Received: 19 September 2021 | Revised: 27 July 2022 | Accepted: 17 April 2023

DOI: 10.1002/evan.21987

REVIEW ARTICLE

Evolutionary Anthropology WILEY
ISSUES, NEWS, AND REVIEWS

Hunter-gatherer diets and activity as a model for health promotion: Challenges, responses, and confirmations

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Abstract

Beginning in 1985, we and others presented estimates of hunter-gatherer (and ultimately ancestral) diet and physical activity, hoping to provide a model for health promotion. The Hunter-Gatherer Model was designed to offset the apparent mismatch between our genes and the current Western-type lifestyle, a mismatch that arguably affects prevalence of many chronic degenerative diseases. The effort has always been controversial and subject to both scientific and popular critiques. The present article (1) addresses eight such challenges, presenting for each how the model has been modified in response, or how the criticism can be rebutted; (2) reviews new epidemiological and experimental evidence (including especially randomized controlled clinical trials); and (3) shows how official recommendations put forth by governments and health authorities have converged toward the model. Such convergence suggests that evolutionary anthropology can make significant contributions to human health.

KEYWORDS

diseases of civilization, evolutionary medicine, hunter-gatherer activity, hunter-gatherer diet, Paleolithic diet

1 | INTRODUCTION

Almost four decades ago, "Paleolithic Nutrition: A Consideration of Its Nature and Current Implications," was published in a leading medical journal.[1] It unveiled an unorthodox dietary paradigm—unorthodox because it was based not on conventional research, but instead on an understanding of nutritional experience during the course of human evolution. This understanding emerged from hunter-gatherer (HG) research and from archeological and paleontological evidence. Although HG diets varied greatly, they did so within definable ranges, which we took to mean that similar limits probably applied to our ancestors during our evolution. We suggested a "mismatch" or discordance hypothesis, which in its simplest form states that our genome evolved in conditions that no longer exist—from the emergence of modern humans to the beginnings of agriculture—a time period when some fundamental genetic matrices underlying our metabolism, physiology, and behavior were refined. We argued that subsequent changes of the environment, socioeconomic conditions, physical activity patterns, and dietary factors have induced only modest genetic adjustments, and that the resulting genome-life style discrepancy, the mismatch, is a causative factor affecting the development of several important chronic ailments, sometimes called "diseases of civilization." Some might liken the evolutionary approach to health promotion science[2] to a Thomas Kuhn-like paradigm shift.[3] The hunter-gatherer model (HGM) might inform future laboratory, clinical, and epidemiological studies; has heuristic value; and approximates the "natural" human experience so appreciated by the public.[4]

The "mismatch" affects atherosclerotic peripheral vascular and coronary artery disease (CAD), cerebrovascular accidents (strokes), type 2 diabetes mellitus (T2DM), chronic obstructive pulmonary disease (COPD), several cancers, essential hypertension (HTN), obesity, diverticulosis, and other diseases which, taken together, constitute a large portion of the global burden of adult disease and

mortality. The biomarkers—serum cholesterol and triglycerides (TGs), aerobic fitness, blood pressure (BP), and body composition—measured in nonindustrial, especially HG, populations confer low risk for these conditions.[5] Various lines of evidence support this thesis. For example, when HGs on different continents transition to market economies, their dietary quality declines, including a reduction in diversity of foods, fewer vegetables, fruits, and animal products, and more sugar, salt, and oil.[6,7] Conversely, Australian aborigines who had become urbanized and had developed T2DM experienced marked improvements in carbohydrate (CHO) and lipid metabolism when experimentally returned to the "bush" where they resumed their former HG diet and physical activity patterns.[8] In the same vein, archeologists have found that (with some exceptions) body size and robusticity decreased as dietary quality declined during the transition to agriculture.,[9,10] although the full impact of the transition is complex.[11] Assumption of upright posture and locomotion millions of years ago led to some of today's spinal pathology,[12] but for the most part today's mismatch began with the Agricultural Revolution; it greatly increased with industrialization. No one thinks our genes have had time to adjust to the diet and lifestyle changes of the past two centuries.

The original depiction of Paleolithic nutrition has been subjected to legitimate criticism. Nevertheless, with some adjustments, it holds up to scrutiny. Using then-available data on the nutrients in specific animal and plant foods consumed by HGs worldwide, together with anthropological data on the composition of HG diets, the 1985 paper estimated HG macro- (and some micro-) nutrient intakes. These estimates were compared to published data regarding the average mid-1980s American diet and to then-existing guidelines from government and health authorities. Similarly, estimates of HGs' aerobic and muscular fitness were compared to published data from the United States and other industrial and postindustrial societies.[5] Together, these comparisons supported recommendations that industrial and postindustrial populations need to increase physical activity, balance caloric intake with caloric expenditure and improve both cardiopulmonary fitness and muscle strength. Health promotion proposals based on an evolutionary perspective were extraordinary[13] and attracted extensive media attention—mainly mockery—ironically foreshadowing the eventual popularity of "Paleo" diets.

"Cavemen cooked up a healthy diet,"[14] "Cave Man Takes a Healthy Bite Out of Today's 'Civilized' Diet,"[15] and "Check Ads for Specials on Saber-Toothed Tigers" were some headlines. *The Fort Lauderdale News/Sun-Sentinel* ran "paleolithic" recipes and a full-color photo of a stooge done up as a caveman—skin, club, tooth necklace, and all. A *Washington Post* editorial claimed we would write a best-seller "inevitably" entitled "The Cave Man Diet," and, "Some day in the near future you'll look out at daybreak and see people all up and down your street come loping out of their homes wearing designer skins and wielding L. L. Bean stoneaxes while every dog, cat and squirrel in the neighborhood runs for cover."[16] *Boston Globe* columnist Ellen Goodman's ridicule was accompanied by an etching of tribal people dancing, captioned "Make mine mastodon;" "But I am convinced," she concluded, "that the average Paleolithic person was the very role model of good health when he died at the ripe old age of 32."[17] *The New York Times* editorialized, "Did the people of the early Stone Age eat more healthily than their urban successors? The issue is being vigorously chewed in the *New England Journal of Medicine*, and it tastes like the myth of the Noble Savage."[18]

Critics have stressed that HG life expectancy was only 30–35 years, not noting that average life expectancy was similar for nonindustrialized people generally, and due more to high infant/child mortality than to shorter maximum lifespan.[19,20] HG deaths often resulted from infectious illnesses that are now controllable (although HIV/AIDS and COVID-19 reprise their past importance). Average HG total serum cholesterol levels were below 135, their typical aerobic fitness matched that of today's superior athletes and their levels of insulin resistance and HTN were minimal.[5] Consequently, older HGs rarely suffered CAD, T2DM, COPD, colon disorders, or certain other currently common noninfectious ailments,[21,22] although they did suffer some spinal disorders common to all human populations due to the imperfect evolution of erect posture.[12]

Mid-1980s health guidelines, based on epidemiological, clinical, and animal research differed both quantitatively and qualitatively from the HGM. HG intakes of sodium and CHO were below official targets, while protein and fiber intakes were higher. Cholesterol intake was about the same for HGs as for 1980s Americans—above the recommended range. Total CHO intake was lower than recommended because HG CHO came chiefly from fruits and vegetables (substantially more than average Americans consumed) while grains and sugars contributed far less than is common today. Total fat intake was similar to that in current diets, but the ancestral diets included far more long-chain polyunsaturated fatty acids (LCPUFA). Within this category, the proportions of ω−6 and ω−3 components were close to equal—much different from the contemporary 20:1 ratio based on studies in the United States, the United Kingdom, and Northern European populations.[23,24]

The HGM has been updated over the years,[25–27] and is the foundation of what is termed "evolutionary health promotion."[2] The present review (1) addresses three decades of questions and critiques; (2) updates the HGM with respect to new archeological findings, more extensive HG research, genomics, and recent clinical tests, including randomized controlled trials (RCTs); and (3) appraises the latest authoritative recommendations to show how these tend to converge toward the HGM.

2 | CHALLENGES TO HGM MODEL

Challenges have included claims that we misestimated Paleolithic nutritional components (#1 and #2 below); that we misconstrued the health effects of the mismatches (#3 and #4 below); that atherosclerosis is an ancient disease (#5 below); that we greatly exaggerated the importance of activity differences (#6 below); that genetic evolution since the HG era negates the mismatch model (#7 below); and that a Paleolithic-type diet (PTD) is environmentally unsustainable (#8 below).

Challenge #1: The 1985 estimate of Paleolithic macronutrient intake was incorrect.

The 1985 article estimated that typical Paleolithic humans consumed (in terms of energy supplied) 24.5% protein, 55% carbohydrate, and 20% fat.[1] This estimate was flawed partly because it was based on analysis of only 44 wild plant foods and 21 game animals consumed by HGs. Now, hundreds of pertinent analyses are available. More importantly, the 1985 estimate assessed only game muscle meat. However, HG's avidly consume the organs and fat stores of the animals they acquire—a factor that necessarily alters dietary macronutrient estimates.[28] Third, early nutritional reconstructions included data from worldwide HG groups, including some from environments immaterial to retrodictions of prediaspora Africans. Marlowe[29] assembled data from 179 warm-climate, nonequestrian HG groups that suggested a median of 53% plants, 26% meat, and 21% fish. Based on these data, the energy sources of typical late Paleolithic diets would have consisted of ~30% protein, ~35% CHO, and ~35% fat. Numerous subsequent studies have arrived at essentially similar proportions (e.g., Kuipers et al.[23]), although new research on HG consumption of the digesta of large herbivore prey could increase CHO estimates.[30] The estimates for protein and fat are within the National Academy of Sciences (NAS) accepted macronutrient distribution ranges (AMDRs)[31]: For CHO, the NAS AMDR is 45%–65%, well above the HGM figure of 35%. However, the NAS range includes up to 25% sugar, a nutrient thought to provide only ~2% of Paleolithic dietary intake.

It has been argued that the human gastrointestinal tract is best suited for omnivory,[32] with a relatively short gut compared to other hominids, although this may also be due to the long-standing importance of cooking, leading some to call humans "cucinovores."[33] The fossil record[34,35] shows that meat became important early in the evolution of the genus *Homo*,[36–39] but plant foods remained in use.[40] Cooking was crucial because it made otherwise poorly digestible meat and plant foods (including legumes[41]) more absorbable, nutritious, and safe.[42–45] Taken together, Marlowe's findings and updated nutrient analyses suggest that a nutritional pattern approximating Protein/CHO/Fat: 30%/35%/35% (in terms of energy provided) prevailed during at least the last 250,000 years of human evolution and likely far earlier.[46]

Like all extant primates, many (probably most) HGs consumed insects,[47–49] and there is evidence of insectivory in hominin evolution.[50] Arthropods offer rich and varied nutrients,[51] but more research is needed before we can estimate their quantitative or qualitative contribution to ancestral diets. However, any necessary alteration is unlikely to change our rough estimates of the relative energy contributions of the three major macronutrient categories.

Challenge #1 is valid, but HGM dietary estimates presented more recently, and in the spirit of the original, are increasingly defensible.

Challenge #2: The 1985 article overemphasized terrestrial, and neglected maritime, lacustrine, and riverine Paleolithic environments.

Most, though not all, of the data on which the 1985, and 1988 papers were based came from inland HG groups. This is understandable because paleoanthropological studies had focused on terrestrial archaeological findings and on savanna/forest HG's like the Hadza, Ache, and San (Figures 1–3). However, it is increasingly likely that our most relevant ancestors inhabited littoral regions both before and during the "out of Africa" diaspora, and that this played a major role in human evolution,[52,53] greatly facilitating worldwide dispersal. Although it is no longer tenable to argue for a single rapid coastal settlement of Asia, the more complex current view still leaves a large

FIGURE 1 The first author with Jun/'hoan (!Kung) San hunters after a traditional gemsbok (oryx) hunt in Northwestern Botswana in 1970. Photo by Nicholas G. Blurton Jones.

FIGURE 2 A Jun/'hoan (!Kung) San woman gathers berries for her family with a child on her back and another picking berries alongside her. Northwestern Botswana, 1969. Photo by Marjorie Shostak.

FIGURE 3 A Jun/'hoan (!Kung) San girl around seven years old is delighted with a bird she has killed. While women do little hunting, every child must be socialized emotionally as well as in skill set. Northwestern Botswana, 1970. Photo by Mel Konner.

role for marine adaptations.[54] Clearly littoral adaptations played a previously underestimated role in modern human evolution,[55,56] with significant implications for paleonutrition.

A greater proportion of oceanic and freshwater foods would likely affect dietary electrolyte intake (see below), but another factor might be of similar significance. The 1985 paper estimated a dietary polyunsaturated to saturated fat (P:S) ratio of 1.41, but provided no figures for long-chain polyunsaturated fatty acids (PUFA). More recently, Kuipers et al.[23] estimated that in East Africa, the HG P:S ratio was ~1.2, and that the diet provided substantial amounts of PUFA with a long-chain PUFA (LCP) ω−3/LCP ω−6 ratio of ~1.38. The Kuipers group also compared Paleolithic diets containing fish to those that did not. The former provided 8.7 g of the ω−3 LCPs DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid) per day (together with 4.0 g of AA). In their model, ancestral diets without fish offered only 2.2 g DHA and EPA per day.

Many epidemiological investigations have suggested that greater dietary intake of PUFA, especially of ω−3 EPA and ω−3 DHA, is correlated with benefits for cardiovascular diseases (CVD), diabetes, cancer, dementia, visual/neurological development, and several other conditions. However, in each case, there are opposing studies that failed to support these findings,[57] so additional RCTs are needed.[58] A 2015 Cochrane Database meta-analysis of 15 RCTs with a total of 59,000 participants found a small but potentially important reduction of cardiovascular risk when saturated fat (SF) intake was lowered; caloric replacement of SF with PUFA was more useful than replacement with CHO.[59] But a recent review concluded that reducing SF intake is not beneficial.[60] For these questions, the 1985 article wasn't germane, but subsequent contributions prompted by it can beneficially influence future trials by establishing experimental parameters that match ancestral PUFA intake patterns.

Challenge #2 was valid, but later research has corrected the original omission.

Challenge #3: The 1985 article implied endorsement of a "high" protein diet, but high-CHO diets are heathier.

Several authors[61–65] advocate very low refined-CHO, near-vegetarian diets with high nonrefined CHO and low fat (HCLF). These diets appear safe and reduce major cardiovascular events[63]; one showed radiologically-proven reversal of atherosclerotic arterial stenosis.[62] Such recommendations are diametrically opposed to those of some "paleo" diets—both low CHO/high fat (LCHF) and low CHO/high protein (LCHP)— and have incited fierce debate.[66,67] Several studies have shown that a HGM diet is also safe, while beneficially affecting cholesterol and TG levels, BP, and weight.[68–71] One meta-analysis of RCTs[72] showed that "The Paleolithic diet resulted in greater short-term improvements in metabolic syndrome components than did guideline-based control diets" (p. 922).

In fact, other meta-analyses show that HCLF, LCHF, and LCHP diets all produce weight loss[73] and improve metabolic measures predictive of CVD.[74] This being so, dietary adherence becomes an important consideration. In turn, adherence is affected by how diets produce feelings of satiety, and RCTs have found a Paleolithic-type diet to be more satiating per calorie than either the Mediterranean[75] or Canadian Food Guide diets.[76] It's important to recognize that "tolerable" and "optimal" are not synonyms. Several dietary regimens seem comparably beneficial as accessed by investigations to date, as might be expected from human omnivory and the spectrum of HG diets. Nevertheless, all such diets vary substantially from typical Western nutritional patterns. Also, satiety is a potentially important but understudied influence on diet adherence, RCTs of the HGM are in their infancy, and on the basis of human evolutionary experience, we continue to predict that future research will eventually endorse the HGM.

Challenge #3 is refuted. HGM diets are as healthy, or more so, than are hi-CHO, low-protein alternatives.

Challenge #4: The 1985 paper implied endorsement of "very" low sodium intake, but this factor is of no relevance to blood pressure.

In 1985, "Paleolithic Nutrition" indicated that inland HGs consumed about 600–1000 mg (26–40 mmol) of sodium (Na^+),[1] a range approaching that for Tsimane forager-horticulturists, ~480 mg/d.[77,78] For coastal HG's consuming substantial amounts of shellfish, Na^+ intake must have been greater; however, for 1960s Pacific islander Pukapukans, average intake was ~1450 mg/day while BP averaged 123/77 mm/Hg.[79] The 1988 Intersalt Study found no hypertension among populations consuming HG levels of Na^+ (483 mg/d),[80] and separate studies of 25 similarly low-salt populations from around the world found they were also normotensive.[5]

Unfortunately, no subsequent epidemiological studies have included groups with intake that low, but nevertheless many have shown a linear relationship between BP and Na^+ intake or excretion, and RCTs show a dose–response relationship down to as low as 400 mg/d.[81] Sodium worsens CVD and all-cause mortality independently of BP.[82] In one global modeling study, "1.65 million deaths from cardiovascular causes in 2010 were attributed to sodium consumption above a reference level of 2.0 g per day."[83] Certain studies have shown a nonlinear (U- or J-shaped) relationship between Na^+ intake and measures relevant to cardiovascular health, suggesting an optimal intake of 3000–6000 mg/d[84–86] Accordingly, some believe that Na^+ consumption for most of the world is in the optimal range and that guidelines are too strict.[87] The low prevalence of hypertension among diverse low-salt populations, contrasted with its near ubiquity elsewhere, argues against such contentions.

In 2022 an analysis of 10,709 participants in six prospective cohort studies assessed major cardiovascular events (e.g., heart attack, stroke, coronary bypass surgery) as predicted by excretion of Na^+ and K^+ in 24-h urine samples.[88] The estimated intake ranges for each were roughly 2000–6000 mg. After controlling for numerous confounding factors (e.g., baseline HTN, smoking, diabetes), Na^+ positively predicted and K^+ negatively predicted cardiovascular events; Na^+/K^+ ratio independently predicted higher risk. (Each 1000 mg increase in Na^+ excretion or decrease in K^+ was associated with an 18% increase in risk. Like most such studies, this one did not extend down to HG levels of either nutrient.)

Higher dietary K^+ also protects against HTN and renal failure.[86,89–91] Hunter-Gatherer K^+ intake is estimated to have been high (~7000 mg/d vs. 2500 mg/d currently) and for all HGs studied, dietary potassium consumption exceeded that of sodium. Away from the coast the K^+/Na^+ ratio was likely 7:1.[1] Coastal HGs' Na^+ intake must have exceeded that of inland foragers, but both shellfish and finfish provide more K^+ than Na^+ (shellfish $K^+/Na^+ = 1.6$; finfish $K^+/Na^+ = 2.4$), so even maritime HG's had K^+/Na^+ dietary levels far healthier than do typical Westerners ($K^+/Na^+ = 0.6$).[92]

Challenge #4 is refuted. Electrolyte intake at the HGM level protects against hypertension.

Challenge #5: Both the 1985 and 1988 articles suggested that an HGM regimen would reduce risk of atherosclerosis. The Horus Study discredited that proposition.

We originally proposed that atherosclerosis is a relatively new disease, largely absent in HGs.[1,5] In 2011, the "Horus Study" found atherosclerosis (AS) in mummies from various cultures and differing time periods.[93,94] "Atherosclerosis was present in all four populations: 29 (38%) of 76 ancient Egyptians, 13 (25%) of 51 ancient Peruvians, two (40%) of five Ancestral Puebloans, and three (60%) of five Unangan hunter-gatherers (Thompson et al.,[95] p. 1211)." The paper concluded that "atherosclerosis in premodern human beings suggests that the disease is an inherent component of human ageing and not characteristic of any specific diet or lifestyle." (Thompson et al.,[95] p. 1221). However, a Horus Study coauthor wrote separately, "The relatively small samples of elite Egyptian individuals who were mummified preclude generalizations about atherosclerosis at the population level."[93] The Peruvian sample is also likely biased toward elites, as any deliberately mummified sample might be. The five Unangans were HGs randomly mummified by Arctic temperatures unlike those that existed in pre-exodus Africa, so none of the Horus populations was particularly relevant to human evolution, which took place as foragers inhabited warm climates.[95,96]

Elites in the ancient world could have had atherogenic diets and lifestyles, but AS was uncommon before 1900. It became much more prevalent thereafter,[97] and is now endemic globally.[98] In the Rotterdam Study, only around 3% of individuals (mean age, early 70 s), were free of arterial calcifications, versus almost 60% of the Horus Study mummies over 50.[94] In a San Diego preventive medicine clinic,[99] "Approximately one-third of subjects younger than 50 were free of calcified disease, whereas all subjects older than 70 were found to have some calcium (p. 331)."

Certain arterial beds carry particular risks. Coronary artery calcification (CAC) predicts myocardial infarction, and in three major studies, the U.S.-based Multi-Ethnic Study of Atherosclerosis (MESA, $n = 6726$), the Dallas Heart Study (DHS, $n = 1080$), and the German Heinz Nixdorf Recall study (HNR, $n = 3692$), the percentages of zero scores for CAC were 50.1 (mean age 62), 33.4 (mean age 53), and 30.8 (mean age 60). In the Horus study, 96% were free of CAC.[94] Of 18 Peruvian and Egyptian mummies, three (17%) had calcifications in the internal carotid arteries, predicting stroke risk; the comparable figures for modern Brazilians and Greeks in that age range were 55% and 46% respectively.[100] Clearly, some ancient populations, particularly elites, had AS, but prevalence in these does not compare with that in industrialized populations.

Clinical studies of non-Westernized Kenyans, Solomon Islanders, Navajos, Masai, Australian Aborigines, New Guineans, and African Pygmies found little or no coronary disease,[5] and stronger evidence comes from evaluation of Tsimane forager-horticulturalists in the Bolivian Amazon. In this group, sophisticated evaluation revealed very low cardiac risk.[21,22] Of 705 Tsimane individuals over 40 years of age (mean = 58), 85% had zero CAC, as did 65% of those over 75 ($n = 48$).[21] Only four in that age group had CAC scores over 100, one-fifth the rate of Americans in the MESA study.[21] More research on arterial calcification in traditional societies will be welcome, but their much lower levels of serum cholesterol, BP, and other CVD risk factors have long been clear.[5,26]

Challenge #5 is satisfactorily addressed. Evidence that an HGM regimen reduces AS risk outweighs the "Horus" study findings.

Challenge #6: Calories dont count: physical activity at the HGM level is unrelated to obesity and thus to Type 2 diabetes.

Muscularity and aerobic fitness critically affect health.[5] Inferences from skeletal remains (postcranial robusticity, trabecular bone structure, muscle insertion areas)[101,102] and observations of HG physical activity[5,103,104] indicate that the muscle strength and aerobic fitness of average HGs were similar to those of today's superior athletes. Recent Hadza foragers typically exert about 135 min of moderate and vigorous physical activity (MVPA) per day,[103] more than six times the current recommendation for MVPA of 150 min/wk.[105] Only 20% of Americans attain even this modest goal.

Despite the low level of physical activity among contemporary Westerners, their total energy expenditure (TEE) is similar to that of Hadza hunter-gatherers.[46,104,106] This suggests that the basic human energy utilization equation, and that of all primates, resembles a "zero sum game." That portion of TEE not devoted to physical activity is otherwise allocated: menarche occurs earlier; people grow taller and fatter; host defenses against infection (e.g., immune activation) are enhanced. In fact, in very hygienic modern environments, immune activation may produce inappropriate inflammation leading to allergies, asthma, and other autoimmune diseases,[107–109] with microbiome differences contributing to intestinal disease.[110] However, the portion of TEE not accounted for by physical activity, growth, reproduction, immune activation, and basal metabolic requirements is stored as adipose tissue, and excess adipose tissue storage—a.k.a. obesity—has become epidemic.

The Hadza studies of TEE, and particularly their interpretation, have been criticized. For example, a leading investigator of the evolution of activity and inactivity observes,[111] "it is important to note that hunter-gatherers tend to have much smaller body masses than people in developed nations, so estimates of their active energy expenditure (TEE-RMR) relative to body mass indicate that they expend on average 30 kcal kg^{-1} d^{-1}, almost twice that of Americans, which is 17 kcal kg^{-1} d^{-1} In other words, hunter-gatherers who are very physically active for only 4–6 h d^{-1} are still nearly twice as active as people in postindustrial economies" (p. 316). Also, there is a growing consensus that even if weight loss can be achieved with dietary restriction alone, the maintenance of weight loss (i.e., the avoidance of weight rebound) cannot be achieved without increased activity as people go off their restrictive diets.[112]

West Point Cadets provide a deep historical database. Between 1843 and 1894, 18 y-o West Point Cadets had *average* body mass indexes (BMIs) of just under 20.[113] Today the minimum BMI allowed for admission at heights between 68 and 74 inches is 19, while the maximum at both heights is 25.8.[114] For a recent sample of 18-year-old American males generally (admittedly less fit than Cadets), BMI averaged 24.7.[115]

Measures of the broader population reflect consistent trends. In 2018 American men aged 20–29 had average BMI's of 26.8.[116] In 2020, the percentage of Americans considered obese (BMI≥30.0) was 31.9, up from 27.4 in 2011.[117] The National Health and Nutrition Examination Survey (NHANES), using the same BMI cutoff but somewhat different methods, found that the age-adjusted percentage who were obese went from 30.5 in 1999–2000 to 42.4 in 2017–2018.[118] As BMI has increased, muscularity has declined. As inferred from skeletal remains, in Europe ~5 kya, women's arms were as muscular as those of contemporary competitive women rowers[119]; similarly, men then were as muscular as are today's athletes.[120]

In sum, human body composition—proportions of muscle and adipose tissue—has changed greatly over millennia, especially during the last century. In turn, this has affected insulin sensitivity and T2DM prevalence because the proportion of adipocyte insulin receptors relative to those on myocytes has been distorted—altering physiological conditions from those for which mammalian glucoregulatory mechanisms were originally selected. Fatty tissue and skeletal muscle engage in a whole-body competition for circulating insulin, so relative tissue proportions play a major role in determining the physiological impact of insulin molecules released during any given pancreatic secretory pulse.

The biochemical impact of myocyte and adipocyte insulin receptors differs. In humans, an insulin molecule activating a muscle insulin receptor induces 2.1–3.1 times more glucose clearance than does one reacting with an adipose tissue receptor[121,122]; insulin molecules interacting with fatty tissue are less efficient so, other factors being equal, lean, muscular individuals have greater whole-body insulin sensitivity than those who are sarcopenic and obese. Insulin receptor imbalance—adipose tissue receptors exceeding myocyte receptors—demands more insulin secretion (hyperinsulinaemia) for a given carbohydrate load. This whole-body reduced responsiveness, due to adipocyte–myocyte imbalance, leads to "intrinsic" insulin resistance as a secondary phase and, ultimately, to T2DM.[123]

Preventive measures, including increased daily activity, aimed at restoring a HGM-type balance, seem desirable on this basis alone. But in addition, activity and exercise have been shown to help prevent the metabolic syndrome and its CVD consequences,[124] hypertension,[125] chronic kidney disease,[126] and depression.[127] A review of 24 systematic reviews and meta-analyses[128] found that, "Physically active older adults (≥60 years) are at a reduced risk of all-cause and cardiovascular mortality, breast and prostate cancer, fractures, recurrent falls, ADL disability and functional limitation and cognitive decline, dementia, Alzheimer's disease, and depression." (p. 816) Elderly Tsimane and Moseten, indigenous Amerindians of the Brazilian Amazon, were recently found to have rates of Alzheimer's among the lowest in the world, despite commonly having mild cognitive impairment and intracranial artery calcification; they may be protected by high levels of physical activity.[129]

Challenge #6 is refuted. Physical activity at the HGM level does protect against obesity and type 2 diabetes, and has many other proven positive health effects.

Challenge #7: Genetic evolution in the past ~10 ky negates the mismatch model.

The discordance or mismatch hypothesis posits that our genomes evolved in living conditions prevailing as modern *Homo sapiens* emerged ~500 to 100 kya. This left us with genes adapted to environmental circumstances existing then. The hypothesis posits that cultural changes during the Holocene, the past 10–12 ky, have been too rapid for genetic adaptation to keep pace. Hence the mismatch and its consequences. However, some argue that recent genetic adaptations have been sufficient to minimize any discordance, calling Holocene evolution "the ten thousand year explosion."[130]

Evidence of recent genetic evolution is growing.[131,132] Life-long persistence of lactose tolerance arose through gene changes in dairying populations and now characterizes around 30% of the human species;[133–135] Basque individuals in 5000-year-old burials had much less lactase persistence than do current Basque

populations.[136] Other "new" dietary adaptations involve salivary amylase,[137,138] fatty acid desaturase,[139,140] and dietary arsenic tolerance.[141] Other instances, outside the realm of nutrition, include high altitude tolerance (perhaps the result of 100,000-year-old Denisovan DNA introgression),[142] lighter pigmentation (skin, hair, eyes),[143] and pathogen resistance.[144–146]

However, such modifications typically reflect mutations affecting one or a few genes that strongly influence phenotypic expression of individual traits, and tend to be geographically limited in their distribution. More complex and universal systems like metabolism, athleticism, and body composition involve multiple interacting physiologic subcomponents each of which may be affected by hundreds of genes. Most polygenic traits are affected by stabilizing selection; consequently, such components of mammalian biology are relatively buffered against alteration.[147,148] On the other hand, it has been puzzling that some genes, like *APOE4*, have persisted despite deleterious effects; part of the answer may be that *APOE4* had a salutary effect on immune defenses in HG-like populations, and its persistence is another instance of mismatch.[149] While the last 10–12 ky have witnessed some genetic adjustments, adaptations sufficient to prevent chronic degenerative diseases have not occurred. As for changes in nutrition and physical activity since the Industrial Revolution, these have outpaced any possible evolutionary genetic response.[150–152]

Challenge #7 is effectively refuted. Genetic evolution is ongoing, but for the species as a whole has been outstripped by cultural change.

Challenge #8: A Paleo Diet is not Sustainable or Affordable.

We did not initially consider the environmental sustainability of Paleolithic-type diets, directing our concern solely at the implications for health, nor did we sufficiently acknowledge the fact that poverty, especially urban poverty, makes all healthy diets difficult to access and pay for.[153] Our consciousness about both has been considerably raised.

Compared with meat-containing diets, vegetarian diets produce 50% less greenhouse gas emissions, need at least 25% less energy for production, and have over 40% less environmental footprint.[154] Diets containing substantial amounts of meat may reprise the many thousand millennia when human population size fluctuated around 10 million, but are nonsustainable for 10 billion. Judicious farming of the oceans can play an increasing role in supplying animal protein,[155] as can insects,[47,51] with which our species has a very long dietary history. However, HGM diets can and must include vegetarian options that fall within the HGM macronutrient and micronutrient range. A whole-food, plant-based 2000 kcal diet appropriately chosen provides 16% of energy from protein.[156] Supplementing this with 90 g (three ounces) of soy protein isolate would add 350 kcal of protein and increase the total protein component to 27% for a 2350 kcal diet. Plant-based simulated meats and laboratory-based cellular meat technologies can play important future roles.[157] A 50% meat/fish version of the Paleo diet accords well with the range of ancestral experience and with our genetic make-up, but plant-based, insect, and laboratory-generated alternatives will be increasingly available for those who wish to fight the climate crisis—ultimately, all of us.

The issue of access to healthy diets among the world's billions of poor people, especially the vast numbers who have migrated to cities, cannot be ignored by any ethical scientist. A systematic review of 68 selected studies of the impact of urban poverty on nutrition worldwide[153] found that the urban poor consume "unhealthy and energy-dense foods associated with a higher prevalence of overweight and obesity," that they experience "chronic undernutrition, leading to higher obesity prevalence" later in life due to food insecurity, and that psychosocial factors promote obesity due to "stress and feelings of despair commonly experienced by people living in urban poverty." (p. 14) Research indicates that this is not an unsolvable problem; a systematic review and meta-analysis of interventions to improve eating behaviors in childhood and adolescence found small but significant effects, and suggested that longer-term monitoring would make a larger and more lasting difference.[158] Despite almost 800 million undernourished and often growth-stunted children in the world, some countries such as Bangladesh and Brazil have had marked success in reducing this childhood scourge.[159] The paradoxical tragedy of undernutrition and overnutrition—known as "the double burden"—now exists in many low- and middle-income countries,[160] and require what *The Lancet* has called "double-duty policy actions" (p. 8) to ensure that economic development and globalization do not exacerbate these results of inequality. Any healthy diets, including Paleolithic-type diets (PTDs), remain an aspirational goal for too many, but we can strive toward that goal.

Challenge #8 is valid, but sustainability can be addressed by creating new versions of the HGM dietary program, and the damaging nutritional results of poverty can be addressed if we raise our level of awareness and commitment.

3 | RANDOMIZED CONTROL TRIALS AND OTHER CLINICAL TRIALS OF HG-LIKE DIETS

Even before "Paleolithic Nutrition" was published, O'Dea conducted an uncontrolled study in which urbanized, sedentary Australian former HGs with T2DM were returned to their HG diet and lifestyle for 7 weeks.[8] The subjects lowered their fasting and postprandial glucose levels, markedly reduced fasting TGs, and increased insulin responsiveness. Inspired by these results, formal trials followed. Of these, a 2020 meta-analysis combining four randomized control trials (RCTs) comparing PTDs to other diets deemed advisable for glucose homeostasis (the Mediterranean, diabetes, and Dutch Health Council diets) found that all produced comparably beneficial effects on fasting glucose and insulin levels, insulin resistance, hemoglobin A1C, area-under-the-curve (AUC) 2-h glucose or insulin.[161] It is clear that the HGM and PTDs are not the only diets that are healthy, and that humans are evolved for a range of healthy diets, with important limitations. We consider it validating that our anthropologically-based recommendations compare favorably with official dietary plans arrived at through thousands of empirical studies and decades of

consultation. However, some studies show that PTDs are superior to these other recommended diets.

A 2021 meta-analysis of 10 RCTs found that, compared with ordinary diets, PTDs produced significant reductions of insulin resistance, fasting insulin, total cholesterol, TGs, LDL cholesterol, BP, and C-reactive protein.[74] Rigorous testing of PTDs is still in its infancy, but studies to date have repeatedly shown that they improve metabolic parameters, in as little as 2 weeks. Four were done with very similar PTDs,[68,70,162,163] broadly defined as comprising only unprocessed meat, fish, eggs, vegetables, fruit, and nuts in variable proportions; dairy, cereal grains, added sugar, and salt were omitted. Control diets were drawn from international or national dietary guidelines. In a meta-analysis, pooled effects from these studies showed that the PTDs led to significantly greater short-term improvements in waist circumference, TGs, and BP.[72] One RCT provided isocaloric meals for 2 weeks to 32 subjects who met criteria for the metabolic syndrome (MS), to see the effect of the diets on MS.[68] The PTD group lost weight, reported less hunger and had greater improvements in BP, TGs, and cholesterol that persisted after statistically controlling for weight loss. Another trial randomized 29 patients with CAD and either glucose intolerance or T2DM to 12 weeks of a PTD ($n = 14$) or a Mediterranean-like "consensus" diet ($n = 15$).[162] The PTD group showed a 26% reduction in AUC glucose in a glucose tolerance test (GTT) compared to a 7% reduction in the Mediterranean group, and (independently) greater reductions in waist circumference.

An RCT of healthy women compared a PTD ($n = 22$) to a diet based on Australian guidelines ($n = 17$) over 4 weeks, and showed greater weight loss in the PTD group (−1.99 kg), $p < 0.001$), but no differences in CVD or MS risk factors.[164] Another trial randomized T2DM patients ($n = 32$) to a PTD with either recommended or supervised exercise. Fat mass, insulin sensitivity, and glycaemic control improved in both groups, but the PTD + supervised exercise group lost less lean mass, had greater improvements in cardiovascular fitness,[165] and had marked reductions in liver and intramuscular fat.[166] For both groups, greater adherence to the PTD predicted lower fat mass, BMI, waist circumference, systolic BP, and serum TGs (independent of weight loss) at 12 weeks.[167] In a randomized cross-over pilot study, 13 T2DM patients (three women) were sequentially placed on a PTD and an American Diabetes Association (ADA) guideline diet for 3 months each. In this small study, the PTD produced lower mean HbA1C, triacylglycerol, diastolic BP, weight, BMI, and waist circumference, and higher mean HDL.[70]

A small, nonrandomized, two-phase diet intervention trial compared the American Heart Association (AHA) "heart-healthy" diet (4 months, phase 1) to a PTD (next 4 months, phase 2) assessing cholesterol and TGs in 20 hypercholesterolemia patients.[71,168] During the PTD phase (vegetables, lean animal protein, eggs, nuts, and fruit, excluding dairy, grains, and legumes),[70] there were significantly lower TGs, total cholesterol, and LDL and significant higher HDL compared to either baseline or the 4-mo AHA phase. Subjects lost significantly more weight on the PTD, yet LDL and HDL improved independent of weight loss. Two small, noncontrolled studies showed significant metabolic improvements, one in as little as 10 days.[69,169]

In sum, the PTD/HG model has gained considerable scientific support. It improves BP, waist circumference, weight, cholesterol, TGs, glucose, and insulin. Furthermore, dietary recommendations by the AHA and other authorities have moved closer to HGM recommendations. Longer duration RCTs with larger sample sizes are needed, but one large-scale epidemiological study used 20 years of prospective data on more than 70,000 women, applying a "Paleolithic diet score" and a "Paleolithic-like lifestyle score" (physical activity, smoking status, and BMI) to baseline data. The PTD predicted T2DM and HTN risk, but the combined diet and lifestyle scores predicted them more strongly.[170]

4 | DISCUSSION: SUPPORT OF THE MODEL AND CONVERGENCE WITH OFFICIAL RECOMMENDATIONS

After 36 years of research, differences between the modern and HG diets have become clear (Table 1). Over that period, official recommendations have shifted towards the HGM and some standards have been adjusted accordingly (Table 2). In 1985, total serum cholesterol below 200 was considered acceptable; now the recommended level is below 180. It's likely that future recommendations and goals will still more closely track the HGM. Differences remain; the AHA diet emphasizes whole grains, a minor component of ancestral diets, which nevertheless provided much more fibre. Contemporary advice supports eliminating added salt and sugar but differs regarding dairy foods, which in any case are ruled out for most humans by lactose intolerance. These differences may matter more generally, because some RCTs show significantly improved metabolism with PTDs compared to epidemiologically-based guidelines. Studies with larger sample sizes and of longer duration are needed to address the issue.

The HGM and the discordance hypothesis suggest that meat and fish consumption can safely be higher than currently recommended; neither protein nor cholesterol consumption at HG levels has been shown to have adverse effects.[176] Very low CHO combined with high protein and fat appears to be a safe weight loss strategy.[177,178] But neither extremely low CHO intake nor a very-high CHO, "meat as a condiment"-type diet is consistent with the HGM. CHO sources matter and, for HGs, refined grains, sucrose, and high-fructose corn syrup played no role. On average, honey provided about 2% of total energy and most CHO sources provided considerable dietary fiber, especially if the digesta of large herbivore prey are included.[30] A modern simulation of HG food pyramid would have a base not of grains but of fruits and vegetables with adequate fiber. The second tier would be lean meat, fish, and (for those who tolerate them) dairy foods. Whole grains might come next, then mono– and

TABLE 1 Widely agreed-upon qualitative differences between average hunter-gatherer and contemporary Western dietary intakes. For references see text, and review papers.[25–27]

	Contemporary Western	Recent Hunter-Gatherers
Total energy	Intake less	More
Caloric density	Higher	Lower
Dietary bulk	Less	More
Total carbohydrate intake	More	Less
Sugars/refined CHO	Much more	Much less
Refined cereal grains	Substantial	Little or none
Glycemic load	Higher	Lower
Fruits and vegetables	Half as much	Twice as much
Antioxidant capacity	Lower	Higher
Fiber	Less	More
Soluble:Insoluble	Much less soluble	Roughly equal
Protein intake	Less	More
Processed meat	Considerable	None
Total fat intake	—roughly equal—	
Saturated fat	—roughly equal—	
Trans fat	~2.5%	Almost none
Total polyunsaturated fat	Less	More
ω6:ω3	Far more ω6	Roughly equal
Long chain essential FAs	Less	More
Cholesterol intake	Equal or less	Equal or more
Micronutrient intake	Less	More
Sodium:Potassium	>1	≪1
Acid-base impact	Acidic	Alkaline or neutral
Milk products	Lifelong	Mother's milk
Free water intake	Less	More

TABLE 2 Changing recommendations for diet and biological markers, as compared with current estimates for HGs. References: Dietary Recommendations,[171,172] Serum Cholesterol,[173] Blood Pressure,[174] Physical Activity,[105] Body Fat Percentages.[175]

	Recommendations		Estimated HGs
	Pre-1990	Current	
Nutrients			
Carbohydrate, % daily energy	55–60	45–65	35–40
Added sugar, % daily energy	15	<10	2[a]
Fiber, g/d[b]	–	38 m; 25 f	>70
Protein, % daily energy	10–15	10–35	25–30
Fat, % daily energy	30	20–35	30–40
Saturated fat, % daily energy	<10	<10	7.5–12
Cholesterol, mg/d	<300	<300	500+
DHA + EPA, g/d[c]	–	0.65	0.7–6.0
Vitamin C, mg/d	60	90 m; 75 f	500
Vitamin D, IU/d	400	1000	4000 (sun)
Calcium, mg/d	800	1000	1000–1500
Sodium, mg/d	2400	1500[d]	<1000
Potassium, mg/d	2500	4700	7000
Biomarkers			
Blood pressure, mm hg	<140/90	115/75	110/70
Serum cholesterol, mm/dl	200–240	<200	125
Body composition, %lean:%fat			
Females	–	<31% fat	35–40:20–25
Males	–	<26% fat	45–50:10–15
Physical activity, kcal/day	–	150–490	>1000

[a]Scientific Report of the 2020 Dietary Guidelines Advisory Committee called for limiting added sugars intake to no more than 6% of total calories. Dietary Guidelines for Americans, 2020–2025 notes that a Healthy U.S.-Style Dietary Pattern provides only 1.5%–2% of total calories as added sugars.

[b]No tolerable upper intake level has been set for dietary fiber.

[c]ω−3 long-chain polyunsaturated fatty acids DHA (docosahexaenoic acid) & EPA (eicosapentaenoic acid); The European Food Safety Authority (EFSA) notes that up to 5 g/d is safe.

[d]American Heart Association suggests ideal upper limit of 1500 mg/d.

polyunsaturated fats and oils; refined CHOs would have a small place at the top, basically as condiments. This would not exactly replicate HG diets in food categories, but would roughly replicate their macronutrient content.

Large prospective epidemiological studies and RCTs have now shown that dietary Na^+ predicts CVD.[81,88,179] However, only a few studies extend down into the HG range, so intakes lower than 2 g/d need further investigation. The CVD effects of higher K^+ intake and K^+/Na^+ ratio also support the HGM.[86,89–91] The earliest archaeological evidence of tobacco use by humans dates to ~12 kya in North America,[180] and Australian Aborigines chewed a nicotine-containing plant before European contact,[181] but neither of these could have been ancestral HG populations. Physical activity above current levels—closer to that required by obligate subsistence tasks in the HG era—is also an HGM component. Ongoing research on HG populations themselves confirms most of our earlier generalizations about them.[182,183] Westernization worsens their diet and health indicators.[6,7,184,185]

Studies of the gut microbiome have found that Hadza HGs have much more diversity of microbiota than Italians;[186] although the Western-diet narrowing of the gut microbiome is well established, its implications for health remain uncertain.[187]

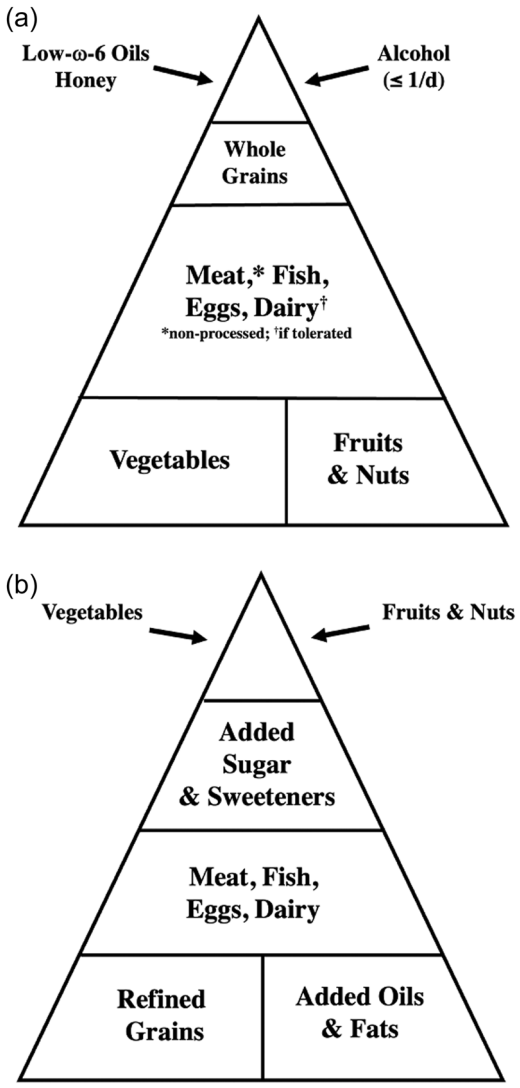

FIGURE 4 Comparison of hunter-gatherer-model update and modern diets as food pyramids. (a) Approximate contribution of major food groups to our proposed diet (which departs in some ways from the median diet of recent hunter-gatherers/HGs) by estimated caloric content. Dairy products are included as tolerated, modest alcohol intake may be an option, and the total proportion of calories from animal products shown here is about 45%, rather than half or more. These are our attempts to accommodate the HG diet to modern conditions and information (see text.) (b) Average per capita consumption by Americans of dietary components, USDA data for 2010, kcal/d: Vegetables, 126; Fruits & Nuts, 153; Added sugar & sweeteners, 369; Meat, poultry, fish, eggs, added animal fats, and dairy, 731; Grains (mostly refined), 581; Added plant-based oils & fats, 518.[188] The CDC estimates that in 2007–2010, alcoholic beverages contributed ~100 kcal/d[189]; it issues cautionary guidelines even for moderate alcohol consumption.[190]

Subsequent to the "Out of Africa" exodus(es), HG lifestyles have varied more, but warm-climate HGs throughout the world had much in common,[29] and it is on these basic components that the HGM is founded. Paleoanthropological, ethnographic, epidemiological, and experimental research all suggest that today's typical Westerner should reduce intake of sugars and simple starches, reduce Na^+ while raising K^+, consume more complex CHOs (fiber), increase ω−3 PUFA intake, and boost physical activity. (See Figure 4 for a rough comparison between estimated HG dietary sources and U.S. averages in recent data, depicted as food pyramids.) Multidisciplinary evidence indicates that these measures will minimize the existing genome/lifestyle mismatch and reduce prevalence of chronic degenerative diseases. Despite disagreement over some details, HG diets and active lifestyles remain a valid source of hypotheses about what is likely to improve and maintain health.[191–195]

5 | CONCLUSION

Research over nearly four decades largely supports the HGM; challenges to it have been adequately answered in the modestly changed version presented here. Despite initial ridicule, HGM offers a sound provisional alternative to the often complex, conflicting, and poorly prioritized barrage of research findings, not to mention diet fads, all of which have failed to stem pandemics of obesity and T2DM. Regrettably, about half of Americans reject the basic facts of evolution, an obvious obstacle to acceptance of the HGM paradigm. On the other hand, most people seem comfortable with the idea of a "natural" diet and lifestyle,[4] and the HGM is a scientific version of that idea. Physicians and medical scientists, at least, can accept it as an organizing heuristic principle for research. While the model cannot be accepted solely on its anthropological merits—without supportive clinical, experimental, and epidemiological findings—it can guide future research.

Climate change, population growth, and the unequal results of globalization pose threats to health and the HGM diet must adapt to this reality; the foods it advocates must be consistent with sustainability and nutritional access. Beyond diet and exercise, the HGM endorses gradual population contraction—as is already occurring in 39 countries[196]—to bring our species into planetary balance, ultimately reprising what existed when humans were much fewer in number. In the HG era, people perceived themselves as part of nature, struggling with it but coexisting, but from the rise of agriculture we have aspired to dominate it. Discoveries during the last generation have enhanced our awareness that we are stewards of our planet and of our manifold fellow species. Humanity's future depends on how well we negotiate this existential crisis. Living in accord with the HGM, adapted for sustainability and the challenge of global poverty, should be a part of our response.

GLOSSARY

AMDR: Accepted macronutrient distribution range of the National Academy of Sciences
AS: Atherosclerosis; fatty inflammation and bulging of arterial walls due largely to blood cholesterol imbalances
BMI: Body mass index; weight in kilograms divided by the square of the height in meters; an indirect (and inexact) reflection of body fat
BP: Blood pressure; expressed as two numbers in millimeters of mercury, one corresponding to heart contraction, the second to heart relaxation
CAD: Coronary artery disease, including coronary artery calcification (CAC)
CHO: Carbohydrates
COPD: Chronic obstructive pulmonary disease (chronic bronchitis and/or emphysema)
CVD: Cardiovascular disease, including heart disease and stroke
DHA: Docosahexaenoic acid, an ω−3 fatty acid considered beneficial
Digesta: Partly digested contents of the gastrointestinal tract of herbivores that are HG prey
Discordance: Hypothesis proposing a mismatch between typical diet and activity in industrial and postindustrial populations and those of HGs
EPA: Eicosapentaenoic acid, an ω−3 fatty acid considered beneficial
GTT: Glucose tolerance test; serial glucose levels over 2 h following drinking a sweetened liquid
HCLF: High carbohydrate low fat (diet)
Hemoglobin A1C: A type of hemoglobin in red blood cells reflecting blood sugar levels over the prior 3 months
HG: Hunter-gatherer
HGM: Hunter-gatherer model (of diet and activity)
HTN: "Essential" hypertension; high blood pressure not explained by other disease processes; most cases of high blood pressure today
K^+: Potassium; healthier substitute for Na^+ in salt
LCHF: Low carbohydrate high fat (diet)
LCHP: Low carbohydrate high protein (diet)
LCPUFA: Long-chain polyunsaturated fatty acids
MS: Metabolic syndrome; combined high blood pressure, high blood sugar, abdominal obesity, high triglycerides, and cholesterol imbalance increasing the risk of CAD, stroke, and T2DM
Na^+: Sodium; key element in table and other salt
ω−3, ω−6: Omega-3, omega-6; components of LCPUFA; ratio should be ~1:2, but is much lower in most current diets; DHA and EPA are ω−3s
PTD: Paleolithic-type diet
PUFA: Polyunsaturated fatty acids
RCT: Randomized controlled trials
SF: Saturated fat
Stenosis: Narrowing, as of an artery or the spine
T2DM: Type 2 diabetes mellitus; diabetes usually associated with high sugar intake and obesity; most cases today
TEE: Total energy expenditure; calories consumed by metabolic processes and activity in a given time period
TG: Triglyceride; fat circulating in blood; the most common type of fat in the body
Zero sum game: As applied to energy expenditure, a way of describing the claim that human energy input minus output always equals zero

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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How to cite this article: Konner M, Eaton SB. Hunter-gatherer diets and activity as a model for health promotion: challenges, responses, and confirmations. *Evolutionary Anthropology*. 2023;1-17. doi:10.1002/evan.21987