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## Atherosclerosis in Indigenous Tsimane: A Contemporary Perspective

### Comments

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# 14 Atherosclerosis in Indigenous Tsimane

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## *A Contemporary Perspective*

Randall C. Thompson, Gregory S. Thomas, Angela D. Neunuebel, Ashna Mahadev, Benjamin C. Trumble, Edmond Seabright, Daniel K. Cummings, Jonathan Stieglitz, Michael Gurven and Hillard Kaplan\*

### 14.1 Introduction

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The Horus and other research teams have found that atherosclerosis is not uncommon in ancient people through the study of their mummified remains (Murphy et al., 2003; Allam et al., 2009, 2011; Thompson et al., 2013, 2014). However, some have postulated that traditional hunter-gatherers are in some ways healthier than modern people and that they had very little atherosclerotic disease (O'Keefe et al., 2010). The aim of this study was to evaluate the burden of atherosclerosis in a population alive today but living a traditional lifestyle similar to that experienced by past populations. This led to the Tsimane Health and Life History Project Team (THLHP) (Gurven et al., 2017) and the Horus Study Team combining efforts to evaluate the prevalence and extent of coronary atherosclerosis in the Tsimane of Bolivia (Kaplan et al., 2017).

### 14.2 The Tsimane of Bolivia

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The Tsimane are forager-horticulturalists in the Bolivian Amazon region. They are an isolated population of approximately 16 000, inhabiting more than 90 villages along the Maniqui, Quiquibey and Mato Rivers in lowland Bolivia (Gurven et al., 2017). Most villages lack running water and electricity and have limited access to market goods. Poling a canoe or raft on a river or walking are their traditional forms of transportation. Recently, small outboard motors have become widely available and can be placed on canoes to shorten the duration of trips to the market town of San Borja.

The Tsimane economy is based on small-scale cultivation of produce including plantains, sweet manioc, rice and corn, as well as fishing, hunting and gathering fruits and honey. Figure 14.1 illustrates some of their lifestyles. The surrounding

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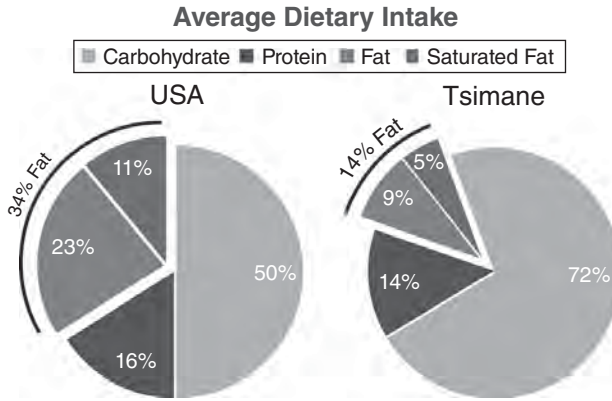
*Tsimane Health and Life History Project team members and other collaborators*: Juan Copajira Adrian, Sarah Alami, Giuseppe Barisano, Bret Beheim, Angela R. Garcia, Andrei Irimia, Margaret Gatz, Raul Quispe Gutierrez and Daniel Eid Rodriguez.



**Figure 14.1** Images of Tsimane lifestyle: (a) Tsimane individual crossing the Maniqui River at sunrise; (b) Tsimane dwellings; (c) inside a Tsimane dwelling; (d) woman crushing dried corn; (e) Tsimane woman retrieving water from a nearby stream; (f) two Tsimane hunters in the forest. Sources: (a) Ben Trumble; (b–d) Jonathan Stieglitz; (e, f) Michael Gurven. (A black and white version of this figure will appear in some formats. For the colour version, please refer to the plate section.)

rivers offer a variety of fish and nearby arable land for cultivation. Arrows, hooks and line, or nets are used for freshwater fishing. Depending on the wild game density around the village, hunting plays an important role in many communities. Guns or bows and arrows are used in hunting neotropical mammals such as the collared peccary, grey brocket deer, the Brazilian tapir and the howler monkey, sometimes with the help of hunting dogs or machetes. The corn, manioc, plantains and rice are high in fibre and low in saturated fats and simple sugars (Gurven et al., 2017).

The Tsimane diet lacks artificial *trans* fats (created by adding hydrogen to liquid vegetable oils to make them more soluble) and people's daily food intake on average contains 11 g saturated fat, 14 g monounsaturated fat and 8 g polyunsaturated fat (Martin et al., 2012). Diets differ from village to village, but a typical Tsimane diet consists of 72 per cent carbohydrates, 14 per cent protein and 14 per cent fat (Martin et al., 2012). In comparison, the typical modern US diet comprises 50 per cent carbohydrates, 16 per cent protein and 34 per cent fat, 11 per cent of which is saturated (see Kris-Etherton et al., 2012 and Figure 14.2). Tsimane days mostly consist of hunting, farming, cooking, parenting, grandparenting and socialising. Hunts often last more than eight hours and cover many kilometres (Trumble et al., 2014). Clearing of fields for horticulture requires heavy chopping of forests with axes (Trumble et al., 2013). A recent increase in access to the market town of San Borja and to intermittent wage labor have, however, been changing the Tsimane diet (Kraft et al., 2018). Men and women spend on average six to seven and four to six hours, respectively, per day carrying out physical activity. Only 10 per cent of the Tsimane waking hours are spent in a sedentary manner (Gurven et al., 2013) compared with



**Figure 14.2** Comparison of major dietary components of US and Tsimane populations. (A black and white version of this figure will appear in some formats. For the colour version, please refer to the plate section.)

approximately 54 per cent in industrial populations (Matthews et al., 2008). This high level of physical activity has rather obvious implications for cardiovascular health (Lee et al., 2012). The THLHP and Horus cardiovascular studies aimed to determine if this population with traditional human lifestyles, but high rates of infection, have low or high rates of atherosclerotic disease.

### 14.3 Material and Methods

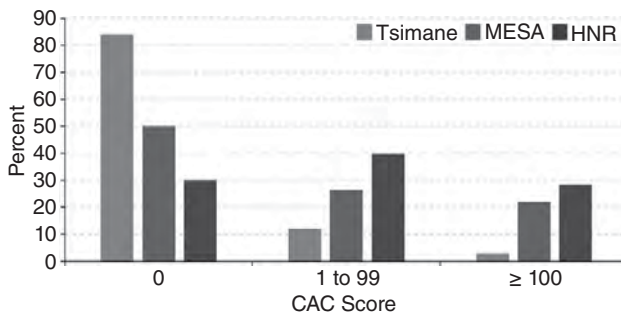
The Tsimane Health and Life History Project began in 2002, and combines biomedical surveillance of health with the anthropology of everyday life to analyse the impacts of ecology and society on the human life cycle. The Tsimane people of Bolivia are a remote-living Amerindian tribe with traditional lifestyles, very high levels of physical activity and limited access to market goods. The THLHP and Horus study teams collaborated in a study involving 705 adult Tsimane men and women who were transported from their villages to the clinics and computed tomography (CT) scanner at the German Busch Hospital in the regional capital of Trinidad, Bolivia between 2014 and 2017 (Kaplan et al., 2017). To reach the city, they typically journeyed one to two days by river to the roads originating from San Borja, followed by six hours in a taxi or bus. The composition of the Tsimane group studied was selected randomly by computer to achieve a cross-sectional study population. Voluntary participation in the study was high (92 per cent) among the Tsimane given the trust that THLHP had engendered over many years. The Tsimane who travelled to Trinidad were also provided with free access to medical care, including medical specialists. Individuals were compensated for their time and travel with subsistence goods. To evaluate coronary atherosclerosis, CT and coronary artery calcium scoring were utilised as sensitive measures of preclinical coronary atherosclerosis. Deposits of coronary hydroxyapatite (a component of atherosclerotic plaque) can be detected on CT scans and are diagnostic of atherosclerosis (Stary et al., 1995). These calcified deposits

occur prior to the development of symptoms, such as those associated with myocardial infarction or angina pectoris (Agatston et al., 1990). The degree of calcification is scored by the number and density of CT pixels that are over a threshold density of 130 HU using the Agatston method, with higher numbers correlating with more extensive coronary atherosclerosis (Agatston et al., 1990).

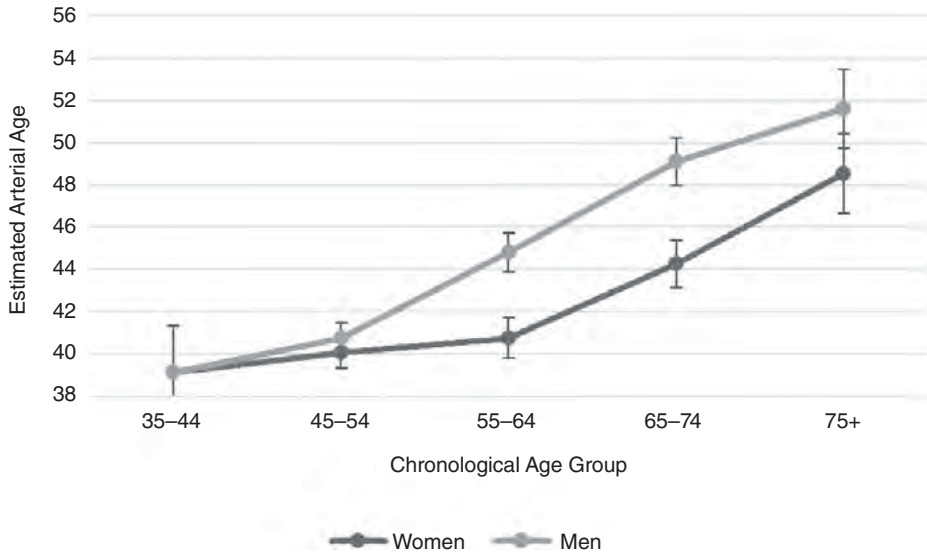
## 14.4 Results

The Tsimane were found to have a very low prevalence of coronary atherosclerosis, as measured by coronary artery calcification (CAC). The vast majority (596 of 705; 85 per cent) of participants had no CAC. A small number had mild coronary calcifications, with scores lower than 100 ( $n = 89$ ; 13 per cent), and only 20 individuals (3 per cent) had CAC of 100 or higher (Figure 14.3) (Kaplan et al., 2017). These results were compared with published calcification scores of general population-based studies in industrialised countries (Schmermund et al., 2002; Budoff et al., 2013). The Tsimane have less CAC than any other population ever described, including two major comparative studies: the cross-sectional population of the US Multiethnic Study of Atherosclerosis (MESA) and the European cross-sectional population of the German Heinz Nixdorf Recall (HNR) study (Schmermund et al., 2002; Budoff et al., 2013). The differences in CAC were further analysed by age across broad categories (Figure 14.3).

Using CAC as a metric for arterial age, the Tsimane have an average arterial age that is about 28 years younger than matched Americans (Figure 14.4). The difference in arterial age is best shown by using the MESA arterial age calculator. Figure 14.4 displays the predicted arterial age of the Tsimane by their actual chronological age, and the difference between the MESA arterial age calculator scores for the Tsimane and their true chronological age. By the age of 80, the estimated arterial age is 52 years for women and 51 years for men. For a Tsimane over the age of 75 years, the mean difference between chronological and arterial age was 33 and 28 years for females and males, respectively.



**Figure 14.3** Percentage of Tsimane CAC scores in three risk categories compared with the general cross-sectional population-based participants from the MESA study (Budoff et al., 2013) and the Heinz Nixdorf Recall (HNR) study (Schmermund et al., 2002). (A black and white version of this figure will appear in some formats. For the colour version, please refer to the plate section.)

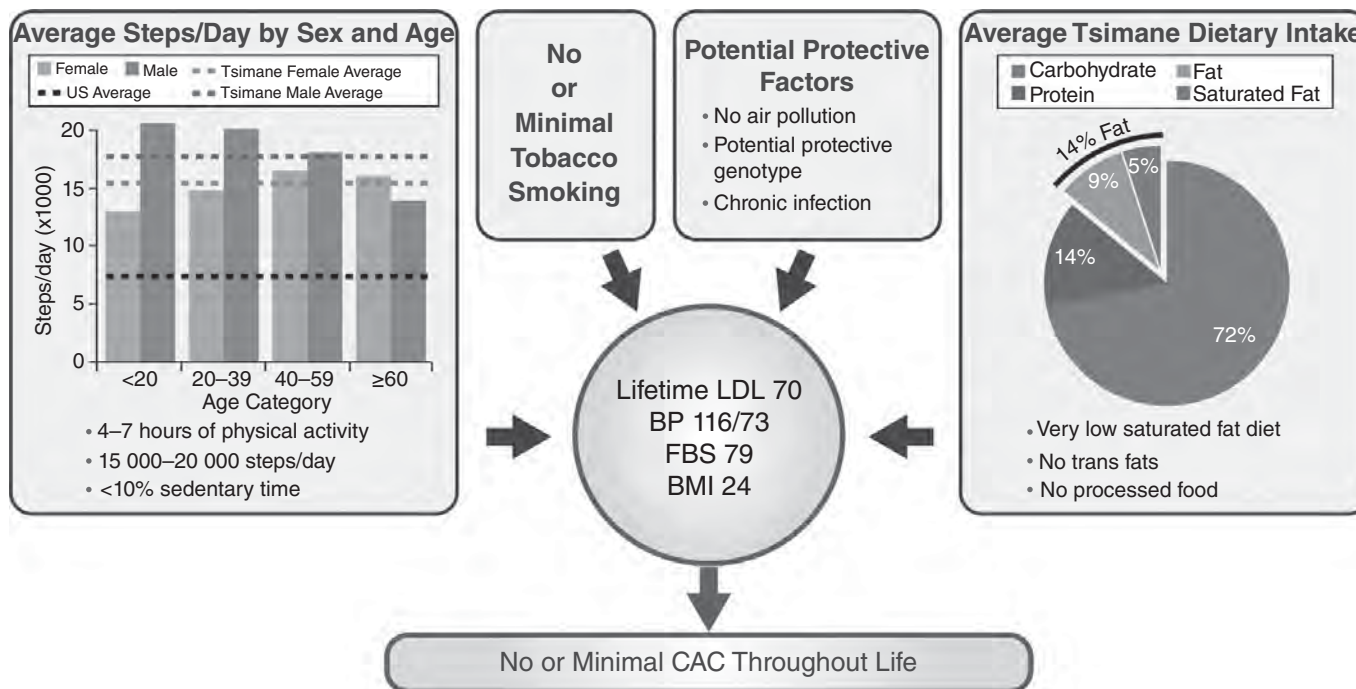


**Figure 14.4** Arterial age versus chronological age for Tsimane women and men.

## 14.5 Discussion

### 14.5.1 Why Do Tsimane Have So Little Coronary Atherosclerosis?

The most obvious explanation for the reason why the Tsimane population has such little coronary calcium and subsequent coronary atherosclerosis is related to their optimal coronary risk factor profile (Yusuf et al., 2004); in other words, the paucity of traditional cardiovascular risk factors. Genes, the presence of inflammation and immune regulation represent three other possible explanations. The Tsimane subsistence lifestyle meets all four of the lifestyle factors that the American Heart Association lists as goals: no or minimal smoking, body mass index (BMI) less than 30 kg/m<sup>2</sup>, a healthy diet and moderate or greater physical activity (Lichtenstein et al., 2006). Although some Tsimane smoke lightly, and they are not particularly lean (almost one-quarter of adults qualify as being overweight according to their BMI), almost all Tsimane meet the goals of the American Heart Association and often greatly exceed them. Their subsistence lifestyle includes a very low saturated fat diet and substantial daily physical activity. As a result, there is little obesity, hypertension or peripheral arterial disease, and their mean low-density lipoprotein (LDL), or 'bad' cholesterol, is quite low. Lifetime LDL is estimated to be 72 mg/dL (Kaplan et al., 2017). Among the 705 Tsimane in this study, mean fasting glucose was 79 mg/dL (desirable <100 mg/dL) and none had diabetes. Figure 14.5 serves as a summary of this discussion. It should be noted that the Tsimane and other indigenous people in South America and Africa are experiencing a rapid change in some of these metrics, as progressive access to market goods increases lipid levels, body weight and rates of diabetes.



**Figure 14.5** Concepts of how multiple factors contribute to the remarkably low rates of coronary arterial calcification in the Tsimane. (A black and white version of this figure will appear in some formats. For the colour version, please refer to the plate section.)



The Tsimane also have potential atheroprotective factors within their environment, including no industrial air pollution (although they cook over an open fire), and the presence of chronic helminthic infections, which some theorise may induce beneficial modulation of the immune system (Gurven et al., 2016 and see below). As the Tsimane have recently experienced increasing levels of cholesterol with advances in acculturation, a genetic predisposition to low cholesterol seems an unlikely cause of their benign lipid levels (Kaplan et al., 2017). If the genetic constitution of the Tsimane is similar to that of other North and South Americans, their subsistence lifestyle and high levels of physical activity, and resultant optimal cardiovascular risk factor profile, set a new standard of achievable metrics when discussing potential preventative measures for avoiding atherosclerosis.

However, the Tsimane live without modern sanitation and have high rates of infection and markers of inflammation. Blood markers of inflammation such as white blood cell count (WBC), high-sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate (ESR) are frequently elevated (Zebrack & Anderson, 2002). In particular, the hs-CRP test measures the level of inflammation and can be used to assess risk for heart disease/stroke (Ridker et al., 2009). The ESR measures how quickly red blood cells move to the bottom of a test tube; if a person has inflammation, their cells may settle at a fast rate.

Infection and inflammation, particularly periodontal disease and elevated hsCRP, have been found to be associated with atherosclerosis in industrialised societies (Chistiakov et al., 2016). However, there is reason to hypothesise that chronic infections of the lungs and skin do not promote atherosclerosis, and other infections, especially those caused by helminths, could be protective against atherosclerosis, especially when a person has low LDL in their cholesterol (Gurven et al., 2009, 2018). For example, intestinal helminths draw metabolic resources from their host, including blood lipids and glucose, and modulate immune function towards greater  $T_H2$  (anti-inflammatory) polarisation. These helminth-induced alterations may be factors in slowing atheroma progression and diminishing the possibility of atherosclerotic plaque rupture, in which a sudden blood thrombosis forms over the rupture causing a heart attack or stroke (Gurven et al., 2016).

#### **14.5.2 Studies of Cardiovascular Disease and Risk Factors in Other Subsistence Populations**

Studies of individuals from cultures living a subsistence lifestyle have found similarly low blood pressure and LDL cholesterol levels, as documented in four reports. Firstly, in 1975 Oliver and colleagues reported a study of 506 men and women out of approximately 15 000 from the Yanomamo tribe in the tropical rainforest of northern Brazil and southern Venezuela (Oliver et al., 1975). Without access to markets, the Yanomamo people farm, hunt, fish and gather their food. While blood pressure in industrialised cultures gradually increases over adult life, the blood pressure of Yanomamo men was 108/69 mmHg during their twenties but remained stable

thereafter through adult life. Blood pressure in Yanomamo women in their twenties was 100/64 mmHg, again without increasing thereafter. LDL levels were obtained and reported in 1990. Mean LDL among 34 men was 68 mg/dL and was 78 mg/dL among 14 women (Mancilha-Carvalho & Crews, 1990). This compares favourably to what is considered desirable (<100 mg/dL) and to the mean in general population-based studies of Westerners (e.g. 132 mg/dL in the PESA study; Fernandez-Friera et al., 2015). Secondly, two cultures in southeastern India living a subsistence lifestyle had mean LDL cholesterol levels similar to those of the Tsimane and Yanomamo. The Kandha tribe of the Eastern Ghat mountains ( $n = 97$ ) who hunt, gather and practice slash-and-burn agriculture, and the Naulia fishermen of the Coromandel coast ( $n = 93$ ) both had mean adult LDL values of 71 mg/dL (Mandal et al., 1994). Thirdly, the long-standing subsistence culture of the Parkateje of northern Brazil experienced a change over a 20-year period in which they gained access to market food and motorised vehicles. While mean blood pressure remained low in a sample of 90 individuals studied (111/73 and 107/70 mmHg for men and women, respectively), LDL was higher than in cultures prior to acculturation (the Tsimane and Yanomamo) at 90 and 93 mg/dL for male and female Parkateje, respectively (Tavas et al., 2003).

Finally, a frequently cited study explored risk factors for cardiovascular disease in a Melanesian population from the Trobriand Islands, Papua New Guinea (Kitava) and compared them with those of a healthy Swedish population (Lindeberg et al., 1994). This study focused on horticulturalists who were thought to have been free from ischaemic heart disease or strokes. A total of 220 people were studied, 151 male and 69 female between the ages of 14 and 87 years. These people maintained a traditional horticulturalist lifestyle and had not been uninfluenced by Westernised diets. Instead, fruits, fish, tubers and coconut were their main foods. The investigators measured blood pressure, height, weight and BMI, and waist, pelvis and upper arm circumference. They also measured serum total cholesterol, high-density lipoprotein (HDL), LDL and the lipid subfractions apolipoprotein B and A1. BMI, diastolic blood pressure and triceps skinfold thickness measurements were all lower in the Islanders compared to the Swedes. Systolic blood pressure was lower in women over age 60 and men over age 20. The authors attributed the very low rates of stroke and ischaemic heart disease to lower blood pressure and lean body weight among the Islanders relative to modern-day Swedish people. The authors believed this difference could be explained by the considerable difference in diet between the two cultures, especially less salt and saturated fat and more soluble fibre in the Trobrianders. However, relative physical activity may have a part to play here, although Lindeberg et al.'s (2014) study was focused on dietary factors.

These studies of the Yanomamo, Kadha, Naulia, Parkateje and Trobriand Islanders are consistent in showing healthy cardiovascular risk factor metrics and apparently low rates of cardiovascular disease, findings similar to those of the Tsimane. All represent physically active populations who consume diets low in Western food items and have a very low burden of risk factors for heart disease.

### 14.5.3 How Do We Reconcile the Absence of Atherosclerosis among the Tsimane with Its Apparent Prevalence among Ancient People?

The Horus study found atherosclerosis among Egyptian mummies as well as pre-Columbian Peruvians, Aleutian Islanders and Ancestral Puebloan Native Americans of the southwestern USA (see Chapter 4). While Egyptian mummies tend to be of people who were elite in life, the two latter cultures lived a subsistence lifestyle that may have been similar to that of the Tsimane. The ancient Egyptian lifestyle (and to a lesser extent the ancient Peruvian) was more hierarchical and even urbanised. In addition, the elite Egyptians were artificially mummified in a costly 40-day process, whereas the human remains analysed in the other cultures were preserved naturally through desiccation (Peruvians and Native Americans of the southeastern USA) or very cold environments (Aleutian Islanders). The Egyptians who were mummified were particularly of the higher social classes, especially in the older dynastic periods (David, 2010). They likely ate a rich diet, in many ways similar to moderns (David, 2010), and were not physically active in life. This may have contributed to the occurrence of atherosclerosis in these people. One study of pathological bone conditions on CT scans of Egyptian mummies revealed numerous examples of joint disease in the bones of the knees, hips and spine, but ankle osteoarthritis was relatively rare (Fritsch et al., 2015). This finding led the investigators to conclude that these Egyptians in life likely did not commonly walk on irregular surfaces because of their high status, which could have resulted in ankle injuries (Fritsch et al., 2015).

The heart is typically not well preserved after either artificial or natural mummification and, in the case of the Egyptians, was sometimes removed. This makes coronary artery calcification particularly difficult to evaluate in such studies. Thus, the presence of atherosclerosis in mummies has usually focused on extra-coronary atherosclerosis. Extra-coronary atherosclerotic calcifications, such as calcium in the thoracic aorta, abdominal aorta and the iliac, femoral and carotid arteries, is known to occur earlier than in the coronary arteries (Allam et al., 2018) and is fairly easy to identify on the CT scan of a reasonably well-preserved mummy. For example, Allam and colleagues have pioneered the study of whole-body calcifications using whole-body CT scanning to investigate extra-coronary atherosclerosis in living people (Allam et al., 2018), with 154 Egyptian patients studied as part of this project. They underwent clinically indicated nuclear cardiology stress testing (myocardial perfusion imaging), but their scans showed no evidence of lack of blood flow caused by coronary artery heart disease. The investigators found that calcification was frequently present in the iliac and femoral arteries of the legs and the abdominal and thoracic aorta. However, calcification in the coronary and carotid arteries was typically seen only in older individuals. As coronary and carotid atherosclerosis result, respectively, in myocardial infarctions and strokes (Kaptoge et al., 2019), they can be termed ‘event-related arteries’. The investigators thus proposed that atherosclerosis moves in a ‘south to north fashion’ with age (Allam et al., 2018), occurring first in the iliac and femoral arteries, then the aorta and then arteries to the head. Based on these findings, whole-body CT scanning in the Tsimane would likely reveal

more atherosclerosis in more 'southern' arterial beds than was seen in the coronary arteries. Extra-coronary atherosclerosis has not yet been fully evaluated in the Tsimane, but thoracic aortic calcium has been observed to be more prevalent than coronary calcification (Thompson et al., 2018). Thus, it is not really possible to say whether ancient people had more atherosclerosis than the Tsimane. However, what can certainly be said is that atherosclerosis has been present in humankind for a very long time. It is also clear that cultures where people are very physically active and eat a lean diet have much less atherosclerosis than people who live in modern Western cultures.

## 14.6 Conclusions

The findings of atherosclerosis in multiple diverse ancient cultures demonstrates a natural human tendency to develop atherosclerosis, the primary cause of cardiovascular death and the number one cause of death in the modern-day world (Yusuf et al., 2015). Finding that the Tsimane experience minimal coronary atherosclerosis demonstrates that coronary disease can be dramatically reduced with a very low fat diet and high levels of low to moderate activity. These two variables appear to produce low LDL cholesterol, low blood pressure, minimal obesity and an avoidance of diabetes. While this lifestyle and diet is not always realistic in contemporary urban populations, it sets a standard of what can be achieved to slow the modern-day scourge of atherosclerosis. The study of the bioarcheology of atherosclerosis has added substantially to our understanding of this very common human disease.

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