



Biological Parameters Explain Why Shorter or Smaller People have Lower Cardiovascular Disease and Greater Longevity

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Aim: To identify biological parameters that are related to the greater longevity and lower cardiovascular disease risk of shorter, lighter people.

Study Design: The study for this paper was conducted over the last 2 years but was based on papers and reports published over the last 40 years, which is when the author started studying the impact of body size on health and longevity. It was decided that the research would focus on how body size affects human health, mortality from chronic diseases and longevity. Human body size factors were height, weight and body mass index. Biological parameters included serum levels of insulin, IGF-1, and adiponectin. Other types of parameters included: blood pressure, the FOXO3 gene, left ventricular mass, telomeres, and DNA damage.

Methodology: Numerous biological parameters were identified by reviewing papers and notes taken over 40 years. These parameters were identified in relation to how height, weight and body mass index impact our health or longevity. Approximately, 5000 papers and reports were reviewed and parameters affecting our health and longevity were recorded.

Results: A list of 36 biological parameters and related factors was created that shows how each parameter is related to one or more body size factors (height, weight or body mass index). In

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addition, undesirable changes in parameters were identified in relation to the increase in height, weight, or body mass index.

Conclusions: Reduction in height, weight, and body mass index is related to improved biological parameters and explains why many studies find shorter, lighter people tend to have delayed incidence of chronic diseases and live longer. However, poor nutrition, excess weight, smoking, genetics, and socioeconomic (SES) status can affect biological parameters independent of body size characteristics.

Keywords: Aging; biological parameters; body mass; body mass index; cardiovascular disease; height/stature; longevity; telomeres.

1. INTRODUCTION

The concept that smaller body size may be related to greater longevity has been espoused by many scientists and is gaining support among various types of researchers based on recent findings in the public and scientific domains. For example, The University of Glasgow issued a news release that stated: "A study looking at how DNA changes with body size may help scientists to explain why taller individuals tend to have shorter lives" [1]. Another news release from Columbia University Medical Center stated: "Short people have several health advantages over tall people, including longer life expectancy" [2]. The Director of the Aging and Longevity Research Laboratory at Southern Illinois University also stated that smaller body size has many benefits in terms of greater health and longevity [3].

While scores of longevity, survival and mortality studies support these observations, many (not all) mortality studies have found that taller people have lower mortality rates from all-causes and cardiovascular disease (CVD) [4]. However, unlike most longevity, survival and centenarian studies, many epidemiological mortality studies do not cover the entire age range of the subjects studied [5]. An exception is Waaler's study that tracked mortality till death and found that up to 70 years of age, tall men had lower mortality rates [6]. However, between 70 and 85 years of age, men over 184 cm had a higher mortality rate compared to men between 170 and 184 cm. This paradoxical pattern is probably related to the fact that after 70 years of age over 70% of deaths are due to age-related chronic diseases. In contrast, most deaths before 60 years of age are primarily due to accidents, infections, suicides, congenital defects, etc. and death before 70 years of age is considered premature.

In contrast to mortality studies, almost all human longevity studies have found shorter people live

longer, including He et al., Salaris et al., Vasto et al., Holzenberger et al., Miller, Samaras, Willcox et al., and Chan et al. [7-16]. Most of these studies were based on deceased populations in Ohio, Spain, Sardinia, Okinawa, and California. In addition, several survival studies have found shorter people tend to reach advanced ages (Maier et al., van Heemst et al., Wilhelmsen et al., and Rantanen et al. [16-19]).

Another paper (Mueller and Mazur) reported on two cohorts of West Point officers who graduated in 1925 and 1950 [20]. These officers were tracked after they retired. They had at least 20 years of active service and were free of any disabilities. The two cohorts consisted of about 900 men tracked up to mid 2008. The researchers found that the taller half of the 1925 and 1950 cohorts experienced higher mortality in the 60 and over age group. An important part of the study was that the officers represented a highly homogeneous background in ethnicity, economic background and lifestyle during their careers.

Populations with the highest percentage of centenarians in the world are almost always short when compared to northern Europeans; e.g., Okinawa, Japan; Bama, China; Nicoya, Costa Rica; Sardinia, Italy; and Ikaria, Greece. (No height data were found for Nicoya or Ikaria, but the populations of Costa Rica and Greece were relatively short when these centenarians were in their youth.)

Additional support for the advantages of smaller body size comes from comparing males and females. For example, American males are 9% taller than females and have a 9% shorter life expectancy [21,22]. Shorter females also have lower CVD vs. men in most parts of the industrialized world. In addition, Brown-Borg et al. found that dwarf male mice lived substantially longer than their normal size female siblings [23]. Miller also found when he compared men and

women of the same height, they had about the same longevity [11]. The relationship between height and CVD is more controversial. However, there are many examples of shorter people having lower CVD/coronary heart disease (CHD) than taller ones [5]. In some pre-Western populations, CHD and stroke were found to be zero.

Animal longevity research has also strongly supported the observation that smaller individuals are longer-lived than bigger individuals within the same species. Studies of mice, rats, and dogs have provided extensive support over the years for both heart disease and longevity being lower in shorter or smaller animals [4]. Based on many mammalian species, Promislow found that as individuals within a species get larger, their mortality rate increases [24]. They also found that when the female is the larger of the species, the mortality rate is higher for females. Moore and Wilson also found similar results. In addition, they found levels of parasites increased with body size [25].

For the preceding longevity studies to make sense, there should be biological factors that explain why shorter, smaller bodies promote greater longevity. The purpose of this report is to summarize 36 biological parameters that support the lower CVD and greater longevity of shorter or smaller humans who also have healthful nutrition and a good environment. These parameters include reduced cell replication, DNA damage, blood pressure, left ventricular mass (LVM), mechanistic target of rapamycin (mTOR), insulin and insulin-like growth factor-1 (IGF-1). Other benefits include greater adiponectin, forkhead box O3 (FOXO3) genotype and sex hormone binding globulin (SHBG).

2. MATERIALS AND METHODS

The material for this study is based on over 5000 papers and reports dealing with human body size, nutrition, chronic disease and longevity. These papers and reports were collected over the last 40 years and provided information on various biological parameters discussed in this paper. In addition, PubMed was searched for biological parameters related to body size, such as height, weight and body mass index (BMI). The internet was also searched for possible sources of information on body size and biological parameters.

Identification of subjects as shorter or smaller in the studies used for this review applies to the

cohorts described in the individual studies. Thus, body size is relative to the specific population examined; e.g. US, European, Asian or African.

3. RESULTS

Thirty-six biological parameters or factors were identified and are presented in Table 1 [3,5,7,16,26-144]. A separate column identifies body size factors, such as height, weight and body mass index (BMI) related to the parameter. A third column describes the harmful effects on health due to undesirable changes in these parameters. The sources of information for each parameter are listed in the last column.

The table covers a wide variety of parameters/factors that favor smaller body size. These include longer telomeres, lower DNA damage, lower left ventricular mass, longevity genes, lower C-reactive protein, lower insulin and insulin-like growth-1 (IGF-1) hormone. Other parameters favoring the hearts and longevity of smaller people include lower mTOR, higher adiponectin, and lower homocysteine. Other factors include higher heart pumping efficiency and lower incidence of atrial fibrillation and venous thromboembolism.

The parameters/factors identified in Table 1 may change in the future as more research is focused on the ramifications of increasing body size. Detailed information on the methodology and analysis of findings on individual parameters/factors is available from the appropriate reference sources.

The trend lines or mortality rate increases for various parameters are covered in the individual references given. Mortality generally increases progressively with undesirable changes in various parameters. A few examples are given next.

Fontana and Hu [64] found that there was a strong linear increase in mortality with increases in BMI for various chronic diseases. Cardiovascular disease increased by 14% per BMI point increase. All-cause mortality has also been found to increase by ~10% per BMI point increase.

A study [85] found as C-reactive protein levels increased there were proportional increases in all-cause mortality and ischemic heart attacks. For example, all-cause mortality ranged from

hazard ratio (HR) of 1 for < 5 mg/L to a HR of > 3 for > 80 mg/L.

Mendall et al. [80] found that C-reactive protein levels increased with BMI and height and correlated with increased mortality from CHD and all-causes.

Giovannelli et al. [45] found that oxidative DNA damage increased with height. The damage was expressed as the % of DNA in tail. The damage increased from 3.28% for a height of 148-164.5 cm, to 4.45% for 165-173 cm and to 6.08% for 173.5-197.5 cm.

4. DISCUSSION

Table 1 shows the relationships among biological parameters, body size, CVD, chronic diseases and longevity based on the assumption that we

are comparing short and tall humans of the same proportions and lifestyles. Obviously, on an individual basis, many factors can alter the results shown in Table 1. Early nutrition promotes growth and increases in body size. However, once adulthood is attained, a larger body requires more food than a smaller one and thereby promotes undesirable increases in the levels of mTOR, insulin, IGF-1, etc.

It is important to note that height is less than 10% of the longevity picture and many other factors can affect one's longevity. For example, a taller person may be at lower risk of undesirable changes in biological parameters if he or she has a low weight for their height, higher socioeconomic (SES) status, eats a healthier diet, doesn't smoke, exercises regularly and is social connected. Genetic factors can also affect results.

Table 1. Biological parameters related to shorter, smaller body size that reduce chronic diseases and increase longevity

Biological parameter	Beneficial anthropomorphic factors related to biological parameter	Harmful ramifications of greater or smaller parameter	Reference sources
Longer telomeres	Lower height, weight, & BMI	Fewer potential cell replications available at older ages due to faster telomere attrition. Unhealthy centenarians have shorter telomeres compared to healthy centenarians. Shorter telomeres are related to cardiovascular aging, type 2 diabetes & reduced longevity.	16,26-28, 34-39,40-43,
Lower stem cell exhaustion	Lower height & weight	Higher erosion reduces longevity due to lost ability to replace damaged cells.	29, 39
Lower DNA damage	Lower height & BMI	Increased height & BMI increases total daily energy expenditure & food intake which damage DNA and promote aging	44-46
Lower left ventricular mass (LVM)	Lower height, weight & BMI	Higher LVM is a risk factor for CVD & all- cause mortality independent of other risk factors.	47-51
Higher sex hormone binding globulin (SHBG)	Lower height, weight & BMI	Lower levels of sex hormone binding globulin are related to increased risk of cancer, cardiovascular disease and type 2 diabetes.	52-56

Table 1. Biological parameters related to shorter, smaller body size that reduce chronic diseases and increase longevity (continued)

Fewer cells	Lower weight & BMI	More cells due to larger body size mean higher risk of cancer because of greater exposure to toxins, carcinogens & radiation.	7, 36, 39, 57-60
Lower body mass	Lower height and BMI	Body mass is strongly correlated with height and is related to increased chronic disease, mortality and reduced longevity in humans and animals.	3, 5, 16, 24, 25, 34, 39, 61
Lower blood pressure	Lower height, weight & BMI	Higher BP r with hypertension and CVD	30-32, 64-72 *
Fewer free radicals	Lower height & weight	A larger body requires more food that produces more free radicals. More free radicals increase damage to DNA, cell structures and components, and CV system.	34,45, 73, 74
Increased incidence of Laminin, Alpha 5 rs4925386-T allele	Lower height	The occurrence of this Genotype is related to longer longevity, especially after 85 years of age	75
Lower Pulse Wave Velocity (PWV)	Lower height, weight & BMI (a decrease in PWV with increasing height has been found in a few studies.)	Higher PWV is an independent predictor of CVD, stroke, & all-cause mortality in healthy people	48, 76, 77

* While Bavdekar [69] did not track from 8 years to adulthood, Sinaiko [100] found that body size and biological parameters tracked from 8 years of age to 24 years of age

Table 1. Biological parameters related to shorter, smaller body size that reduce chronic diseases and increase longevity (continued)

Larger organs in relation to weight	Lower height	Smaller organs in relation to body mass have lower functional capacity; Exceptions: heart and lungs are proportional to weight	78, 79
Lower C-reactive protein (CRP)	Lower height, weight & BMI	Higher CRP levels promote CVD, cancer, type 2 diabetes and all-cause mortality (one study showed a r with BMI but a -r with height in older subjects)	43, 80-87
Lower BMI	Lower weight for height	Assuming same body types are compared: Chronic disease & all-cause mortality increase in a strong linear trend with increasing BMI BMI r with height in children A number of studies have found a decreasing BMI within the normal	33, 64-66, 80, 89-93

range increases mortality. In view of the many undesirable trends of most biological parameters vs. BMI, it appears these findings are confounded by other factors. The WCRF report (based on review of about 7000 papers and reports) recommends keeping BMI low (21 to 23).

Table 1. Biological parameters related to shorter, smaller body size that reduce chronic diseases and increase longevity (continued)

Lower insulin-like growth factor-1 (IGF-1)	Lower height, weight, & BMI (Some studies show a increase in IGF-1 with increasing BMI over the normal BMI range but a decrease in IGF-1 with a BMI in the obesity range..)	IGF-1 -r longevity. IGF-1 is also related to cancer; Laron dwarfs in Ecuador have low IGF-1 levels and no deaths from cancer or diabetes.	3, 16, 17, 61, 94-99
Lower insulin	Lower height, weight & BMI	Lower insulin levels are related to greater longevity	16,17, 69, 100-104
Higher insulin-like growth factor binding protein-1 (IGFBP-1)	Lower weight, BMI, & height (after 65 yr of age)	Lower IGFBP-1 is related to higher cancer, CVD, & type 2 diabetes	98, 105,106
Lower parasites	Lower body mass	Body parasites increase with increasing body mass independent of sex & are related to increased mortality	25
Higher FOXO3 gene expression	Shorter height	Lower levels of FOXO3 gene are related to CVD and lower longevity	7, 107
Lower mechanistic (mammalian) target of rapamycin (mTOR)	Lower weight & BMI	Higher levels of mTOR promote cell replication, growth and reduce longevity; mTOR also promotes chronic disease	3, 108-110
Higher adiponectin	Lower weight & BMI; lower height only in childhood	Lower adiponectin is a risk factor for heart disease and increases the risk of other chronic diseases. Also reduces longevity.	111-116
Lower Cystatin-C	Lower height & weight	Higher levels related to increased risk of CVD & kidney disease	117, 118
Lower creatinine	Lower height & weight	Higher levels related to increased risk of CVD & kidney function or disease	117, 118

Table 1. Biological parameters related to shorter, smaller body size that reduce chronic diseases and increase longevity (continued)

Lower food toxin intake	Lower weight & BMI	Higher weight is r with increased intake of food and related toxins that damage cells.	62, 119
Higher heart pumping efficiency	Lower height, weight, & BMI	Larger hearts pump a lower percentage of blood out of left ventricle	47, 120
Lower homocysteine (Hcy)	Lower weight & BMI (not all studies show r with body weight or BMI)	Higher weight is r with higher Hcy levels which promote CVD and telomere attrition	35, 121-123
Higher HDL	Lower height, weight, & BMI	Lower levels are related to heart problems; some studies show shorter people have lower HDL but this appears to be due to higher BMI, lower economic status or other factors.	33, 66, 82, 100, 124-126
Lower triglycerides (TG)	Lower height, weight, & BMI	Higher levels are related to heart problems	65, 66, 69, 88, 100
Lower ApoB	Lower BMI	Higher levels of ApoB are related to heart disease & metabolic syndrome, especially a high ratio of ApoB/ApoA-1	88, 127
Higher ApoA-1	Lower BMI	A lower level of Apo A and a higher ratio of ApoB/ApoA-1 are related to greater heart disease & metabolic syndrome	88, 127

Table 1. Biological parameters related to shorter, smaller body size that reduce chronic diseases and increase longevity (continued)

Lower low-density lipoprotein (LDL)	Lower BMI, weight & height	Heart is damaged by higher LDL. As BMI increases, LDL increases as well. (There are conflicting findings on height and LDL; however, these stand in contrast to the low levels of LDL in short hunter-gathers.)	65, 69, 88, 100, 129-131
Lower glucose	Lower BMI	Glucose levels > 83 mg/dl increase CHD, stroke, type 2 and all-cause mortality. Note: shorter height appears to increase or have no effect on glucose levels	65, 66, 88, 132-135 136-138
Lower fibrinogen	Lower BMI	Higher fibrinogen is related to heart problems.	88, 139
Lower atrial fibrillation (AF)	Lower height	Higher AF increases risk of stroke	140, 141
Lower venous thromboembolism (VTE)	Lower height & BMI	Higher VTE increases risk of death in men	142, 143
Lower Total Cholesterol (TC)	Lower BMI & height	Higher TC increases risk of CVD	65, 66, 69, 88, 144

The findings presented in Table 1 are consistent with a review of eight types of studies that support the “smaller lives longer” thesis. These eight areas are: (1) within a species smaller individuals live longer, (2) animal studies show caloric restriction (CR) produces smaller animals that live longer, (3) smaller females live longer than males, (4) US studies show that as ethnic groups get taller, age-adjusted all-cause mortality increases; e.g., Asians have the lowest mortality vs. Blacks and Whites who are the tallest and have the highest mortality. (However, subsequent generations of Asians may lose much of the longevity benefits of their parents and grandparents.) Other types of studies supporting the increased longevity of shorter or smaller people include (5) survival studies, (6) centenarian body size, (7) life expectancy, and (8) research based on deceased populations [5].

It is important to keep in mind that the findings presented here are based on the assumption that we are comparing similar body-type people. Obviously, tall, thin people would have different parameters compared to short, overweight people. For example, many epidemiological studies find taller men have lower mortality rates than shorter men. However, insurance findings from the 1979 Build Study found that shorter men were more overweight than taller men [21]. When they compared tall and short men with the same degree of overweight, the shorter men had a slightly lower mortality.

Socioeconomic status is biased towards taller people who may average a 5-year longer life expectancy. However, few studies adjust accurately for many SES confounders [21,145]. SES factors favoring taller people include a higher standard of living, better medical care and substantially lower stress. A higher percentage of shorter people tend to be in lower SES. They tend to be heavier in proportion to their heights and suffer from higher blood pressure and glucose levels. They also smoke more and don't exercise as much during their free time. Another disadvantage is that their diet is not as healthful as higher SES individuals. Their diets tend towards fast foods that are high in calories, animal protein, fats, and salt. Another problem is that childhood infections or other illnesses tend to stunt growth and some of these diseases can have a health impact in adulthood. Another confounder that is rarely considered is that shorter people born in lower SES classes are negatively impacted in adult health although they may have risen to higher SES levels. A study of

US West Point graduates provides an exception to most of the preceding confounders. Mueller and Mazur [20] studied 900 West Point officers who had retired and were 50 or more years of age. These officers represented a similar family background and life history and thus provided a less biased view of shorter people within this cohort. The researchers found that after 60 years of age, shorter officers had a lower mortality rate. Another study [30] found when the benefits of higher SES are removed, taller low SES people had ~ 40% higher risk of heart attacks compared to low SES shorter people [30].

The confounders just discussed may be changing. For example, some reports have found that taller people are gaining weight at a faster rate than shorter individuals. If this change continues, it could alter the confounders that are related to shorter and taller people.

Based on the traditional viewpoint that taller height is related to lower mortality, it seems reasonable to assume that tall people would dominate in centenarian studies. However, it is just the opposite. Although some people over 183 cm reach 100 years of age, the vast majority of centenarians are short and lean [15].

Another confounder involves low birth weight individuals who experience catch-up growth during early childhood. Studies show these individuals tend to remain somewhat shorter than normal weight peer group and have higher risk for chronic diseases in adulthood [3,32]. School children that are shorter than their peers may also suffer from pathological conditions that predict adult health problems with shorter height being a consequence of the pathological conditions.

Even when cohorts with the same BMIs are compared, this can lead to incorrect results. Taller populations should have BMIs that are equal to the percentage difference in height between the two cohorts. For example, a 10% taller cohort should have a 10% higher BMI compared to the shorter cohort. The reasons for taller people having a higher BMI with the same body proportions are described by Samaras [33].

Research as to whether height is an independent factor vs. BMI is limited. However, a study of baseball players with virtually the same BMIs (~23 kg/m²) but 10 different height groupings (165 -188 cm) showed a substantial decline in lifespan for increasing height groupings [146]. A

second cohort of baseball players with a heavier BMI (26 kg/m²) also showed an inverse trend between height and average lifespan with a constant BMI throughout the height range of 165-188 cm. (The grouping with the lower BMI had a higher overall lifespan compared to the higher BMI group for the same range of height categories.)

In addition, there were other findings that showed the percent height increase and decrease in longevity was inversely related [146]: A partial sample follows:

Taller US males vs. shorter females: men 9% taller and 9% shorter life expectancy
Taller US Asian males vs. shorter females: men 8% taller and 8% shorter life expectancy
Taller baseball players vs. shorter players: 4% taller players had 4% shorter life spans.
Taller US veterans vs. shorter veterans: 6% taller veterans had 7% lower life spans

Other findings involved loss of longevity with increasing height [146]. Seven populations were analyzed. They varied from .35 to .63 years per cm of increased height. The average for seven populations was .5 year per cm of increased height. Data from three other researchers showed the same value (.5 year/cm) for populations of Ohio, Sweden and Finland [12]. It is unlikely that a recurring figure of .5 year/cm between height and longevity would be due to coincidence.

5. CONCLUSIONS

The findings in this paper provide evidence that the levels of many biological parameters or factors are related to shorter, smaller bodies. Desirable changes to these levels tend to be associated with lower CVD risk, better health and greater longevity in smaller bodies based on the assumption that shorter height or low body weight was not caused by childhood health problems. For some biological parameters, higher levels are harmful; for others, lower levels are harmful. However, differences in an individual's life history, body proportions, nutrition and genetics can provide conflicting results.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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