.

**JAMA:** Are there any resources available for physicians who want to talk to their patients who have South Asian ancestry about a healthy lifestyle?

**DR KANAYA:** On our website, [masalastudy.org](https://masalastudy.org), we have a health resources page, which has up-to-date information about diet, exercise, diabetes, and heart disease. There are really important carb-counting tools for patients with diabetes that actually look at the carb content of South Asian-specific foods because that's not easy information to find. ■

**Published Online:** July 13, 2022.  
doi:[10.1001/jama.2022.11417](https://doi.org/10.1001/jama.2022.11417)

**Conflict of Interest Disclosures:** Dr Kanaya reported current and pending grants from the National Institutes of Health and the John Templeton Foundation for the MASALA study or research related to cardiovascular disease, diabetes, and obesity prevention. Dr Kandula reported receiving funding from the National Institutes of Health for the MASALA, SAHELI, and SAATH trials and the Northwestern University Division of General Internal Medicine for the SAATH trial.

**Note:** Source references are available through embedded hyperlinks in the article text online.