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## **Article Type**

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## **Title**

Adult Height, Nutrition and Population Health: A Review

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## **Abstract**

In this review, we summarize the potential causes and consequences of adult height, a measure of cumulative net nutrition, in modern populations. We discuss the mechanisms linking adult height and health with a focus on the role of potential confounders. Evidence across studies indicates that short adult height (reflecting growth retardation) in low- and middle-income countries is driven by environmental conditions, especially net nutrition during early years, and potentially reflects the association between these conditions and several adverse health outcomes. These conditions are manifested in the substantial differences in adult height that exist between and within countries and over time. This review suggests that adult height is a useful marker of variation in cumulative net nutrition, biological deprivation, and standard of living between and within populations and should be routinely measured and monitored. Linkages between adult height and health, within and across generations, suggests that adult height may be a potential screening tool for select diseases and that programs focused on offspring outcomes may consider maternal height as a risk factor.

## **TITLE**

Adult Height, Nutrition, and Population Health: A Review

## **INTRODUCTION**

Human anthropometric history as it relates to standards of living has long been a focus of research in a range of social science disciplines.<sup>1-35</sup> Indeed, an abundance of studies describe relationships between child and adult height, nutrition, socioeconomic status and health, and show links between secular increases in height and key indicators of development and population health, and a recent review discusses variation in height from an evolutionary perspective.<sup>36</sup> Given that average adult height has significantly increased in a short period of time in high-income countries (HICs), the pace of change cannot be attributable to changes in the gene pool.<sup>37</sup> Previous studies suggest that overall improvements in access to food, dietary diversification, sanitation, water, living standards and decreasing exposure to disease are responsible for the secular increases in height occurring in the 19<sup>th</sup> and 20<sup>th</sup> centuries across many developed countries.<sup>19,38,39</sup> Notably, these factors are also related to nutrition and, ultimately, to mortality. Thus, adult height may be a potential marker for tracking cumulative net nutrition and population health over time.

Despite the large volume of published information on modern adult height, there has been little integration of the epidemiological and the population health perspectives on modern adult height. (By modern adult height, we refer to height of humans from approximately the last 100 years). This lack of a conceptual map clouds understanding of the potential role of adult height in population health and development, and hinders the argument for including adult height as key indicator of cumulative net nutrition and other

exposure-related improvements. Therefore, a review of results across studies on modern adult height (as both an outcome and an explanatory factor) would help clarify the role of adult height in tracking nutritional improvements, biological deprivation, and population health. Building on previous papers discussing some of the pathways linking height and health,<sup>12,40,41</sup> we present an integrated discussion on the complete set of potential mechanisms and pathways by which various factors affect adult height and by which height affects health, including intergenerational linkages. Specifically, in this review, we aim to:

- (1) summarize the patterns, determinants, and health and development consequences of modern adult height as described in studies identified as salient to this review;
- (2) outline known mechanisms linking modern adult height to nutrition, socioeconomic status, health and intergenerational outcomes;
- (3) identify challenges for causal inference when examining the consequences of height; and
- (4) discuss the relevance of adult height to tracking nutrition and population health improvements.

Before addressing these aims, we review growth periods related to stature, which will reflect attained adult height via cumulative net nutrition. This information provides a foundation from which to understand the discussions that follow regarding determinants and consequences of adult height, and the basis on which we suggest using adult height, and its distribution, as potential measures of cumulative health stock at the population level.

## **AUXOLOGY: THE STUDY OF LINEAR PHYSICAL GROWTH AMONG HUMANS**

Two growth periods are important for determining adult height: growth occurring from conception to age two and growth occurring during adolescence before the onset of puberty. Adult height is primarily established during the first growth period in early childhood<sup>42</sup> when nutritional requirements are greater than at any subsequent time and when infections, particularly diarrheal diseases, occur most frequently. The second growth period presents an opportunity for 'catch-up growth', defined as body growth that is more rapid than normal for age and follows a period of growth inhibition.<sup>2,43</sup> The principal mechanism of catch-up growth appears to be delayed onset of puberty and therefore a longer period of growth in individuals with previous growth-retardation. The timing and duration of catch-up growth may vary. Although there is debate as to the extent to which catch-up growth can occur after two years of age,<sup>44,45</sup> it appears that catch-up growth is not sufficient to fully make up for deficiencies in the first growth period and achieve full growth potential.<sup>45-49</sup> In terms of gender differences, age at menarche is linked with adult height in girls and has shown large changes over time,<sup>50,51</sup> which may explain diverging male-female height ratios,<sup>52</sup> though girls generally start growing earlier, attain adult height earlier than men, and are shorter.<sup>53</sup> Growth trajectories are similar across countries during the first few months of an infant's life, lag behind during the post-weaning period in low- and middle- income countries (LMICs), and are again similar after the age of 2 years.<sup>54</sup>

In sum, adult height represents the balance between nutritional intake and losses over time (particularly during the growth periods), including losses due to physical activity, psychological stress, and disease from conception to maturity.<sup>55</sup> As such, adult height is the product of cumulative net nutrition during the two growth periods (as well as genetics), and is relatively fixed as compared to child or youth height (which may not yet

fully represent any effects of catch-up growth). Moreover, adult height, as a measure of *cumulative* net nutrition, differs from BMI (Body Mass Index or weight-for-height), which is a measure of *current* net nutrition and reflective of the immediate environment.

## **IDENTIFYING ARTICLES ON THE EPIDEMIOLOGY OF HEIGHT**

Articles cited in this review were found through a search of PubMed and ISI Web of Knowledge, using the terms “height”, “stature”, “body height”, and “anthropometry” as keywords. We selected papers deemed relevant to a narrative review specifically addressing modern adult height, and included systematic reviews and meta-analyses where available in favor of individual papers discussing the same relationships. We focused on publications from the past 25 years, and included seminal papers regardless of publication date. We additionally searched for conference presentations and book chapters, and reviewed reference lists of publications and reports identified by this search strategy. Articles on non-human height and those related to specific stature disorders were excluded.

While height is generally defined as the distance from the bottom of the foot to the top of the head when standing erect, across publications adult height was measured in different ways, and the biases associated with each method can lead to incomparability of recordings of adult height between sources and across time. For example, biases in recumbent or free standing height, although taken as a the gold standard, may arise due to inaccuracy of person taking the measurement, lack of precision and standardization of measurement instruments, diurnal variation (loss of about 1% of overall height during the day), subject behavior, change in instruments used, and whether shoes were removed.

Finally, although self-reported height data is the easiest to collect, accuracy is upwardly biased in older individuals, shorter men, and heavier women, and in general there is greater bias in men than women.<sup>56-58</sup>

## **PATTERNS OF MODERN ADULT HEIGHT**

### **Secular increases**

Since the Industrial Revolution, records of adult stature have shown unprecedented increases in average adult heights.<sup>19,38,39</sup> There is evidence, however, that growth in average modern adult heights has been stagnating or actually declining, particularly in Africa relative to Western European countries.<sup>17,59-61</sup> Using data from the World Health Surveys (2002-2004),<sup>62</sup> to assess these claims, we calculated the correlation of mean adult self-reported height with increasing birth-cohort (1934-1948; 1949-1963; 1964-1978) representing decreasing age cohorts (55-69, 40-54, and 25-39 years). The smallest increases in adult height during this time period occurred in Africa (correlation = 0.01) and the greatest increases in adult height occurred in Europe (0.25) (**Figure 1**). The four other regions defined by the World Health Organization (WHO) had correlations ranging from 0.11 to 0.15, across the three age cohorts. Including data from the World Bank, we ran a regression of adult height on year of birth while adjusting for wealth quintile and country fixed effects and stratifying by sex and World Bank income classification. We estimated that average adult heights experienced the largest gains for people born from 1930 to 1980 in the richest countries while height gains in the poorest countries stagnated, on average, during the same period (**Figure 2**).

Given its association with economic development, the average adult height of a population may be a useful indicator of access to nutrition and exposure to disease environments, representing a "biological standard of living."<sup>12</sup> A recent study found that between 43% and 68% of increases in adult height in Brazil between 1950 and 1980 were associated with increases in GDP per capita.<sup>63</sup> In addition, adult height may be a better indicator of overall population health and development than some traditional measures, such as infant mortality. A study of trends in height, health and infant mortality in Sub-Saharan Africa showed that although infant mortality had improved since 1961, average adult heights had not increased.<sup>64</sup>

### **Between- Versus Within-Country Variation in Adult Height**

According to country-average adult heights calculated from self-reported data obtained through the World Health Surveys, there is large variation in height globally, even within HICs (**Figure 3**). The tallest countries are in Western Europe whereas the shortest are concentrated in Sub-Saharan Africa and Southeast Asia. The biggest gender differences are in the tallest countries (the correlation between average height and the gender gap is 0.7), suggesting that sexual dimorphism is more pronounced where undernutrition and childhood disease are mitigated. However, within-country variance dominates differences between countries and country averages mask group differences within countries, particularly between socioeconomic and ethnic groups.<sup>59</sup> There are strong positive associations between adult height and household wealth and education across many countries (and within-country urban-rural differences in height appearing to largely depend on socio-economic circumstances).<sup>11,59,65,66</sup> Moreover, trends in the relation between socioeconomic status and adult height may not have changed much in recent



decades, indicating persistent social inequalities in height.<sup>67</sup> It is possible, however, that the link may be nonlinear and weaker for women.<sup>68</sup>

Notably, social and environmental differences both within- and between- countries dominate any genetic variation between groups in determining average adult heights.<sup>59</sup> This is exemplified by the greater height of children of Mayan immigrants in the United States as compared to Mayan children in Guatemala<sup>69</sup> or in the difference in height between the Koreas, where South Koreans, on average, are 13 cm taller than North Koreans.<sup>70</sup> There may, however, be a genetic component to some cross-country differences, with adaptation of height to different environments, most notably for Pygmy populations in isolated rainforests.<sup>71</sup>

## **DETERMINANTS OF ADULT HEIGHT**

This section reviews the etiology of adult height in modern populations, extending previous work on the determinants of modern adult height.<sup>14</sup> It first focuses on the key proximal roles of nutrition and disease, describes genetic factors, and finally discusses the critical distal role of socioeconomic status.

### **Nutrition**

Nutrition is the most important external factor affecting linear growth.<sup>72</sup> Growth retardation is often a response to a limited supply of nutrition at the cellular level whereby maintenance of basic metabolic functions takes precedence and resources are diverted from growth.<sup>42</sup> Critically, different nutritional components received during both in-utero and post-natal periods are linked to adult height.<sup>73</sup> For example, nutritional factors during pregnancy are associated with intra-uterine growth retardation (IUGR), premature birth,

and low birthweight.<sup>74-77</sup> In turn, these consequences are associated with adult height. A recent study found that birthweight was inversely associated with adult height across five LMICs after adjusting for several confounders.<sup>78</sup> In addition, being small-for-gestational-age (SGA) (a condition when the weight and crown-heel length of infants are less than two standard deviations below reference<sup>48</sup>) is related to adult height.<sup>79</sup> Maternal supplementation with micronutrients, iodine, iron folate and calcium, has been found to reduce risk of SGA births.<sup>80</sup>

However, nutrition affects growth more in the post-natal period than in the pre-natal period.<sup>73</sup> In general, protein is the most essential single nutrient, followed by minerals and vitamins A and D.<sup>73</sup> A study of geographic differences in stature among young men from 45 countries of European origin demonstrated that nutrition level explained most of the differences in adult height, particularly the consumption of high-quality proteins from milk, pork, fish, and wheat.<sup>81</sup> Similarly, milk consumption was positively associated with adult height among a nationally representative sample from the United States.<sup>82</sup> In particular, increased cow's milk is associated with linear growth,<sup>83</sup> though there may be something specific to milk itself, and not milk protein. One trial in India showed that children born within a community-based intervention offering nutrition supplementation during pregnancy and early childhood were 14mm taller than the control group and had a reduced risk of cardiovascular disease upon reaching adolescence.<sup>84</sup> However, evidence of impact on adult height of post-natal nutrition interventions remains weak overall. A small trial from Guatemala indicated no effect of maternal and childhood nutrition protein supplementation on later young adult blood pressure, and no attributable impact on adult height.<sup>85</sup> Another study from the Gambia demonstrated no difference in late adolescent

height due to supplementary maternal feeding during pregnancy compared to supplementation during lactation.<sup>86</sup>

## **Disease**

Nutrition and disease are synergetic, with decreased nutrient intake making infections more likely. In turn, disease can affect growth by hindering food intake, absorption, and nutrient transport to tissues, causing direct nutrient loss, increasing metabolic requirements, or affecting bone growth or density.<sup>73</sup> Indeed, in addition to poor nutrient intake, diarrheal diseases are the other main reason for growth failure in early childhood. Infections (most notably those causing diarrhea), hookworm and intestinal parasites can affect stature while fevers and respiratory tract infections can sap nutrients and inflammatory diseases can hinder growth of long bones.<sup>73,87,88</sup> In addition, asthma has also been associated with reduced stature in HICs, as has having experienced any major disease in childhood.<sup>73,89,90</sup> Moreover, treatments for some diseases may themselves retard growth.<sup>91,92</sup>

## **Genetics**

Height is one of the earliest human traits for which heritability, the component of phenotypic variance within a population that is attributable to genetic variation, was discussed and investigated.<sup>93,94</sup> According to twin studies in HICs, estimates of genetic variation in height are about 80%, with lower estimates for women than for men.<sup>95-97</sup> The underlying assumptions for heritability estimates based on twin studies, however, can be problematic.<sup>98</sup> In recent years, genome-wide association studies (GWAS) have allowed estimation of the contribution of identified and common genetic variants (SNPs) to the proportion of variation in height that is attributable to genetics.<sup>99</sup> Various GWAS

showed that confirmed or specific variants account for a small proportion of the variance in height that is attributable to genetics (about 20% or less).<sup>100-102</sup> Studies using a conglomeration of common SNP variants, but not specific genetic loci, and studies using Genome-wide Complex Trait Analysis (GCTA), which combines information from all common, rare, and imputed SNP variants that in principle exist, find that those variants all together are associated with about 60% of the variation in height that is attributable to genetics.<sup>103,104,105,106</sup> These modern methods show, however, that known genetic loci only account for a small proportion of the estimated heritability of height.<sup>107</sup> In general, GWAS studies have shown that height is a polygenetic trait, controlled by many genes each with a small effect. Notwithstanding the contribution of genetics to explaining variation in height among individuals, genetics is unlikely to be a major contributor to explaining mean differences in height across populations. Furthermore, height heritability estimates may be lower in LMICs due to increased importance of height determinants such as nutrition, disease, and socioeconomic status during the critical periods of growth. Indeed, several twin studies have demonstrated lower estimates of heritability for people in LMICs.<sup>108,109</sup>

### **Socioeconomic Status**

Parental social class, poor socioeconomic conditions (e.g. income, education, and occupation) and maternal education, are all important predictors of adult height because these characteristics represent access to resources, exposure to risk factors, and health behaviors of the mother.<sup>73,87</sup> Indeed, they are critically intertwined with nutrition and disease during the two critical periods of growth. Challenges to growth include overcrowding, reduced access to health care, poor infant feeding practices, poor nature of local diet and contamination of foods/liquids, all of which impact net nutrition.

Environmental exposures in poor socioeconomic areas, such as the consumption of aflatoxin, may also retard growth.<sup>110,111</sup>

The dependence of height on socioeconomic circumstances, however, may lessen as populations become wealthier. For example, the socioeconomic gradient in adult height, though still existing, decreased (by about 2cm) among Swedish men from 1818 to 1968.<sup>112</sup> A similar trend was found across men born in Spain from 1859 to 1967.<sup>113</sup> The social gradient of adult height in young adults in a UK birth cohort appears to be entirely dependent on the height of their parents.<sup>114</sup> While discussing the relationship between income and height, it is important to note that the relationship between average adult height and income is nonlinear. It should be acknowledged that average population height is somewhat dependent on socioeconomic distribution; transferring income to poor families would increase average height because, while children from poor families would grow, children from rich families would not lose any part of their cumulative net nutrition (as they already have more than enough).

In sum, variation in modern adult height substantially reflects differences in environmental conditions, which ultimately affect cumulative net nutrition. 'Environmental conditions' refers to all factors within a context that affect availability of, access to, and use of resources, as well as exposure to health risks. Such factors include appropriate nutrition, socioeconomic status of individuals, characteristics of households or places, and access to, and quality of, health services, and certain diseases and climates. Importantly, these factors do not operate in isolation nor in sequential order; conditions may be relevant at multiple time points, operate across multiple levels and exhibit substantial effect modification. The level of exposure to factors negatively affecting net

nutrition remains high in many LMICs experiencing minimal nutritional, sanitation and water-related improvements in the past decades. These exposures can lead to undernutrition, child stunting, and ultimately to a failure to reach one's genetic adult height potential. While there is variation at the individual level, average adult height in low-resource contexts is lower than genetically possible. By comparing average adult height across populations, the extent of variation in exposures affecting cumulative net nutrition for cohorts, particularly during the first growth period, can be determined. Indeed, modern adult height may offer an important window into understanding population health, nutrition and development improvements over time.

## **CONSEQUENCES OF HEIGHT**

In this section, we examine the role of adult height as a determinant of adult health, access to resources, and the health of future generations. To do so, we first present evidence of the relationship between adult height and various manifestations of morbidity and causes of mortality. We then provide evidence that links adult height to socioeconomic status and education, well-being, and the health and height of offspring.

### **Mortality and Morbidity**

In general, the association between adult height and cause-specific mortality is heterogeneous.<sup>115</sup> However, some disease-specific associations are strong enough that the use of height as a variable in screening for these conditions may be explored. The strongest negative associations between adult height and cause-specific mortality (and morbidity) are found for respiratory and cardiovascular diseases across different populations.<sup>115-119</sup> A review of 52 studies on coronary heart disease (CHD) concluded that there was enough

evidence to indicate a real relationship between adult height and CHD-related morbidity and mortality; shorter adults had about 50% greater risk than taller adults.<sup>117</sup> In addition, a recent study found a positive relationship between sudden cardiac arrest and adult height.<sup>120</sup> Yet, a prospective study among men and women in Japan found that there was no relationship between height and coronary heart disease after adjusting for education though height was inversely associated with total risk of hemorrhagic or ischemic stroke.<sup>121</sup> In contrast, adult height is positively associated with risk of pulmonary and aortic aneurysms,<sup>115</sup> coronary artery calcium,<sup>122</sup> weight gain and obesity,<sup>123</sup> and venous thromboembolism among men.<sup>124</sup> A recent study found that tallness was associated with lower risk for ischemic heart disease and premature death, but was associated with increased risk for atrial fibrillation (AF).<sup>125</sup> In that study, stature was not associated with stroke or venous thromboembolism among men. Another study also found that independent of gender, adult height was positive associated with risk of AF.<sup>126</sup> Separately, tallness may confer protection against glucose intolerance<sup>127</sup> and high cholesterol.<sup>128</sup>

Several studies have found a positive association between adult height and various types of cancer including colorectum, breast, head and neck, ovaries, skin, endometrium, central nervous system, blood, liver, intestine, thyroid, gliomas, and lymphatic malignancies.<sup>115,116,129-131,132,133-138</sup> Conversely, tallness may confer protection from neoplasm of the stomach,<sup>116</sup> esophagus, and mouth, though discrepant findings have been reported.<sup>131,132,139</sup> No consistent differences between sex, regions or populations have been found.<sup>132</sup>

Despite the mixed relationships between adult height and cause-specific mortality and morbidity, the historical epidemiological literature indicates a strong inverse

relationship between adult height and all-cause mortality.<sup>6,140,141</sup> Moreover, the increase in life expectancy in the 19th and 20th centuries has been attributed to key determinants of stature (i.e. improved nutrition and lowered rates of infection and trauma)<sup>142</sup> and the risk of mortality has been shown to increase with decreasing height.<sup>73,129,143</sup> Subpopulation differences are less clear across studies even though a dose-response relationship between height and all-cause mortality has been suggested for men and a threshold effect for women.<sup>143</sup> A recent study of the association between adult height and health in later life found that height was positively associated with lung function, grip function, good self-reported health, no difficulties with activities of daily living or instrumental activities of daily living across six LMICs.<sup>144</sup>

### **Socioeconomic Status and Education**

Adult height is strongly associated with both higher income and education in modern populations and is a predictor of economic productivity, with taller people earning more and more likely to be in the workforce,<sup>145</sup> even after controlling for education<sup>146,147</sup> and productivity.<sup>148</sup> Taller people have also been shown to be more socially upwardly mobile,<sup>73</sup> which will perpetuate the socioeconomic gradient in height. For example, in the Philippines, higher length-for-age at age 2 years was associated with a 40% increase in likelihood of formal work as an adult.<sup>149</sup> In addition, data from the US showed that comparing women and men of below-average to above-average height corresponded to an 18% increase in family income for women and a 24% increase for men.<sup>150</sup> While part of this association may reflect the positive correlation of height and intelligence,<sup>151,152</sup> it is not possible to reliably separate socio-environmental from genetic contributions to this correlation.



Finally, within populations, some studies have found that adult height was positively correlated with cognitive function, such as memory and numeracy.<sup>153,154</sup> A recent study found that height among adults aged 50 or older was positively associated with cognitive ability (measured as a summary score of memory, numeracy, and verbal fluency) even after adjusting for an extensive set of controls.<sup>155</sup> This study also provided some evidence of a height-cognitive ability association across countries for pre-1950 birth cohort respondents and that being taller was associated with smaller decreases in age-related cognitive function. Another study among the urban elderly in Latin America and the Caribbean found a positive association between height and later-life cognition, and that the relationship was stronger among women than men.<sup>156</sup> Separately, stunting has been noted as a marker for poor psychological performance<sup>157</sup> and as being associated with lower school attainment resulting from late school entry, more grade repetition, and increased likelihood of early drop out.<sup>158</sup> Supporting these findings, a review of height in LMICs reported that height-for-age at 2 years was the best predictor of human capital.<sup>159</sup> While some twin studies have shown that the taller twin completed more education, and earned higher wages,<sup>160</sup> another suggested that genetic factors explained both adult height and intelligence or that they could be interacting with environmental factors to explain the association.<sup>161</sup>

### **Well-being**

Overall, taller individuals consistently report better health and less illness,<sup>162</sup> and better results on various well-being measures, including enjoyment, happiness, sadness, physical pain, and social activity.<sup>150,163</sup> Tall people, however, are also more likely to report stress and anger and, for women, worry.<sup>150</sup> Most of the associations between stature and these measures may be accounted for by income and education.<sup>150</sup> Yet, even when

controlling for socioeconomic position, adult height is inversely associated with lowered risk of depression and suicide,<sup>164</sup> and demonstrates a positive association with psychological well-being<sup>165</sup> though there may be gender differences in this association.<sup>166</sup> Adult height is positively correlated with higher IQ<sup>167</sup> and higher achievement in cognitive testing.<sup>168</sup> Although these associations are evident in modern societies, they may not appear in traditional ones.<sup>169</sup>

### **Offspring Health**

Maternal height is strongly associated with reproductive success.<sup>170,171</sup> For example, several studies have shown inverse associations between maternal adult height and risk of congenital malformations,<sup>172</sup> fetal growth,<sup>173</sup> preterm births,<sup>174</sup> premature labor,<sup>75</sup> low birthweight,<sup>175</sup> stillbirths,<sup>176</sup> assisted delivery,<sup>177</sup> and Caesarean-sections.<sup>178</sup> One study among women from different countries found that maternal height was associated with child height during all development periods (intrauterine, birth to age 2 years, age 2 years to mid-childhood (MC), and MC to adulthood).<sup>179</sup> In addition, lower maternal height may be a risk factor for child mortality, underweight, and stunting across LMICs.<sup>180,181</sup> Moreover, parental height (and in particular maternal height) may also be inversely associated with offspring coronary heart disease<sup>182</sup>, and maternal childhood growth may be linked to offspring growth.<sup>183</sup> Indeed, maternal adult height is an exemplary intergenerational factor, which are “those factors, conditions, exposures, and environments experienced by one generation that relate to the health, growth and development of the next generation.”<sup>184</sup>

In summary, adult height is associated with a myriad of health and well-being outcomes, relationships that often remain even when adjusting for potential confounders. Moreover, height may affect multiple outcomes, which may, in turn, affect each other. Given

the potential for shorter adult height to produce intergenerational consequences at the individual level, which can, in aggregate, lead to continued high levels of child stunting at the population level particularly in contexts of limited nutrition,<sup>185</sup> average adult height, if tracked over time, can be an important indicator of changes, or lack thereof, in health, well-being and socioeconomic inequalities in populations.

## **MECHANISMS LINKING ADULT HEIGHT TO HEALTH AND SOCIOECONOMIC STATUS**

This review of potential determinants and consequences suggests that adult height is both affected by, and affects, health, nutrition and socioeconomic status outcomes, and that these ‘environmental conditions’ are critical to the height and health of future generations. Unfortunately, few studies examining height have a design that would facilitate clear causal inference (e.g. determination of which factors are most relevant and in which order they are likely to affect each other). Discussing what may be behind these associations, however, will help to reveal both the usefulness of adult height as a screening criterion for biological deprivation, standard of living and nutritional deprivation, and the degree to which the causal factors potentially underlying the associations are amenable to intervention. Therefore, we next parse out the mechanisms linking adult height to health, socioeconomic status and intergenerational factors while allowing for the possibility that these relationships may be partially or entirely due to unobserved factors.

### **Mechanisms**

There are five possible mechanisms that could underlie the associations between adult height and health, socioeconomic and intergenerational outcomes:<sup>186</sup> (1)

*Biomechanical*<sup>42</sup>: height confers advantages and disadvantages related to body and organ

size and function which have health and reproductive consequences; (2) *Biological*<sup>14</sup>: height is an indicator of health capital, and growth, and rate of growth at different periods, has metabolic impacts that translate into lifelong and intergenerational health consequences; (3) *Genetic*<sup>104</sup>: factors influencing growth may be tied to risks for disease or ability, and their joint transmission creates associations between height and these outcomes; (4) *Psycho-social*<sup>129</sup>: society places a premium on height and those who are taller are conferred greater social status and exhibit greater confidence; (5) *Epigenetic*<sup>104</sup>: changes in gene expression (without a change in DNA sequence), which may be related to external (i.e. environmental) influences.

Although these mechanisms are comprehensive, they are not distinctly bound; some of the categories are likely to overlap and all are likely to be functioning to some extent, and variable extents, within and across generations. Given the essential interconnectedness of these mechanisms, conventional observational epidemiology approaches are not powered to distinguish between them. However, we provide specific examples of how these mechanisms may link height to a) health and well-being, b) socioeconomic status, and c) intergenerational outcomes in **Table 1**.

### **Confounding, Effect Modification and Mediation**

Other factors associated with both modern adult height and health outcomes may play a role in creating the associations observed. Evidence from across studies included in this review suggests that income and education are positively correlated with both adult height and health and are thus potential confounders in the relationship between adult height and health. Indeed, there are several pathways linking height and socioeconomic status (**Figure 4**). However, the association between adult height and health remains

robust in studies adjusting for adult income, education and other measures of socioeconomic status.<sup>6,89,115,124,125,129,137,141,200,201</sup> Yet, there certainly is a strong argument that childhood conditions may confound part of the association between adult income, education and height and that socioeconomic status during childhood is linked to both adult height (through nutrition and disease) and to adult socioeconomic status. For example, wealthy and more educated parents are likely both to provide better nutrition and to invest more in their children's education. Finally, there may be effect-modification of the role of height on health by socioeconomic status (e.g. shorter height was more strongly associated with coronary heart disease among men in high employment grades than among men in lower employment grades).<sup>202</sup>

Adult height is also associated with risk factors for health, which possibly confound the association between height and health outcomes. For example, taller people smoke less, have lower blood pressure, and better diets. Controlling for these factors, however, does not diminish observed associations.<sup>129</sup> Other potential confounders between height and outcomes include medical conditions, socioeconomic conditions, or nutritional conditions leading to both shorter stature and lower cognitive ability (e.g. via fetal alcohol syndrome, growth hormone, or brain volume)<sup>203,204</sup> or height loss and observed disease.<sup>205,206</sup> However, a study of son's height as an instrument to predict parental mortality found little confounding due to pre-existing health conditions in the relationship between own height and mortality.<sup>207</sup> Finally, although humans shrink with age,<sup>208,209</sup> two reasons counter this as a general confounding mechanism: (1) the robustness of the associations between adult height and outcomes across all ages before shrinkage occurs, and (2) the differential association between how different components of height (e.g. leg length and trunk length)

are linked to different stages of early growth and health outcomes.<sup>210</sup> Indeed, leg length and trunk length may give insight into the importance of different childhood conditions in adult disease. For example, the components of height are differentially associated with some cancers<sup>131</sup> and leg length is linked to both chronic heart disease and non-fatal coronary events<sup>211</sup> and diabetes.<sup>212</sup> Moreover, a recent study found little bias due to potential height loss in the estimates obtained from models using stature to predict health when controlling for age.<sup>213</sup>

Potential confounding should not be ignored in the observed association between mothers' adult height and the health of their children. If adult height is a surrogate for health, then healthier mothers may get more education (through better school attendance) or have better cognitive function.<sup>214</sup> Height is similarly related to socioeconomic status: taller mothers may earn more and be better off than shorter mothers. Indeed, there is evidence that healthier, more educated and richer mothers have healthier children,<sup>215</sup> thus potentially confounding the relationship between maternal height and child health.

**Figure 5** presents a conceptual diagram displaying links between these factors and outcomes, and demonstrates pathways for confounding and mediation, with potential mechanisms and interactions noted. The various relationships among determinants of height and health across generations, including the role of 'environmental conditions' and genetics are depicted. These visual demonstrations of the complex interrelationships eventually affecting child health present a starting point for future research: to elucidate these relationships, and to assess the relevance of the various mechanistic processes occurring within these relationships, which in turn determine outcomes. This conceptualization may assist future studies to measure the role of confounders and

determine how some outcomes themselves may impact adult height (reverse causality), and how adult height may be on the pathway between a third factor and outcomes of interest (mediation). Utilization of novel techniques such as Mendelian randomization,<sup>216,217</sup> and use of family data,<sup>199,218</sup> will further our understanding of these mechanisms, causal pathways and potential confounders/mediators. Other techniques to establish causation may include reliance on instrumental variables, regression discontinuity design, differences-in-differences estimation, panel data, vector autoregression, and Granger-Sims causation methods.

Finally, although it has been suggested that expression of genetic factors associated with height may change according to environmental factors experienced, there is currently little robust evidence on molecular epigenetic processes in relation to adult height. Moreover, the similarity in mother-offspring and father-offspring height correlations in large scale studies does not reflect heritable changes,<sup>91</sup> arguing against the importance in population terms of epigenetic inheritance mechanisms.

## **DISCUSSION**

This review identifies four salient observations summarized from reviewed studies regarding patterns, determinants, and consequences of adult height. First, substantial differences in modern adult height exist between and within countries, reflecting both past and current distribution of disease and nutrition in early life. Second, environmental conditions (representing nutrition, disease, access to resources, and socioeconomic status) play a critical role in establishing adult height, especially during the first two years of life and especially in LMICs. Third, shorter height is associated with adverse consequences for

mortality and morbidity even when adjusting for education, occupation, and income. Finally, the strong intergenerational linkages observed between parental height and offspring stunting and subsequent short adult stature in LMICs, along with stagnation in the average adult height in many countries, suggest that future inequalities in health will persist and may even increase unless immediate attention is paid to improving nutritional (and socioeconomic) circumstances for children during critical growth periods.

In general, the high levels of short adult stature observed in many LMICs strongly suggest that growth retardation is not primarily attributable to genetic factors. Rather, short stature reflects the cumulative net impact of nutrition, and, therefore, the roles of disease and more distal environmental conditions, such as socioeconomic status, on height over time and across generations. That the two regions of the world with the lowest average adult heights are also the regions with the greatest prevalence of undernourishment (Sub-Saharan Africa) and the great number of undernourished people (Southeast Asia)<sup>219</sup> support this claim.

Moreover, at the individual level, the relative roles of net nutrition and genetics appear to differ across the growth periods; the impact of nutrition (and other environmental factors) may be relatively stronger during the first period while the genetic component may be relatively stronger during the second period.<sup>220,221</sup> Estimates of height heritability, however, may lead to confusion on the relative importance of genetic and environmental factors in determining adult height despite the evidence against the contribution of genetics to observed patterns of stature. To clarify, there is no inherent contradiction between the estimated heritability of height and evidence of secular changes (usually increases) in adult height at rates too rapid to be associated with changes in the



genetic structure of a population. Heritability relates to differences between individuals within a particular population at a particular time. Thus, when environmental factors are changing across the board within a population, these changes can lead to substantial, and entirely environmental-based, changes in population mean height, which are in no way incompatible with high heritability.<sup>222</sup> Nonetheless, it is important to distinguish short stature related to polygenic genetic influences from those related to environmental influences. Indeed, it is processes leading to failure to meet genetic potential for height or “target height” that are of interest.

Height is associated with improved social and economic development and has consequences for current and future population health and well-being. As such, adult stature is a measure that, at least partially, captures current human capital and human capability at the population level. There is strong evidence that adult height (and maternal height, in particular) is linked to offspring undernutrition, stunting and mortality. Therefore, shorter average adult height of today can be viewed as a reflection of tomorrow's burden; on average, stunted children, will not meet their full genetic potential for height (even after experiencing catch-up growth). Indeed, achieving national and global goals related to reducing child undernutrition and mortality, poverty, and inequality may require consideration of the strong generational and intergenerational linkages in height.

## **Conclusion**

From the biological/anthropological perspective, adult height is a relatively easy indicator to routinely collect. Evidence of the robust relationship between adult height and outcomes, as well as between determinants and adult height, even after controlling for potential confounders, points to the utility of adult height as a measure of population

cumulative net nutrition, health and development. At the same time, the remaining questions about causality and associated mechanisms point to the importance of continuing investigation on how nutrition and other environmental factors (particularly during early childhood years) are related to adult height, and how adult height in turn predicts subsequent outcomes. Notably, understanding the impact of adult height on future generations does not mean that continuous increases in average adult height are the ultimate goal. Rather, the summary provided in this review supports utilizing adult height as a key indicator for comparison of both between- and within-country population-level improvements over time, particularly those that may be related to inequality in nutrition and environmental factors. From a macro perspective, average adult height can be considered a critical indicator of human capability and reflect the quality of a nation's workforce. By at least partially representing past health, current health and future health, and the impact of environmental conditions through time on cumulative net nutrition, adult height can be used as an marker of long-term progress in global health and development.

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### **Declaration of Interest**

No competing interests.

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## FIGURE LEGENDS

**Figure 1.** Average height (in cm) of adult men and women by year of birth category and WHO region. The data are obtained from the 2003 World Health Surveys. The correlation of height with age-group (represented by birth cohorts) for each WHO region is AFRO - 0.01, SEARO - 0.10, AMRO - 0.13, EMRO - 0.13, WPRO - 0.15, and EURO - 0.23.

**Figure 2.** Predicted association between height and year of birth by sex and World Bank income classification. The data are from the 2003 World Health Surveys and the World Bank. Models were adjusted for wealth quintile (derived from an asset index) and country fixed effects, and estimates were calculated using robust standard errors, taking into account clustering by primary sampling units.

**Figure 3.** Mean height (in cm) of adult men and women across countries. The 2003 World Health Surveys (WHS) measure self-reported heights for de facto populations though surveys in India and China were not nationally representative. Country mean heights are sample-weighted and age standardized by sex to the average WHS population, and calculated by the authors.

**Figure 4.** Disaggregation of the pathways through which environmental factors (socioeconomic status, disease and nutrition) and genetics determine stature, and through which stature determines socioeconomic status and other outcomes.

**Figure 5.** Conceptual model exploring the mechanisms that may link socioeconomic status, height and health across generations. Boxes are factors and outcomes, and circles are mechanisms and interactions. The following points present information on how determinants and consequences are related: (1) The additive endowment component, affecting both maternal stature and health and child outcomes; (2) The multiplicative (epigenetic) endowment component (gene-environment interaction); (3) Socioeconomic conditions of the mother during childhood can mediate her exposure to disease and nutrition through a number of pathways including food resources, access to medical care, and environmental sanitation; (4) The intergenerational persistence of education and income not working through health; (5) The balance between nutritional intake and losses, including losses due to physical activity, psychological stress, and disease; (6) Potential interactions between stature, income and education; (7) Biological pathways working through the viability of the uterine environment during pregnancy; (8) Biomechanical pathways working through the relationship between stature and pelvic size; (9) Socio-economic pathways whereby education of mothers may affect childhood outcomes through health behaviors or autonomy of women to make health-decisions for their children. In addition, links between parental income and child outcomes are well established.



**Table 1.** Potential mechanisms linking height with health, socioeconomic status and intergenerational outcomes.

Mechanisms	Outcomes		
	Health & Well-being	Socioeconomic status	Intergenerational
Biomechanical	Taller people have increased pulmonary function (protective against CHD and respiratory disorders), larger coronary vessel diameter (protective against CHD), and larger organs (higher risk for malignancies due to increased number of cells).	There may be a biomechanical component to the link between stature and economic productivity. Taller people are healthier and may be more physically capable and robust.	Taller women have wider pelves, allowing easier births and a reduced likelihood of fetopelvic disproportion, <sup>187</sup> obstructed labor, and Caesarian-section. <sup>188</sup>
Biological	Childhood nutrition and disease have consequences that impact mortality and morbidity in adulthood. Specific hormones associated with growth are also associated with risk for disease (e.g. insulin-like growth factor (IGF-I)). Early deprivation followed by catch-up growth, partly through delayed onset of puberty, may be linked to risk of diabetes and CHD (partially masking the link between early growth insults and stature). Overall energy intake is associated with both growth and, at the upper end, with cancer risk. <sup>189</sup>	Childhood malnourishment impacts both stature and health, including cognitive development which in turn can lead to fewer years of schooling completed <sup>159</sup> and reduced capacity to work. <sup>190</sup> Higher rates of morbidity are associated with increased absenteeism and decreased attentiveness and capacity to learn. <sup>149</sup> Higher cognitive test scores of taller children have been proposed to explain the association between adult heights and wages. <sup>168</sup>	Maternal stature is related to low birth weight (LBW) in offspring. LBW is due to intra-uterine growth retardation (IUGR) or prematurity (or both). Shorter mothers may have smaller organs, affecting pregnancy primarily due to reduced cytoplasmic-nuclear ratio but also because of reduced cell number. Poor nutrition in early life may induce adaptations in organ function or size, metabolism, or cause gene expression to adapt in order to raise survival probabilities through the early years which may cause problems later in life. <sup>6,191</sup> Similarly, inflammation, caused by infections, has a variety of

			deleterious long-term health consequences, which may be transmitted to offspring.
Genetic	Genetic factors influencing growth may be tied to mortality or risk of specific diseases through pleiotropic effects or because the variants controlling both height and disease may be transmitted together (i.e. are in linkage disequilibrium). For example, the association between short stature and increased LDL-C may be partly of genetic origin <sup>192</sup> ; SNPs associated with adult height may also share an association with risk of testicular cancer. <sup>193</sup>	As with health, height and cognitive abilities may be transmitted together, with height being related to social mobility and thus socioeconomic position. Taller parents, who are in more favored socioeconomic circumstances, will transmit both their genes and their social advantages to their children. <sup>114</sup>	The association between maternal height and child health may be due to underlying genetic control of both, with short stature transmitted along with increased risk of mortality and disease from mother to child. Comparing associations of child outcomes with both maternal and paternal height allows for separation of transmitted germ line genetic variants (balanced between mother and father) and other mechanisms of intergenerational transmission of phenotype. <sup>199</sup>
Psycho-social	Height as a socially desirable trait may result in better self-care and preventive behaviors.	Tallness is a desired trait and is rewarded by society with higher conferred status and wages. This preference may have evolutionary roots; taller men may be both more attractive <sup>194</sup> and have higher marriage rates. They may also exhibit greater interpersonal dominance. <sup>195</sup> The wage-height premium may be due to taller people having higher self-esteem. Self-esteem and social	Confident and successful tall parents may raise more confident and healthier children.

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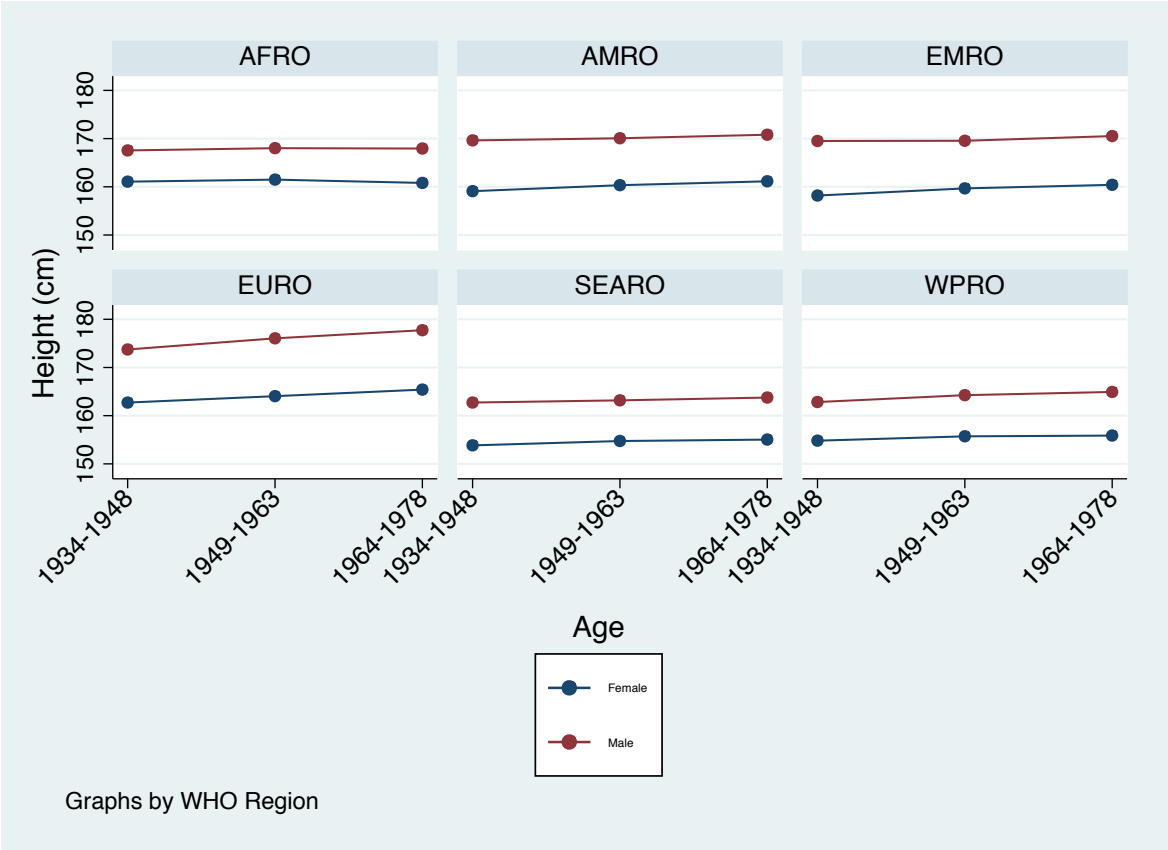
skills that lead to human capital accumulation may be most important in adolescence. Height as a teen may explain the stature-wage association.<sup>196</sup>

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Epigenetic	Environmental conditions result in epigenetic effects through the control of gene expression by DNA methylation and histone modifications impacting both stature and risk of disease specific mortality and morbidity. <sup>197</sup>	The molecular mechanism of controlling gene expression over relatively long periods of time may be affecting gene expression related to both stature and traits impacting socioeconomic outcomes.	In utero conditions may play a role in alterations of many genes involved in metabolism and growth, impacting outcomes in children. <sup>198</sup>
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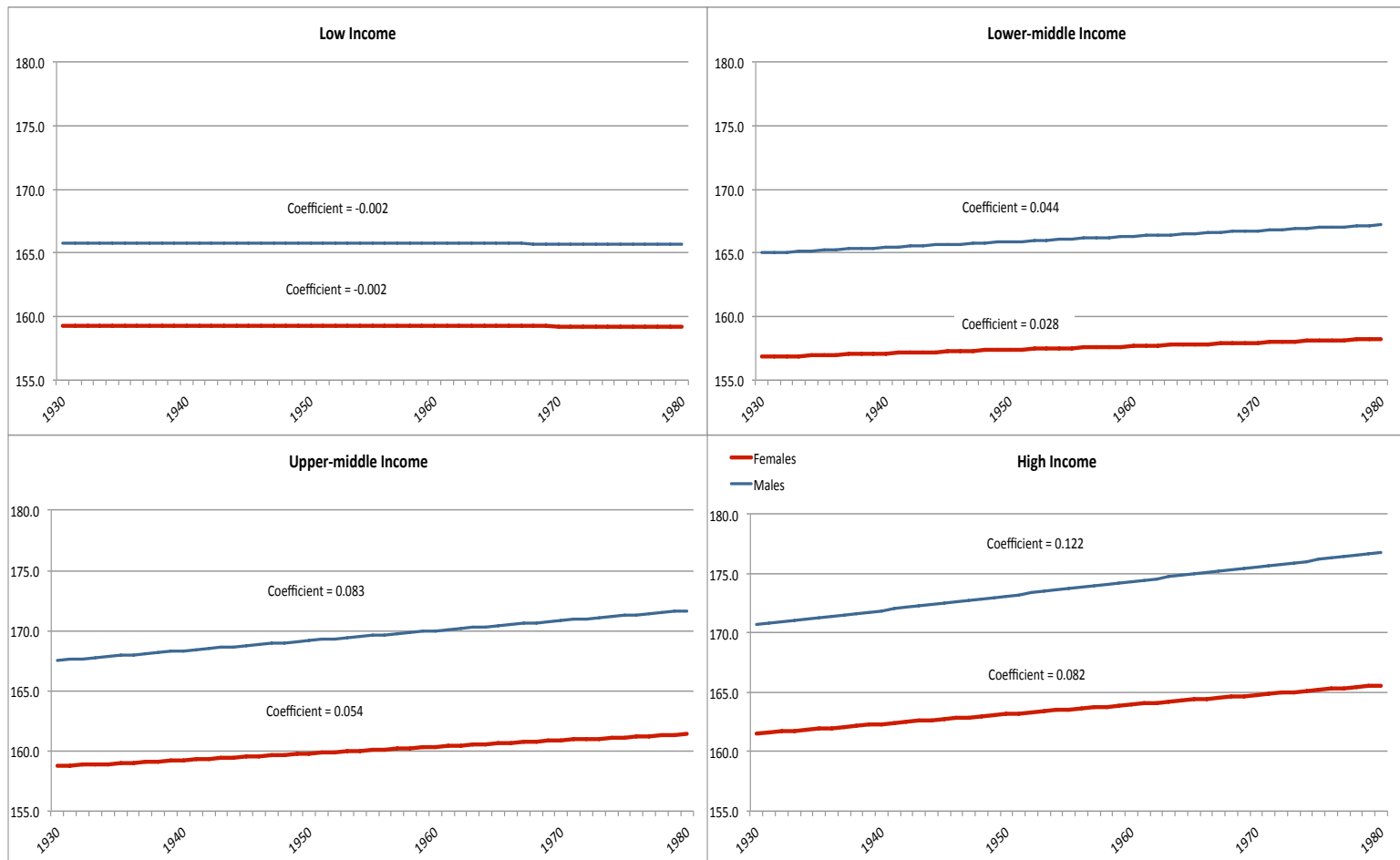
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**Figure 1.** Average height (in cm) of adult men and women by year of birth category and WHO region.



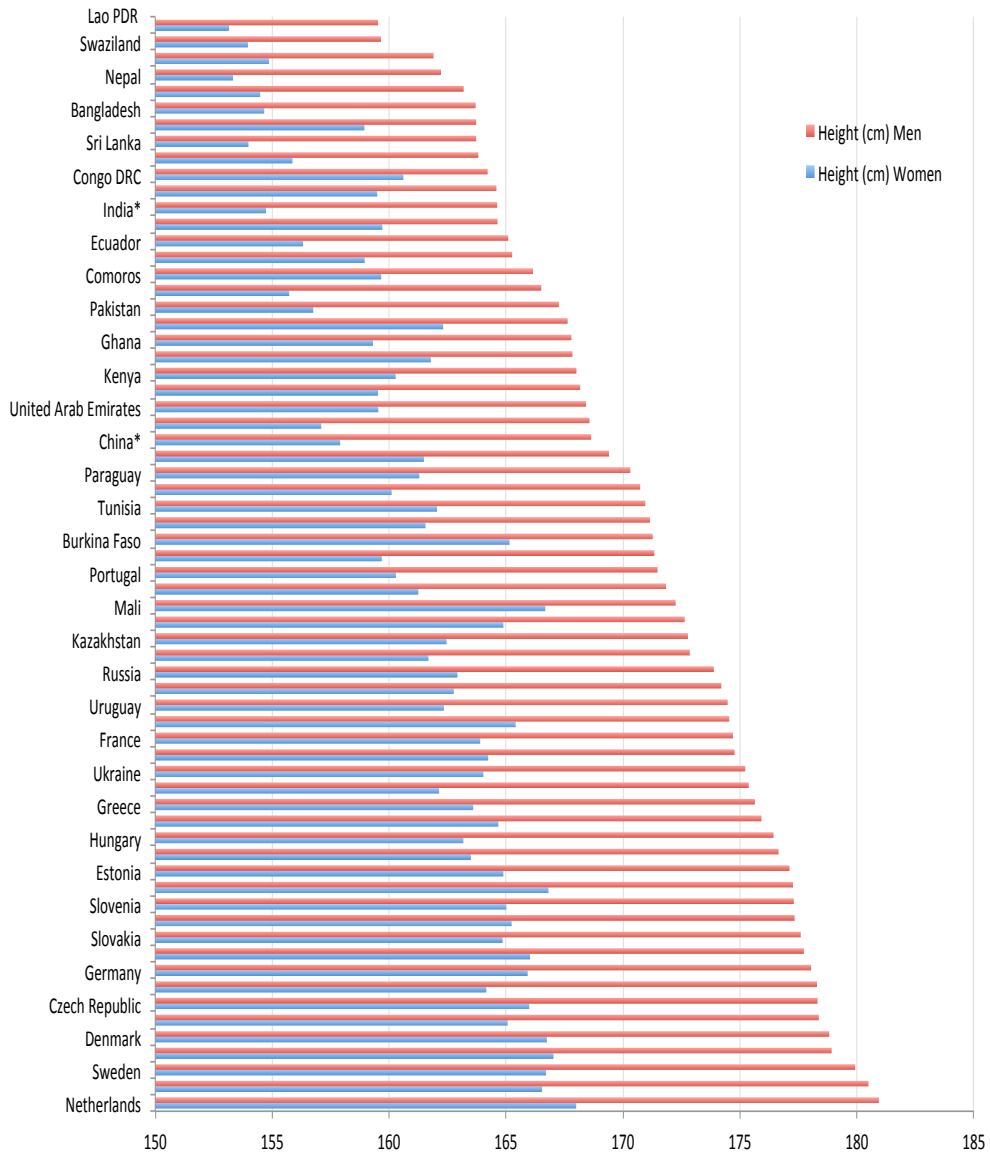
Notes: Data obtained from the World Health Surveys 2003. Correlation of height with age-group for each WHO region: AFRO 0.01, SEARO 0.10, AMRO 0.13, EMRO 0.13, WPRO 0.15, EURO 0.23

**Figure 2.** Predicted association between height and year of birth by sex and World Bank income classification.



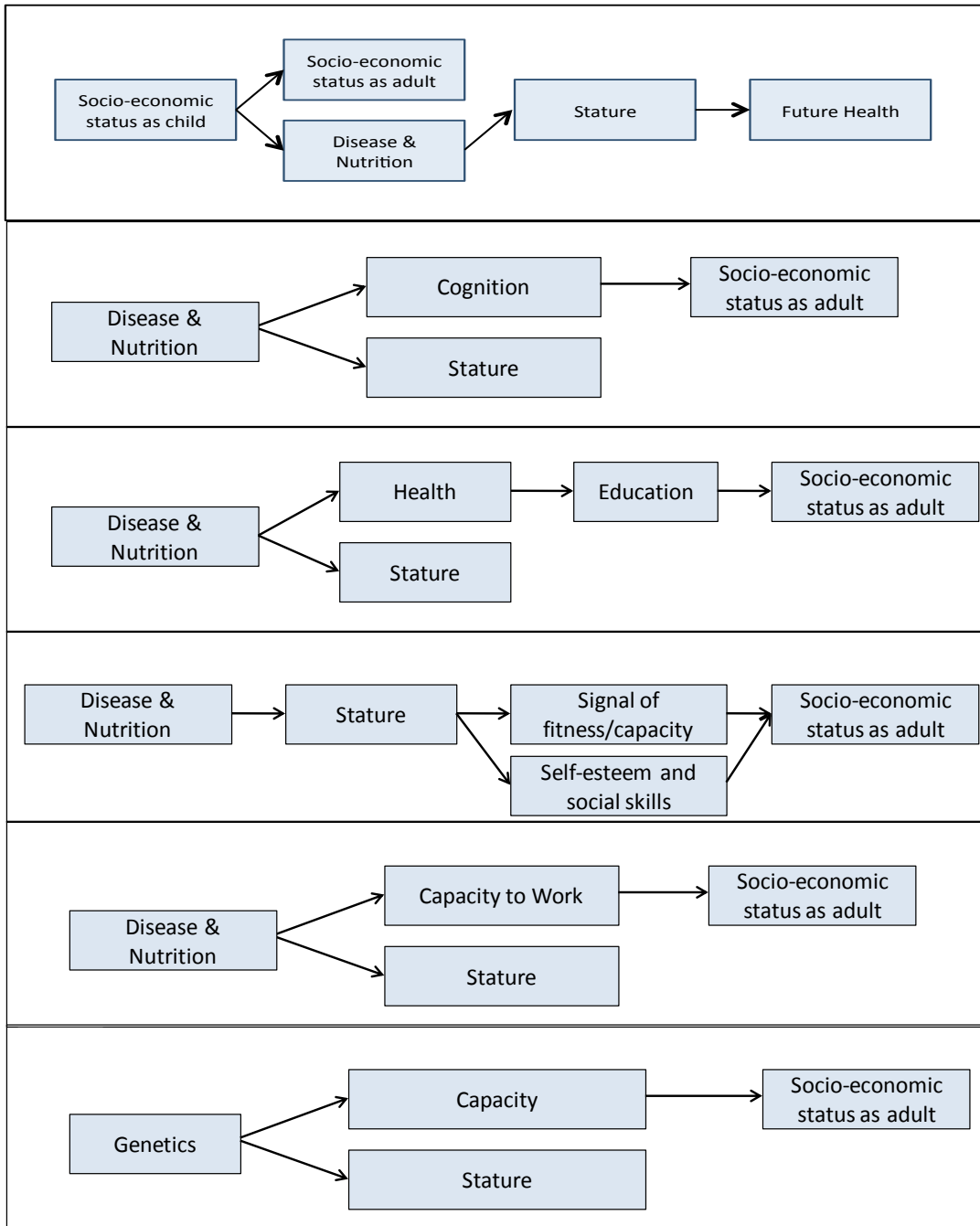
Notes: Data came from the World Health Surveys 2003 and the World Bank. Models were adjusted for wealth quintile (derived from asset index) and country fixed effects, and estimates were calculated using robust standard errors, taking into account clustering by primary sampling units.

**Figure 3.** Mean height (in cm) of adult men and women across countries.

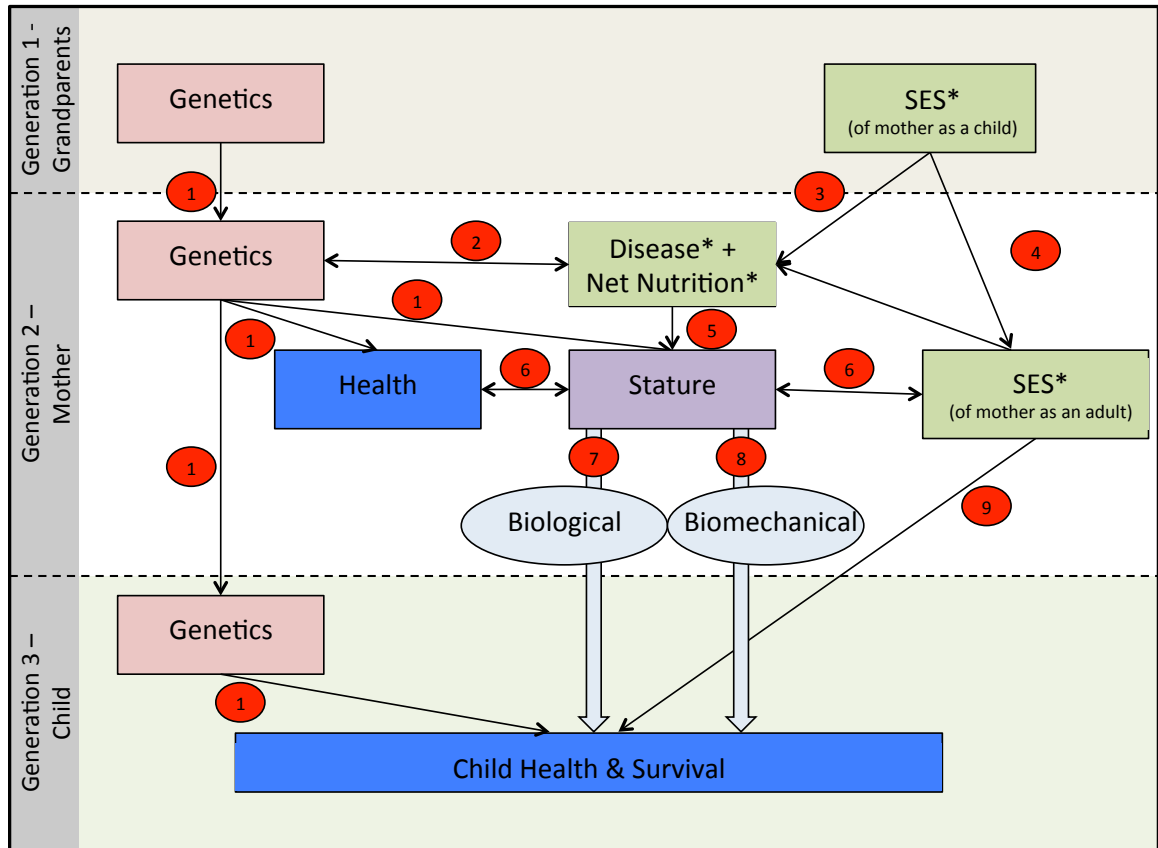


The World Health Surveys measure self reported heights for de facto populations  
 \*Surveys in India and China were not nationally representative  
 Country mean heights are sample-weighted and age standardized by sex to the average WHS population  
 Source: Author's calculations, data from the World Health Surveys 2003

**Figure 4.** Disaggregation of the pathways through which environmental factors (socioeconomic status, disease and nutrition) and genetics determine stature, and through which stature determines socioeconomic status and other outcomes.



**Figure 5.** Conceptual model exploring the mechanisms that may link socioeconomic status, height and health across generations.



**Legend**

Boxes are factors and outcomes: Blue = Outcomes; Green(\*) = Environmental factors; Pink = Biological factors. Circles are mechanisms and interactions.