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Urbanized South Asians' susceptibility to coronary heart disease: The high-heat food preparation hypothesis

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ABSTRACT

Objective: Known risk factors do not fully explain the comparatively high susceptibility to coronary heart disease (CHD) in South Asians (Indian, Pakistani, Bangladeshi, and Sri Lankan populations in South Asia and overseas). The search for explanatory hypotheses and cofactors that raise susceptibility of South Asians to CHD continues. The aim of this study was to propose "the high-heat food preparation hypothesis," where neo-formed contaminants (NFCs) such as trans-fatty acids (TFAs) and advanced glycation end-products (AGEs) are the cofactors.
Methods: We reviewed the actions of AGEs and TFAs, the burden of these products in tissues and blood in South Asians, the relationship between these products and CHD, the effects of preparing food and reheating oils at high temperatures on NFCs, and the foods and mode of preparation in South Asian and Chinese cuisines.
Results: Animal and human studies show NFCs increase the risk for CHD. Evidence on the consumption and body burden of these products across ethnic groups is not available, and comparable data on the NFC content of the cuisine of South Asians and potential comparison populations (e.g., the Chinese with lower CHD rates) are limited. South Asians' cuisine is dominated by frying and roasting techniques that use high temperatures. South Asian foods have high TFA content primarily through the use of partially hydrogenated fats, reheated oils, and high-heat cooking. Reheating oils greatly increases the TFA content. In comparison, Chinese cuisine involves mostly braising, steaming, and boiling rather than frying.
Conclusion: We hypothesize that South Asians' susceptibility to CHD is partly attributable to high-heat treated foods producing high NFCs. Research to accrue direct evidence is proposed.

Introduction

The susceptibility to coronary heart disease (CHD) of urbanized South Asians remains incompletely explained [1,2] (*South Asians* refers to people from the Indian Subcontinent especially India, Pakistan, Bangladesh, Sri Lanka, including those living overseas). For example, there was 62% increased mortality from ischemic heart disease among Pakistani-born men compared with the population of England and Wales [3]. Such high mortality reflects

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high incidence, not high case fatality [4]. The susceptibility of urbanized South Asians to CHD is international [3,5–11].

This susceptibility has been linked to diabetes and metabolic syndrome. The insulin resistance hypothesis [11], however, does not explain the higher CHD risk in South Asians compared with white Europeans [2]. New ideas include the adipose tissue compartment hypothesis [12], the mitochondrial efficiency hypothesis [13], and the variable disease selection hypothesis [14,15]. These augment the longstanding thrifty genotype and thrifty phenotype hypotheses [16,17]. (A short account of these hypotheses can be found in online Supplementary Data.) Collectively, these evolutionary and developmental hypotheses have not yet explained the problem.

Unhealthy diets are important in CHD [18–20] and the type of food and its preparation might matter. We have, therefore, formulated the high-heat food preparation hypothesis. This is a cultural, rather than evolutionary, hypothesis and moves in a new direction. High-heat cooking promotes neo-formed contaminants (NFCs) such as trans-fatty acids (TFAs) and advanced glycation end-products (AGEs) [21–24]. The present study compares the potential for producing NFCs in South Asian cuisine with Chinese cuisine, as the Chinese do not have special susceptibility to CHD, whether in China or overseas [25]. The search strategy used for this study is presented in Box 1.

Neo-formed contaminants and CHD: Human and animal evidence

We prioritized human studies [26,27] despite their limitations, given our focus on the South Asian ethnic group, and NFCs in human foods. Limitations included that food intake data, usually based on a 3-day record or memory based-recall [28], do not equate to long-term exposure. Also, AGE levels from a food database may not always be the same as the food actually consumed by those surveyed. Nonetheless, evidence that NFCs influence human CHD is strong enough to underpin our hypothesis.

Animal studies show an effect of dietary NFCs on metabolism dysregulation and chronic diseases and improvement when NFCs are limited [29–32]. A 50% decrease in diet NFCs could extend animal life span [33].

> Box 1. Search methodology used in the study
>
> We searched for information on high-heat cooking, specifically TFAs and AGEs, on CHD on Medline, PubMed, and Google (for grey literature). The key search terms used were *neo-formed contaminants, Maillard reaction products, advanced glycation end-products, trans-fatty acids, cardiovascular disease,* and *type 2 diabetes*. We examined reference lists of key articles to identify additional data sources. Key journals based on the articles found were also screened (i.e., *Journal of Food Science*; *Food Chemistry*, etc.) for relevant articles.
>
> Due to the scarcity of literature on NFC levels in both Chinese and South Asian foods, we reviewed grey literature. Articles on NFCs in both South Asian and Chinese food were reviewed. We employed informal methods such as meeting experts via conferences such as European Food Information Resource; subscribing to INFOODS mail list (an international network of Food Data Systems with a worldwide network of food composition experts); searching the International Maillard Reaction Society (IMARS) website, and contacting Dr. Reykolnagi, president of IMARS. We took advice from colleagues Antonis Vlassopoulos, currently working on AGEs, and Fu-Shing Lee, who gave expert insight on Chinese food preparation methods.

Box 2 and Figure 1 summarize the nature and action of AGEs and TFAs, which affect health [34]. Human and animal studies highlight that AGEs act through reactive oxygen species and receptors to alter intra- and extracellular proteins, and calcium channels, resulting in endothelial dysfunction, inflammation, and oxidative stress, which may lead to hypertension and atherosclerosis [35–43]. Figure 1 also shows effects on CHD via insulin resistance and diabetes [35–43].

AGE-rich meals contribute to body AGE content and circulating AGEs. One study investigated diets with high versus low NFCs on indicators of cardiovascular and diabetes risk [26]. Plasma high-density lipoprotein (HDL) and total cholesterol, TGs, fasting insulinemia, and homeostatic model assessment were higher after the 4-wk high NFC diet compared with the low NFC diet, whereas vitamins C and E were lower. Lower vitamins E and C suggested oxidative stress [26,44].

Animal evidence shows an increase in AGEs leads to intimal thickening of the aorta [45], increased vascular permeability and dysfunction [46], and increased intimal hyperplasia [47]. AGE deposition is more pronounced within atherosclerotic plaques than normal arterial walls, with atherosclerotic changes correlating with AGE deposition [48,49]. The mechanisms include reduction of nitric oxide activity, interaction with specific receptors, and oxidizing low-density lipoprotein cholesterol (LDL-C). AGEs contribute to disease through expression of procoagulant activity and the production of reactive oxygen species leading to increased endothelial expression of endothelial leukocyte adhesion molecules [50].

Although an optimal dietary AGE intake is unclear, >15,000 to 16,000 kU/d is considered to increase risk for CHD [27,51]. One group of researchers suggests reducing AGEs by lowering cooking temperatures [27].

TFA consumption is associated with CHD in humans [52]. Figure 2, adapted from Centre for Research on Nutrition Support Systems, summarizes the link between TFAs and CHD [53]. TFAs increase LDL-C while decreasing HDL-C [54,55]. TFA-rich diets increase activity of cholesteryl ester transfer protein, which transfers cholesterol esters from HDL-C to LDL-C and VLDL-C [56]. TFAs are associated with markers of endothelial dysfunction and inflammation, including soluble intercellular and vascular cell adhesion molecule-1, e-selectin [57], soluble tumor necrosis factor (TNF)-α receptors [58], interleukin (IL)-6, and high-sensitivity C-reactive protein. TFAs are proinflammatory, leading to atherosclerosis, diabetes, and sudden death due to heart failure [56,58].

TFAs influence adipocytes, reducing TG uptake and increasing production of free fatty acids [59,60]. TFAs raise the fasting TG levels [61], decrease insulin sensitivity, and are associated with metabolic syndrome (including in animals) [62–64], promoting insulin resistance and abdominal adiposity [65].

Approximately 5 g/d of TFA is associated with a 23% increase in the risk for CHD [66]. The Food Safety and Standard Authority of India advocates a TFA level of <10% in hydrogenated vegetable oils [67]. The consensus dietary guidelines for Asian Indians recommend a TFA level of <1% of daily energy intake [68].

Evidence for the high-heat food preparation hypothesis: Indian and Chinese cuisines

If NFCs in food produced during cooking increase South Asians' susceptibility to CHD, they should be both comparatively high in diets and body tissues and associated with CHD in South

Box 2. A brief introduction to neo-formed contaminants

Thermal treatments of food (whether commercial or at home) contribute to the development of NFCs. These compounds are not external, but are formed naturally during thermal processing of food through complex chemical reactions resulting in the formation of various NFCs (i.e., TFAs and Maillard reaction products including AGEs and acrylamide). NFC formation is directly proportional to heat treatment during food processing.

TFAs: TFAs are fatty acids that contain at least one nonconjugated double bond in the trans-configuration, that is, the hydrogen is on both sides of the carbon atom. A series of changes occurs when oil undergoes thermal treatment: degradation of fatty acids, increase in free fatty acids, and conversion of some unsaturated fatty acids into saturated and TFAs. They are formed during the partial hydrogenation of vegetable oils and in small amounts during refining of vegetable oils. Additionally, significant amounts of TFAs are also present when oil/fats are reused. Owing to their harmful effects on human health. TFAs have been banned in several countries, however, they continue to be a significant part of the diets in South Asian countries.

AGEs: Thermal treatments (such as frying) that achieve temperatures >150°C/170°C, help to break down carbohydrates and proteins to monosaccharides and amino acids, respectively, the primary ingredients required for the Maillard reaction, which through a series of reactions forms the Schiff bases and Amadori products that undergo slow rearrangement, dehydration, and condensation reactions to form irreversible compounds called AGEs. These reactions produce the desirable quality of fried foods contributing to their characteristic texture, aroma, brown color, and flavors. AGEs can be absorbed in the gastrointestinal system, contributing to the total AGE body burden. One of the most studied AGES is N-(carboxymethyl) lysine.

Asians. Our literature searches yielded no data on this. Therefore, we have supported our hypothesis on indirect observations we compiled on cuisine and cooking methods (Tables 1–3) and recently published empirical data on oils and TFAs (Table 4) [73]. The data on Indian and Chinese cuisines in relation to NFCs also were limited [69,73,74]. We acknowledge the limitations of the evidence underpinning this hypothesis.

South Asian food is diverse; therefore, pragmatically, we focus on Indian cuisine as an example, compared with Chinese cuisine. Table 1 shows the methods of food preparation, estimated frequency of use, and the estimated temperatures reached during food preparation. Indian cuisine can be crudely divided as South and North. South Indian diet is founded on rice with sambhar. Sesame, peanut, vegetable, coconut oil, and ghee are the primary fats used. Vanaspati (partially hydrogenated fats), a major source of TFA, frequently replaces ghee. North Indians predominantly eat a wheat-based diet consisting of rotis, vegetables cooked with ghee, chicken and mutton, and milk and yogurt [75]. Roasting and frying are the main cooking methods. Ghee, vanaspati, butter, and nuts are widely used.

Deep-fried snacks eaten across India include pakora, samosa, and the like. Currently, there is a nutritional transition in India

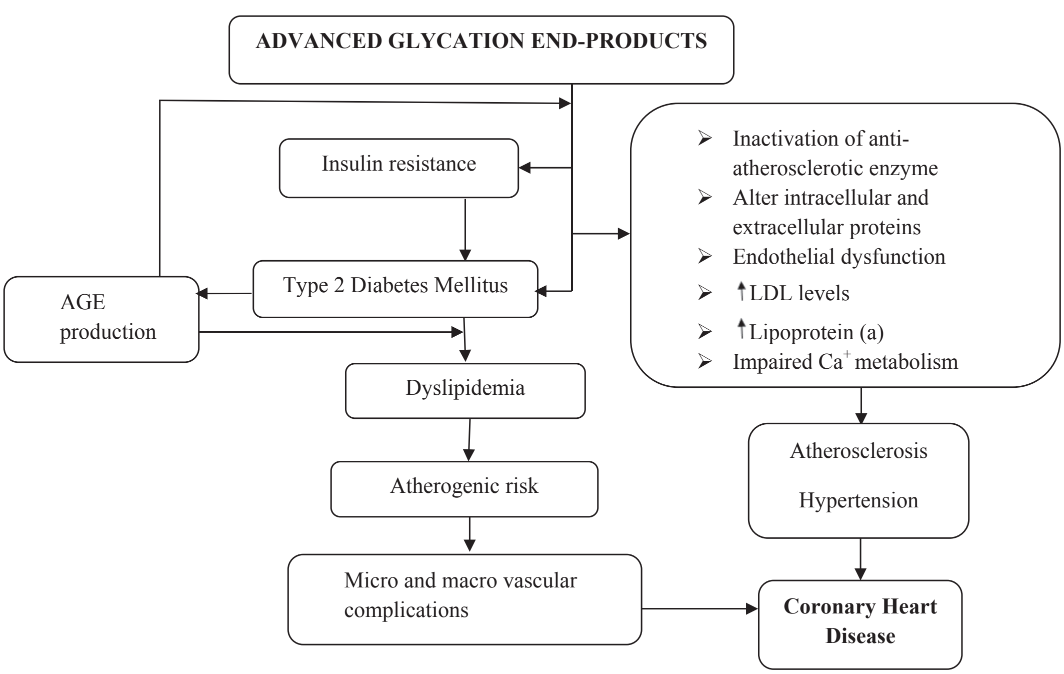

Fig. 1. Potential role of dietary AGE on CHD risk. AGE, advanced glycation end-product; Ca, calcium; CHD, coronary heart disease; LDL, low-density lipoprotein. Based on references [21–27].

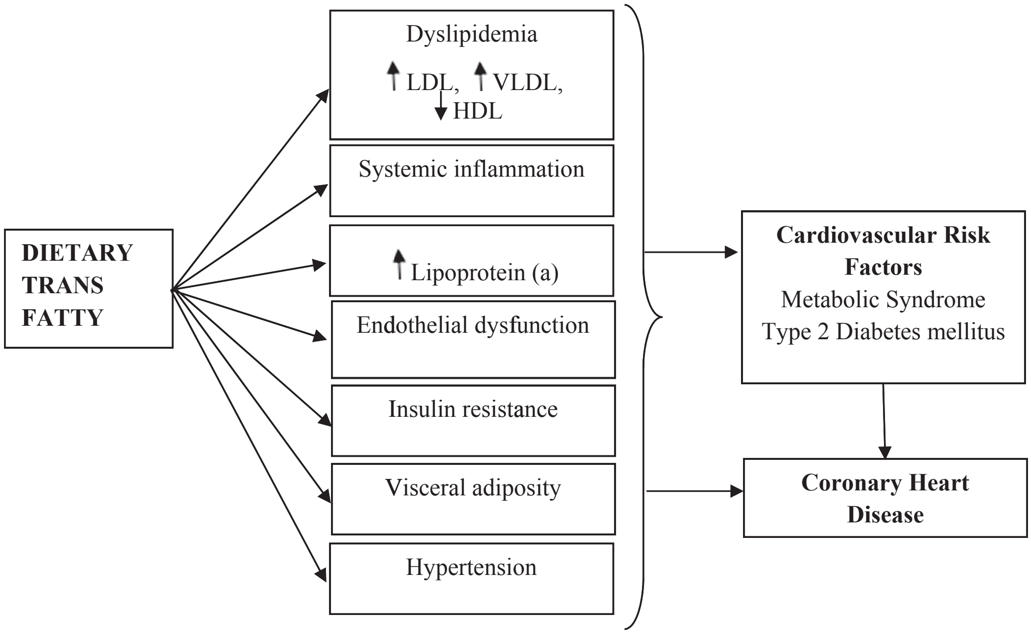

Fig. 2. Potential role of dietary TFAs on CHD risk. CHD, coronary heart disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TFAs, trans-fatty acids; VLDL, very low-density lipoprotein. Adapted from Centre for Research on Nutrition Support Systems (2011) [53].

Table 1
Temperature range and frequency of different cooking techniques used in traditional South Asian and Chinese cuisines

Method of food preparation	Definition	Examples of Indian food	Examples of Chinese food	Temperature range (approx)	South Asian	Chinese
					Frequency of use	
Clay oven or Tandoor	A cooking method that uses a clay oven (tandoor) in which a hot fire is built. The food item is lowered in the clay oven and cooked in the smoky and extremely hot environment.	Butter naan, tandoori chicken, Balochi Aloo	Shao Bing	500°C	Common	Sometimes
Frying	Cooking food in oil or fat (includes deep/ shallow frying)	Chicken pakora, onion bajji, bonda	Spring rolls	150°C–375°C	Very common	Common
Stir frying	Cooking food quickly over a high heat with little oil; tossing and turning it with a spatula until it is just cooked.	Carrot beans vepudu, aloo gobi	stir-fried vegetables	200°C–340°C	Common	Very common
Baking	Prolonged cooking by dry heat acting by convection, normally in an oven, but also in hot ashes, or on hot stones.	Cakes	Cakes	150°C–290°C	Seldom	Seldom
Oven-frying	Cooking food, usually meat or ready to cook foods in a pan in the oven	Oven-fried chilly chicken	Oven stir fry Chinese chicken	230°C	Seldom	Very rare
Roasting	Cooking food using dry heat, whether an open flame, oven, or other heat source	Chicken Bhunna, pork roast	Peking duck	95°C–200°C	Common	Sometimes
Bake stewing	Slowly cooking a ceramic dish of broth and other ingredients by placing it in or close to hot embers	Indian lamb curry	Beef stew Pork stew	76°C–137°C	Very rare	Rare
Braising	Braising ingredients over medium heat in a small amount of sauce or broth and simmering for a short period of time until completion	Chicken curry	Red braised pork	130°C	Common	Common
Pressure cooking	Cook in a sealed dish that does not permit air or liquids to escape below a preset pressure	Chilly pork, lamb chops	–	121°C	Very common	Very rare
Quick boiling	Adding ingredients and seasonings to boiling water or broth and immediately serving the dish with the cooking liquid when everything has come back to a boil	–	Hot pot	100°C–130°C	Very rare	Common
Boiling	Cooking food in boiling water, or other water-based liquid such as stock or milk	Kheer, kesari bath, payasam	Congee	100°C	Seldom	Very common
Steaming	Cooking food with steam	Momos	Dumplings	100°C	Sometimes	Common
Scalding	Par cooking through quick immersion of raw ingredients in boiling water or broth sometimes followed by immersion in cold water	Used with other techniques (e.g., pickling)	Noodles	65.5°C–121°C	Very rare	Common

Table 2
AGE levels in some of the foods consumed by South Asian and Chinese people

Food	Cooking technique	AGE levels/100 g (kU or U10³)*	Indian food	Chinese food
Meat				
Chicken (skinless)	Frying	9722*	Common cooking technique	Common cooking technique
	Curry	6340	Common cooking technique	Used sometimes
	Pan-frying	4938*	Common cooking technique	Common cooking technique
	Roasting	4768*	Common cooking technique	Used sometimes
	Boiling (60 min)	1123*	Rarely used	Common cooking technique
Fish (salmon)	Pan-frying	3083*	Fish is usually pan-fried	Salmon and other dark-colored fish are usually pan-fried
	Boiling (18 min)	1082	Although fish is not typically boiled, it is cooked as a curry in India	Steaming is preferred if it is fresh
Pork	Sausage: microwave (1 min)	5943	Rarely used	Commonly used
	Pan-frying	4752	Used sometimes	Common technique of cooking
Egg	Frying	2749	Common cooking technique	Commonly used
	Scrambled with butter	337	Commonly used with oil	Commonly used with oil
Vegetables and cereal				
Potato	Frying (fast food)	1522*	More common in urban areas	More common in urban areas
	Frying (homemade)	694*	Common cooking technique	Usually stir fried
	Boiling (25 min)	17	Rarely used	Sometimes for sweet potato soup
Tofu, soft	Boiled for 7 min	628	Not part of Indian cuisine	Common
Tofu, soft	Raw	488	Not part of Indian cuisine	Common
Corn flakes	–	427	Common among urban Indians	Consumed by the rich mostly
White rice	Boiling	9	Common in South India	Common in South China
Milk and milk products				
Paneer (cottage cheese)	Frying	1744	Very common, particularly among vegetarians	Not part of Chinese cuisine
Milk, whole (4% fat)	Raw	5	Used widely to make traditional Indian desserts; Used in coffee/tea	Traditionally not used; however, has recently been included as part of the diet
Fat and liquids				
Oil, sesame	Raw	21 680	Used for deep-frying, cooking, and pickling	Used as a dressing rather than for cooking
Oil, peanut	Raw	11 440	Used for cooking and frying	Used for cooking and frying
Oil, sunflower	Raw	3940	Used for cooking and frying	Used for cooking and frying
Coconut cream	Raw	933	Used as a main ingredient in curries	Used in drinks in South China

AGE, advanced glycation-end products
* AGE levels in the table are based on N-(carboxymethyl) lysine levels, adapted from references [27] and [51].

Table 3
TFA levels in some of the foods consumed by South Asian and Chinese people

Item	Description of food	TFA levels*, g/100 g serving
Indian food		
Sweets		
Jalebi	Fried fermented flour, in sugar syrup	17.7
Mathari	Deep-fried pastry made of flour, ghee, and sugar	16.3
Balushahi	Flour, ghee, yogurt in sugar syrup	7.6
Laddu	Round balls of flour, minced dough, and sugar	6.8
Gulab-jamun	Deep-fried heat-dried milk in sugar syrup	6.1
Sweet rice	Rice, ghee, sugar syrup, and nuts	3.5
Savory/Snacks		
Meat puffs	Baked pastry containing spices and meat	19.8
Chaat	Fried flour with yogurt, onions, sev, coriander, and spices	16.4
Paapri	Deep-fried white flour with shortening	10.2
Plain khichri	Steamed cooked rice pulse and ghee	4.0
Samosa	A triangular deep-fried pastry containing vegetable	3.3
Indian bread	Leavened baked flour	1.9
Chinese food		
Sweets		
Sa Qi Ma	A sweet snack consisting of flour, butter, and rock sugar/rock candy	0.08
Chinese moon cake	A rich, thick filling usually made from red bean or lotus seed paste is surrounded by a thin (2–3 mm) crust and may contain yolks from salted duck eggs	0.04
Savory/Snacks		
Sandwich biscuits	Typical biscuit with cream center	0.65
Cheese bread	Type of bread made from tapioca flour, cheese, egg, milk, and corn oil	0.41
Egg roll	Egg roll refers to biscuit roll made from egg, flour, and sugar	0.21
Spring rolls	Deep-fried puff pastry filled with vegetables/meat	0.14

TFA, trans-fatty acid
* TFA levels in the table are adapted from references [69–71]

Table 4
Trans-fatty acid[*] content of edible fats and oils before and after subjecting to frying (g/100 g) [72]

Oil/Fat	Unheated mean ± SD	180°C mean ± SD	220°C mean ± SD	180°C reheat mean ± SD	220°C reheat mean ± SD	Absolute (net) change[†]
RSO[‡]	UD	0.36 ± 0.16	1.37 ± 0.21	2.07 ± 0.72	3.27 ± 0.21	3.27 ± 0.21
RGO[‡]	UD	1.50 ± 0.36	1.87 ± 0.09	2.24 ± 0.39	3.70 ± 0.56	3.70 ± 0.56
RRO[‡]	1.60 ± 0.62	2.09 ± 0.23	2.60 ± 0.35	3.20 ± 0.36	3.90 ± 0.27	2.30 ± 0.89
CB[‡]	0.68 ± 0.29	1.20 ± 0.17	1.60 ± 0.56	2.62 ± 0.38	3.28 ± 0.26	2.60 ± 0.38

CB, clarified butter; RGO, refined groundnut oil; RRO, refined rapeseed oil; RSO, refined soybean oil; UD, undetected levels
* Sum of all unsaturated fatty acids in "*trans*" configuration.
† Absolute change; difference between baseline value (value of unheated fat/oil) and final value (value after subjecting to frying in reheated fat/oil at 220°C).
‡ n = 3.

with an increase in meat, sugar, and fat consumption [76], and a shift toward "fast food" cooked at high heat.

Traditional Indian cooking involves frying and browning. Most Indian food is spice based, and meat and vegetables are cooked in a sauce after frying the base ingredients ("curry"). Such foods have high NFCs [77,78] compared with food that is boiled (e.g., chicken curry: 6340 kUAGE/100 mg; boiled chicken: 1123 kUAGE/100 mg) [27,51]. Indians drink tea and coffee, usually with boiled full-fat milk heated for prolonged periods, thus increasing the AGE levels. Roasting coffee beans also increases AGEs [79]. Indians are consuming modern fast foods containing high levels of NFCs (e.g., pizza: ~6824 kU/100 g) [27]. French fries produce about 843 kU/100 g of AGEs [27].

Fats and oils are important in Indian cuisine. The National Sample Survey reported that in India, oils and fats accounted for ~25% of calorie intake [80]. Individuals in a high socioeconomic group, those in whom the CHD epidemic appeared first in South Asians [81], had higher consumption. Fat intake in the top decile social class of the urban sector at >83 g, for example, was about three times that of the lowest decile class (21.4 g) [80].

Consumption of beverages, biscuits, processed foods, salted snacks, prepared sweets, and other purchased foods constituted 100 to 427 g/capita daily, from the lowest to the highest expenditure class. These are foods rich in NFCs in India [82].

Table 3 reports data on the TFA content of some commonly consumed snacks and sweets in India [67,69–71]. TFA consumption through vanaspati and ghee alone among North Indians was >1% and 0.75% of total energy in men and women, respectively, and 1.1% among adolescents. TFA in hydrogenated vegetable oil was 1.95 times the limit set by the Food Safety and Standards Authority of India (FSSAI) [83]. TFA consumption among South Asians likely exceeds the World Health Organization's recommendations of <1% of daily energy intake [68].

Ingestion of reused oil/fat used for deep-frying increases NFCs and endothelial dysfunction [84,85]. Table 4 provides data showing TFA formation during the process of frying at different temperatures with four oils commonly used in India and TFA formation during oil reuse [72]. TFA formation increased during frying at different temperatures and further after reheating.

Traditional snacks such as chaat and samosa prepared from vanaspati further increase TFA levels [69]. Packaged Indian snacks had high TFA content [70]. Additionally, TFA content in popular fast-food outlets in South Asia was higher than in equivalent outlets in China, the United States, and the United

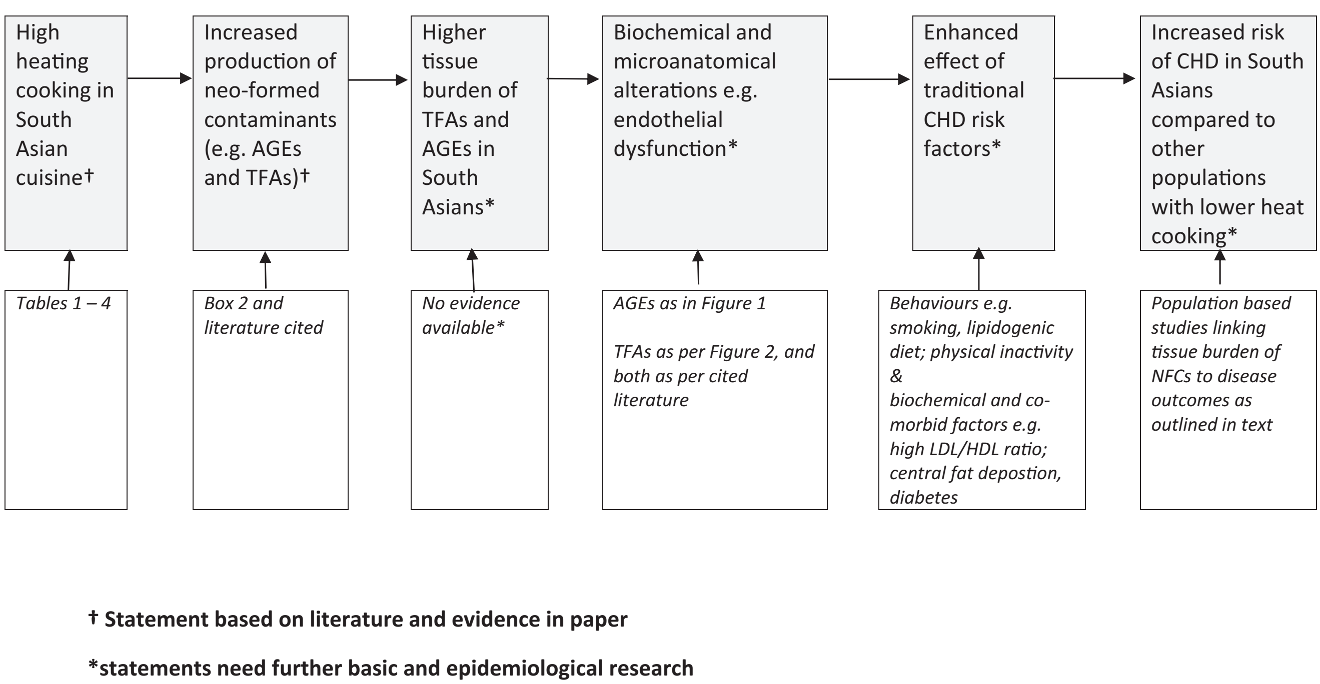

Fig. 3. Summary of the high-heat cooking hypothesis in relation to South Asians' risk for CHD as demonstrated in the present study. AGE, advanced glycation end-product; CHD, coronary heart disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NFC, neo-formed contaminants; TFA, trans-fatty acid. *Statement based on literature and evidence in this study; †statements need further basic and epidemiologic research.

Kingdom [86]. Table 2 shows the AGEs of some foods commonly eaten by Indians [27,51].

In general, people from Northern China eat wheat-based foods, whereas their southern counterparts eat rice-based foods [87,88]. Chinese cuisine includes frying, but food is mainly cooked by braising, steaming, and boiling, which produce less NFCs given the lower cooking temperatures and lower fat content [87,88]. Table 1 compares Indian and Chinese cooking methods in relation to temperature to highlight the differences in cooking temperatures. With the exception of frying, traditional Chinese cooking uses temperatures <130°C, lower than that needed for the rapid formation of NFCs (i.e., >150°C) [79].

Herbal tea, popularly consumed by the Chinese, may have cardioprotective effects. Research has demonstrated that the catechin present in green tea is inversely associated with mortality due to CHD and associated with a 20% reduction in CHD mortality risk [89,90]. These ways of drinking tea are different from India, and less likely to produce NFCs.

Compared with Indians, Chinese consume less fried and baked foods, reducing their exposure to NFCs [91]. Results from one study reported that 80% of Western-style snacks contained 1.44% to 12.07% TFAs, whereas 67% of Chinese snacks contain <0.83% TFAs [92]. Table 3 describes some of the typical bakery foods in China and their TFA content [71]. The China National Center for Food Safety Risk Assessment found that TFA averaged 0.16% of the energy intake. Even in Beijing and Guangzhou, where higher levels are consumed, TFA account for only 0.34% of total energy intake, lower than recommended [93].

The INTERHEART study highlighted that a diet high in tofu and soy (Chinese cuisine) had no association with CHD, whereas a diet high in fried foods (Indian cuisine) nearly doubled the risk [18].

Based on the differences in cuisine, cooking techniques, cooking temperatures, and lower oil utilization in Chinese cuisine, we infer that Indian cuisine contains higher levels of NFCs compared with Chinese, and if so, this supports our hypothesis.

Testing the high-heat food preparation hypothesis

Our hypothesis, outlined in Figure 3, proposes that high-heat food preparation is a potentially important risk factor for South Asians. Despite searching for evidence carefully (Box 1), at this point, our hypothesis can only be supported indirectly, as no direct, comparative studies of either NFCs in South Asian cuisine, body or plasma NFC burdens, or on the relationship between NFCs and the relevant disease outcomes in South Asians were found. We recommend ways of testing the hypothesis, primarily using human population-based research. Animal research, invaluable as it is in elucidating mechanisms, cannot contribute to understanding ethnic variations in CHD.

Given limited data available on NFCs in South Asians and their diets, ongoing and new studies on NFCs in humans should recruit South Asian populations. These studies might also include NFCs and other substances increased by heat [94]. Cross-sectional studies should examine NFCs in diet using techniques such as a food frequency questionnaire, food diaries, and duplicate diet methods among South Asians and their Chinese/European counterparts. The studies should examine cooking practices, especially heating or frying of foods and reuse of oils. They also should measure NFCs and other cardiovascular risk biomarkers in plasma. We hypothesize that NFC levels will be higher in the body tissues and dietary content in South Asians living in industrialized countries than in their counterparts in India, and higher in South Asians than in many other populations including the European origin white and Chinese populations, and higher in South Asians with CHD than those without. We also predict an association between plasma TFA and AGE levels and biomarkers of cardiometabolic risk in South Asians [57,65,95,96].

Assuming the evidence accrued is supportive, the next step would be a case–control study that includes individuals with and without CHD and assesses the level of NFCs (TFAs and AGEs) in cases and controls in South Asians and comparison ethnic groups. The hypothesis would be that South Asians with CHD had higher levels of NFCs than controls.

Small-scale, experimental, diet controlled studies on South Asian volunteers could examine the effect of NFCs on intermediate indicators of cardiovascular risk (e.g., endothelial dysfunction). Important trials of this kind have been done on volunteers elsewhere [26].

If new evidence supports the hypothesis, we recommend that NFC consumption and body burden be measured in cohort studies, where South Asians (without CHD) can be followed up. We hypothesize that the subgroups with higher consumption and body burden would develop more intermediate outcomes (e.g., endothelial dysfunction) and in the long term, incident CHD.

Randomized controlled trials on community samples with disease and points are not currently justified, as evidence is not strong enough, but such studies will be required before public health policy advocates change in high-heat cooking practices.

We acknowledge the limitations of this review and the hypothesis. We do not propose that the hypothesis is the complete answer, but it may be contributory. Our analysis of the health effects of NFCs, the evidence that high-heat cooking induces NFCs, empirical evidence on heating oils in the production of TFAs (Table 4) [72], and the compiled evidence on cooking practices in Indian and Chinese cuisine (Tables 1–3) justify debating and then testing our hypothesis.

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Supplementary data

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