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Physiological Differences Across Populations Reflecting Early Life and Later Life Nutritional Status and Later Life Risk for Chronic Disease

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Introduction

Ageing takes place in widely varying environments which influence the observed physiological characteristics of the population as it ages. People who are ageing, have lived in environments that not only differ across place but also change over time; childhood environments as well as early adult and old-age environments are all likely to influence the physiology of ageing populations. In childhood, the availability of nutrients and their ability to be effectively used influence the development of an organism before the process of aging is recognized (Barker 2004; Crimmins and Finch 2006; Fogel 2004). The ability to use nutrients as well as the demand for nutrients is affected by the level of infectious and parasitic disease in the environment. Later-life environments build on early life physiological characteristics to speed or retard some of the physiological changes that reflect increasing risk for developing chronic diseases and conditions observed at older ages. This paper will examine national differences by age in physiological status that reflect early nutrition and development and current nutritional status in a wide range of past and present epidemiological conditions to clarify how the physiology of aging populations differs across time and place and how physiology is related to current life expectancy and level of childhood infection. We examine the variability within countries in social and demographic differences in indicators of past and current nutrition, as we assume the association of these markers with demographic and socioeconomic indicators will differ depending on epidemiological circumstances. We then relate these nutritional characteristics and current demographic and social indicators to current levels of risk for metabolic and cardiovascular conditions among persons 50 years of age and older to see how early development, current nutritional status and demographic and social characteristics affect risk for chronic conditions related to aging in different environments..

Environmental conditions are related to past and present social, epidemiological, and technological conditions. During the lives of the now older population, all countries have either gone through or are going through demographic transitions, epidemiological revolutions, and technological changes. The epidemiological revolution results from ability

Conflict of Interest

The author has no conflict of interest.

to control infection (Omran 1971) which, in turn, results in reductions in deaths from infections, and spending less time with active infections over one's life (Gurven et al. 2008). Recent observation in a society that would be characterized as pretransitional in epidemiological terms found about 2/3 of people reported having a respiratory or intestinal infection at a given time (Gurven et al. 2009). Less infection not only affects survival but also affects physiological development as reduced infection leaves more resources for physical growth and development instead of maintenance and repair. Infection is very physiologically demanding of both energy and nutrients. The fever and lassitude which accompany infection reflect the intense inflammatory response as energy is being used to fight infection (Finch 2007). When energy to fight infection is not needed as consistently, the body is able to more efficiently use its nutrients and people grow taller and heavier (Crimmins and Finch 2006). Height is achieved by the end of childhood, generally by age 20, and is highly affected by conditions in the first few years of life. Links between height and subsequent adult health provide evidence of the positive link between early and late life health: lower overall mortality in adulthood (Davey Smith et al. 2000; Song et al. 2003), fewer strokes (McCarron et al. 2000; McCarron et al. 2001; Song et al. 2003), and less cardiovascular disease (Davey Smith. et al. 2000; Gunnell et al. 1996, 2003).

With reduction in infection there should also be less damage to organs during development, leading to stronger bodies throughout the lifecycle. Early life infection has been linked to damage to the heart, kidneys, and lungs and changes in metabolic set points (Barker 2007; Lynch and Davey Smith, 2005). As an example, prenatal exposure to the 1918 influenza pandemic appeared to be associated with an increase of more than 20 percent in late life cardiovascular disease, relative to cohorts born without exposure to the influenza epidemic among Americans 60 to 82 years of age (Mazumder et al. 2010). This study also reported increased late life diabetes with fetal exposure to influenza; however, effects on subsequent heart disease and diabetes differed by trimester of exposure and gender. These findings suggest the role of maternal infections in the fetal programming of cardiovascular and diabetes risk factors emphasized by Barker (Barker 2004; Barker and Osmond 1986; Hales and Barker 2001).

At the same time as the epidemiological revolution changed the expenditure of nutrients to fight infection within individuals, technological changes made it possible for societies to increase the production of food with a given amount of labor and change systems of food supply to increase the regular availability of food. The increased production of food and the reduced need for physical labor to produce food along with the reduced need for calories to fight infection and increased ability to use ingested calories all resulted in less malnutrition and increasing height (Floud et al. 2011; Fogel 2004). Barker has emphasized the role of improved nutrition in increasing birth weight and to the link between improved mother's nutrition and less hypertension, insulin resistance and diabetes in offspring (Barker 2004; Barker and Osmond 1986; Hales and Barker 2001).

The heightened inflammatory response required for fighting infection, which is all important for survival, can also have a negative side for the development of chronic disease. Inflammatory substances are a substantial part of the atheromas, or deposits of plaque in the vascular system that increase with aging. If you survive to old age and have had heightened

inflammatory response throughout much of your life, you may have more deposits and arterial damage. When this is reduced throughout the lifespan with improving environmental conditions, the development of cardiovascular diseases and arterial stiffness should be delayed (Crimmins and Finch 2006; Finch and Crimmins 2004).

The inflammatory response to infection is also related to subsequent blood lipid levels as lipids act as mediators during the acute phase of innate immunity (Vasunilashorn et al. 2010). Infection and inflammation typically lower blood total cholesterol and high density lipoprotein cholesterol (Finch 2007; Jahangiri et al. 2009; Khovidhunkit et al. 2004; McGillicuddy et al. 2009). With reduction of infection there will be less remodeling of cholesterol resulting in higher levels of cholesterol, particularly HDL cholesterol (Vasunilashorn et al. 2010). Since high levels of HDL cholesterol are thought to be good; while high levels of LDL cholesterol are a risk factor for cardiovascular disease, the overall effect of this change is not clear.

To this point we have emphasized the positive aspects on physiology of the control of infection and the improved technology that has allowed increased food intake with reduced physical labor. But the resulting increases in weight beyond a certain level may also have had negative consequences in many countries (Beltran Sanchez and Crimmins 2013; Crimmins et al. 2013; Popkin 2006). Higher adult weight has been linked to multiple negative physiological outcomes including hypertension, insulin resistance, dysregulated lipids and diabetes (Clarke et al. 1997; Zheng et al. 2009).

This paper examines age differences in indicators of growth and development, and past and present nutritional status in a number of countries. While the entire analysis is cross-sectional, observed age differences will be used to suggest patterns of cohort change. Because these countries are currently at different stages of epidemiological and technological transition and have had different histories over the lifecycle of the age groups studied, intuiting different cohort patterns is an exercise in “reading history sideways” in the words of Arland Thornton (2004). For some biological indicators determined early in life, age differences clearly reflect different life experiences by cohort as - e.g. height. For others current physiological status, e.g. current BMI, reflects more recent conditions. Examination of the association of national levels of nutritional indicators with current levels of life expectancy and levels of infant mortality during the childhood of older persons, allows us to test the hypothesis that some indicators will be more strongly related to current life expectancy (e.g. BMI) and some to childhood conditions (e.g. height).

Then the paper clarifies how demographic and social factors are associated with variability in physiological indicators within countries. The links between indicators of physiology and nutrition and gender, education and place of residence are expected to differ across countries in ways that might indicate how epidemiological change is linked to individual nutritional differences (Beltran-Sanchez et al. 2011; Strauss and Thomas 2008; Vasunilashorn et al. 2013). For instance, rural/urban and education differences may reflect differential epidemiological and social histories as well as current circumstances. Gender differences in some markers, both across and between countries, may be suggestive of how both the epidemiological and technological revolutions differentially affect the lives of women and

men. Finally the associations between indicators of past and present nutrition, development, and demographic and social factors and cardiovascular and metabolic risk factors for chronic disease are examined within each country as links between nutritional indicators and risks for chronic conditions have also been shown to vary across countries (Tuan et al. 2009; Vasunilashorn et al. 2013; Yeom et al. 2010). This provides an assessment of how risk for chronic disease may be differentially influenced by past and current nutritional and developmental factors as well as social and demographic factors in different environments. We expect that the variability in associations will be greater for the more biologically rooted associations and not as strong for the socially determined associations, recognizing that the both influences are common in most of the associations.

Materials and Methods

Data

Data used in this analysis come from relatively recent nationally representative surveys, with one exception, which have included measurement of physiological status and blood-based biomarkers. Data sets include the US National Health and Nutrition Examination Survey (NHANES); the English Longitudinal Study of Ageing (ELSA); the Chinese Health and Retirement Longitudinal Study (CHARLS); the Social Environment Biomarkers of Aging Study (SEBAS) in Taiwan; the Indonesian Family Life Survey (IFLS); the Mexican Family Life Survey (MxFLS) and the Mexico-National Health and Nutrition Survey (ENSANUT 2006); the Japanese National Health and Nutrition Survey (JNHANS). For comparison data from the Tsimane Health and Life History Project are also included. The Tsimane are forager-horticulturalists who live in the lowlands of Bolivia and represent a population with relatively low levels of life expectancy and high levels of infant mortality (Gurven et al. 2007). For some of the samples, we have measures on adults age 20 and over (U.S., Japan, Mexico, Indonesia, Tsimane) for others (China, England and Taiwan) the sample includes individuals over age 45 or 50.

All of the data sets have included both surveys and the collection of biomarkers through direct measurement and the collection of blood. Venous blood was collected in all but the IFLS and the MxFLS where dried blood spots were collected. Most of the measures are based on relatively comparable venous blood based assays. We use the DBS data on C-Reactive protein from IFLS, which is not comparable to the values in other countries (Hu et al. 2013). In addition, while all of the labs used are certified to perform venous blood assays, differences in cholesterol values due to collection or assay procedures should be minimized by the use of the cholesterol ratio. All data, except those for the Tsimane, are derived from public use data files and are exempt from human subjects review. IRB approval was obtained from the University of Southern California for analysis of the Tsimane data.

Measures

All of the data sets include height as an indicator of physical status that reflects early effective nutrition and growth and development. We examine height and stunting or very short height ($\leq 155\text{cm}$ for male, $\leq 140\text{cm}$ for females) which serves as an indicator of both severe nutritional deprivation and severe experience with infection. We will also examine

current nutritional status using both low weight ($BMI \leq 18.5$) and high weight (obesity or $BMI \geq 30$) and the presence of anemia ($<130\text{g/L}$ for males; $<120\text{g/L}$ for females) as indicators of poor current nutritional status. Anemia, or low levels of hemoglobin, can be caused by undernutrition; it can also result from having parasitic infections and thus be related to current epidemiological conditions. Anemia is generally thought of as an indicator of malnutrition but in the elderly it can also be related to the presence of chronic disease (Clark 2008; Mittrache et al. 2001).

We have chosen four indicators of cardiovascular and metabolic risk for chronic disease related to ageing. The ratio of total cholesterol to high density lipoprotein (HDL) cholesterol which represents the ratio of “bad” cholesterol to “good cholesterol” (Crimmins et al. 2008). The level of C-Reactive Protein (CRP) which is a general systemic marker of inflammation. The level of glucose as represented by glycosylated hemoglobin (HbA1c) in most countries as is appropriate for nonfasting samples and fasting plasma glucose in China. Finally, pulse pressure (Systolic Blood pressure - Diastolic Blood Pressure) which is the best blood pressure indicator of the arterial stiffness characterizing aging (Crimmins et al. 2008). High levels of these markers indicate an increased risk for cardiovascular disease and mortality. In an earlier analysis we documented age differences across countries in these measures (Crimmins et al. 2013).

Environmental and Epidemiological Characteristics

Our set of studies includes information from countries at different stages of their epidemiological transitions. The Japanese are one of the world's longest lived populations, while the Tsimane are a pretransitional short-lived foraging-farming population in Bolivia. Table 2 shows the current level of life expectancy -and infant mortality along with the infant mortality in 1950 for each of these populations. Infant mortality in 1950 reflects the level of infection among children when people now 50–59 were babies; the change in infant mortality over the 50 years is a good indicator of epidemiological progress over the period. In 2005, Japanese males and females lived on average 83 years and had a very low level of infant mortality (3). At the other end of the continuum, the Tsimane are have a relatively short adult life expectancy and high infant mortality rate (Gurven et al. 2007). After Japan, England has the next highest life expectancy 80. While life expectancy in Taiwan is now similar to that of the US (78 years). Because of advances in medicine including the development of antibiotics countries with high levels of infant mortality in 1950 subsequently experienced rapid decline. Taiwan has undergone a much more recent and rapid epidemiological and demographic transition than the United States as evidenced by the change in infant mortality from 1950 to the present. Mexico, China and Indonesia are countries that have also had rapid changes in life expectancy and infant mortality although infant mortality remains relatively high.

Methods

We examine the age specific patterns within and across countries of each of the indicators of growth and development representing past nutritional status and current nutritional status across the entire adult age range where available. For these descriptive analyses we show data for only one gender in order to reduce the number of figures but the patterns are

generally the same for both men and women. The percentage of males and females 50 years of age and older with poor nutritional status according to each indicator is shown in Table 3. We examine the associations of these indicators at the country level with macro level past infant mortality for those 50–59 to show how they are associated.

In micro level regression analyses of those 50+ for each country except Japan, for which we do not have individual level data, we examine how age, sex, current rural residence and having a low level of education are related to past and current nutrition within each country. Low education is defined as up to middle school (up to 8 years for US; up to 9 years for Taiwan; through middle school for England; up to middle school for China; up to 9 years for Mexico). Rural residence is not available in the U.S. or English data set; the Tsimane have no formal education and non-rural residents are indicated as those who live close to settlements. We then examine how being stunted, having current low or high BMI, and having anemia and the social and demographic factors are related to continuous measures of cholesterol, blood pressure, glucose dysregulation and current levels of inflammation within each of the countries using OLS regression. Mean levels of the indicators of risk for chronic disease are also shown in Table 3.

Results

Early Growth and Development

In most of the populations average height of adults is lower at older ages indicating the increasing growth of subsequent cohorts; however, some of the drop in height at the oldest age is likely to reflect the loss of height with age among the old (Huang et al. 2013). There is significant variation by country in female height, Americans and English are the tallest and the Tsimane and Indonesians are the shortest (Fig 1). The Tsimane have little change with age reflecting a long period of relative stability in childhood environmental conditions for those over 20. While the Mexicans are also quite short, the Asian countries are in the middle with fairly similar levels. Americans also show little change between age 20 and 50 as maximum height was reached with cohorts born around in 1955–1965 without significant increases since then.

In these countries, stunting is much reduced for those younger than 50 (Fig 2). Stunting is extremely rare in the US and England but still quite high in Indonesia, up to 50% at the oldest ages. It is also high in Mexico, China and among the Tsimane, increasing markedly in those older than 50. The age pattern clearly indicates childhood growth deficits among those over age 50 in a number of countries, all of which are now reduced among younger people. Taiwan has much less stunting than China and has little pattern by age. Countries with lower infant mortality in 1950 have taller 50–59 year olds. It is likely that the heights of older people not only reflect poor development in childhood but shrinkage in older age. People over 60 in China are estimated to have experienced height shrinkage of about 3.5 cm on average and the shrinkage is greater among those with less schooling, lower family expenditures, and who do not live in urban areas (Huang et al. 2013). This implies that shrinkage at older ages could be greater in countries with lower heights to begin with.

The correlations between national height and stunting levels of persons 50–59 and the IMR for 1950 shown in Table 4 are very strong (–0.89 and 0.74 respectively with $N=7$), much stronger than those for current life expectancy. This supports our hypothesis that height would be more strongly related to indicators of childhood environmental circumstances.

Current Nutritional Status

Anemia is very high among the Tsimane, which could be related to their diet but may be related to a high level of parasites (Gurven et al. 2009; Larocque et al. 2005; Olsen et al. 1998; Pritchard et al. 1991; Vasunilashorn et al. 2010) (Figure 4). It is also very high in Indonesia and relatively so in China some of which may be related to malaria. Most of the other countries have fairly low levels of anemia. National levels of anemia among those 50–59 are equally associated with current life expectancy and past infant mortality but in the opposite direction (Table 4). Countries with high past infant mortality and low current life expectancy have high levels of anemia.

Current BMI indicates relatively recent conditions but it is certainly affected by conditions over the life cycle. The proportion with low BMI is very low in most of these countries except Indonesia, where it is fairly high at older ages (Figure 4). There is also a somewhat higher level of among older Chinese than in other countries. Thus, for most of these countries, except Indonesia, there is not much indication of undernutrition as indicated by low weight for height.

Countries with higher infant mortality in their past and lower current life expectancy have a higher percentage of 50 to 59 year olds with low BMI (Table 3). The relationship is stronger for the level of infant mortality.

The other side of the coin is overweight or obesity. Mexican and American women have the highest level of obesity (Figure 5). The English also have very high levels of obesity. We do not show any data for the Japanese because they do not report BMI in the obese category because it is so rare. The other four countries have low levels of obesity. Levels of obesity among the oldest age group are very low in many of the countries. This could partly reflect mortality at older ages among the obese but more likely it reflects past cohort history of little obesity.

Obesity is higher among 50–59 year olds who live in countries with higher life expectancy and who were born in places with lower infant mortality (Table 4). Again the association is stronger with our indicator of childhood levels of infection than with current life expectancy.

Associations of Demographic and Social Conditions with Indicators of Past and Current Nutrition

Within countries among those at least 50 years of age, older age which is also earlier cohort, is associated with being stunted. While the relative effect among the Tsimane is about the same as in other countries, the N is so low for the Tsimane that we ignore the significance level in this case. Older people are also more likely to have anemia and be underweight; China is the exception where the relative effect of age indicates that older people are less likely to be underweight. Older people are less likely to be obese than younger people

everywhere. So the older populations have more indicators of past and current under nutrition and/or exposure to poor environmental conditions but younger people are more likely to have the problem of being overweight or over nutrition. The associations between age and indicators of nutritional status are fairly similar across countries.

Females are significantly more likely to obese than males in all of the countries. The other nutritional differences by gender are less consistent. Women are less likely to be stunted in most countries; but not in China where the relative likelihood of stunting for females is almost 3 times that of males. There is no consistent gender difference in anemia. Females are more likely to be currently underweight in the U.S., England, and China. Thus gender is related to the indicators of nutrition quite variably across settings.

Where coefficients are significant, rural dwellers are more likely to be stunted and less likely to be obese. Underweight is more common among rural dwellers in Mexico and Indonesia but not in China where the odds ratio indicates that the likelihood of a rural dweller being underweight is 43 percent less than that of an urban dweller. There is modest consistency in the associations of rural living with the indicators of nutrition.

Links between education and stunting are quite consistent across countries; low education is linked to more stunting. Low education is also associated with more anemia but the relationship is not significant in 3 countries. Links between current weight and low education are not consistent. In the U.S. people with low education are relatively less likely to be underweight or obese. In Indonesia people with low education are more likely to be underweight; while in England, Mexico, and China, obesity is more common among those with low education. There is quite a bit of variability in the links between the nutrition indicators and education across countries.

Associations of Social and Demographic and Nutrition Indicators with Risk for Chronic Conditions of Old Age

We investigate associations between risks for chronic disease and social and demographic variables (model1) and then add past and current nutritional status (model 2): the ratio of TC/HDL, HbA1c, pulse pressure, and CRP (Table 6). We do not have measures of HbA1c in Indonesia and we do not have access to individual level data for several markers in Mexico. The variance explained in the ratio of TC/HDL is about twice as great in most countries when the set of nutritional makers are added to the equations indicating that they provide substantial explanatory power of variability within countries. In most countries being obese is associated with an increase in the lipid ratio; while having anemia or being underweight is associated with a lower value. Only in China is stunting associated with a reduction in the lipid ratio. There appears to be greater consistency in the associations for the nutritional variables than for the social status indicators. The U.S. and England are noteworthy as there is a significant educational difference with low education being associated with higher ratios; in Indonesia and China rural residence is significantly associated with lower ratios. Females in most countries have a lower ratio; and where age is significant, older age is associated with to a lower ratio.

Date for HbA1c are limited to 4 countries; and plasma glucose levels are analyzed for China. Results for the U.S. and England are fairly similar; the variance explained for HbA1c is about 5 percent in these countries; and the same coefficients are significant with similar signs and relatively similar values, only age is significantly positive in England but not in the U.S. Explanation is much poorer in both Taiwan and China, with only 2% of the variance explained in Taiwan and almost none in China. In England, the U.S., China and Taiwan obesity is related to higher glucose levels; and underweight to lower levels in China. Stunting is not related to HbA1c levels anywhere and anemia is positively related in England and the U.S. Women have higher level of plasma glucose in China, in contrast to the findings for HbA1c for the U.S. and England. While the sample size is quite small for the Tsimane, 22% of the variance in HbA1c is explained and the only significant variables is the indicator of rural residence which is associated with lower HbA1c.

A fairly high proportion of the variance is explained in pulse pressure by these equations: about a quarter in the U.S. and England and between 15 and 20 percent in Taiwan, China, and the Tsimane. In contrast to the two prior risk indicators, there is not much increase in the variance explained when the nutrition indicators are added to the equation. Among all but the Tsimane obesity was associated with higher pulse pressure; and in 4 countries underweight was significantly associated with lower pulse pressure. Stunting was associated with higher pulse pressure only in China. Females had significantly higher pulse pressure in most countries but there was no gender difference among the Tsimane and in England females had lower pulse pressure. In all countries, higher age was associated with higher pulse pressure.

Inflammation levels are associated with obesity and anemia in the U.S., England, Indonesia and China; and with low education in the U.S., England and Taiwan. Once other variables are controlled, older persons have higher levels if inflammation only in China and England. The relationship of gender is not consistent; women have higher inflammation in the U.S. and men in China. The variation explained is increased markedly in most countries once the nutrition variables are added.

Discussion

We asked whether there is evidence of physiological differences indicating past and current nutritional differences among older people across different environments. We find strong evidence that people in countries that have lower life expectancy and higher childhood infant mortality which also means a more recent epidemiological transition and increase in nutritional availability have aging populations who are shorter, more likely to be anemic, and more likely to be underweight. With epidemiological and nutritional increases underweight becomes rare and overweight becomes more prevalent. Patterns of age differences in nutritional indicators within countries indicate that these factors are likely affected by cohort experiences at specific ages.

Gender was not consistently related to past and current nutrition with the exception that obesity was more common among women everywhere. China stands out as a country where being female is more likely to be associated with indicators of poor nutritional experience.

Females are more likely to be stunted only in China; and China is the only country with relatively recent epidemiological and nutritional change where women were more underweight than men. China is also the only recently transitioning country where rural dwellers are less likely to be underweight. In Mexico and Indonesia it is rural dwellers who are more likely to be underweight. This may be indicative of different patterns of epidemiological and nutritional change in China and other countries. The roles of men relative to women may have differed in China from other countries as the relative development of rural and urban areas may have differed.

Within countries, the risk factors for chronic disease appear to be more associated with current nutritional status, particularly obesity, than to early life nutritional status. Obesity is related to higher levels of TC/HDL, HbA1c (or plasma glucose), and higher pulse pressure in all countries examined. It is related to higher inflammation in four out of six countries. This would suggest that improved nutrition and increasing weight could be a force for increasing risk factors of multiple types in all of these countries.

Underweight is significantly related to a lower lipid ratio in most countries and to lower pulse pressure in four countries. Underweight is not related to levels of inflammation or HbA1c except in the case of China where anemia is associated with lower HbA1c. Reductions in the level of underweight could thus be linked to increasing risks from lipids and pulse pressure.

Anemia is associated with lower levels of some risks and raised levels of other risks. Anemia is significantly negatively related to the lipid ratio in five countries. In the U.S. and England anemia is associated with higher HbA1c and inflammation and higher pulse pressure in the U.S.

Stunting, our clearest indicator of poor nutrition and/or infection in childhood, is not related to any of the risk factors for chronic conditions in most of the countries. Only in China is being stunted related to lower levels of the lipid ratio but to higher levels of pulse pressure. This seems to indicate that extremely poor development in early life has little association with these risk factors in later life in most countries.

Our analysis showed that undernutrition is very infrequent among younger adults in most of these countries; while overnutrition appears to be becoming increasingly prevalent in younger adults in most countries. Such trend would be an influence increasing risk from adverse levels of cholesterol, glucose, pulse pressure, and inflammation.

Human physiology has been honed over thousands of years. For most of this time, humans lived in a world that provided scarce resources and required hard work to acquire those resources. In addition, humans evolved in a highly infectious world. Now we live in a world of nutritional plenty, with low physical demands for many and markedly reduced levels of infection. Decline in infection and improved nutrition may have changed physiology for the better; but continuous increase in nutritional intake is now changing physiology adversely.

This analysis adds to the literature emphasizing the links between affluence and improved nutrition and increasing risks for chronic disease (Ezzati et al. 2005). It is unique in

providing individual level analysis in a number of countries, including indicators of both early life and later life nutrition, and in having measured biomarkers indicating risks for chronic disease characterizing multiple physiological processes. The significance of obesity on higher levels of all risk factors in most environments is remarkably consistent. The socioeconomic and demographic variables were less consistent perhaps indicating variation in these links with developmental stage as has been noted for obesity by Strauss and Thomas (2008) or sensitivity to past development strategies resulting the repeated differences between China and other countries.

This analysis has some limitations. Not all measures were available in all countries; sample size varied and was very small for the Tsimane; and individual level data were not available for the Japanese, a country for which more detail might provide important insights. In addition, it is possible that variability in procedures for blood collection and analyses could have affected the differences observed across countries in some of our blood-based measures. For this reason we focus on associations within countries. Another factor that may affect the levels of risk for chronic conditions is the use of medications which is not taken into account here. Finally, we are unable to directly measure nutritional intake nor infectious exposure as our measures are indirect indicators of overall growth and development. Nevertheless, the wealth of comparable data does allow us to assess the level of risk and the relative importance of early life and later life conditions on a set of risk factors for chronic conditions spanning major physiological systems.

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Fig 1.
Average Height by Age: Females

Fig 2.
Prevalence of Stunting ($\leq 155\text{cm}$): Males

Fig 3.
Prevalence of Anemia (Hemoglobin <13 g/dl): Males

Fig 4.
Prevalence of low weight – Current Undernutrition (BMI < 18.5): Males

Fig 5.
Prevalence of Obesity: Females

Table 1

Data Sources

	Study	Time of Data Collection	Age Range	N for study
US	National Health and Nutrition Examination Survey (NHANES)	2001–2006	20+	14,542
England	English Longitudinal Study of Ageing (ELSA)	2004	20+	7,081
Japan ^{<i>l</i>}	National Health and Nutrition Survey (NHNS)	2004	20+	6,509
Mexico	Mexican Family Life Survey (MxFLS) 2002	2002	20+	19,995
	National Health and Nutrition Survey ^{<i>l</i>} (ENSANUT06)	2006	20+	
Indonesia	Indonesian Family Life Survey (IFLS)	2007–2008	20+	26,045
China	Chinese Health and Retirement Study (CHARLS)	2011	45+	17,314
Taiwan	Social Environment Biomarkers of Aging Study (SEBAS)	2000, 2006	54+	1,284
Tsimane	UNM - UCSB Tsimane Health and Life History Project	2004–2010	20+	512

^{*l*} No individual level data

Table 2

Indicators of Mortality

	Life Expectancy at Birth 2010	Infant Mortality 1950–55	Infant Mortality 2000–2010
Japan	82.7	50	3
England	79.5	29	5
United States	77.9	30	6
Taiwan	78.0	49	5
Mexico	76.2	122	17
China	72.7	121	23
Indonesia	67.8	192	27
Tsimane	53.0	180	105

Data Sources: All countries except Taiwan and the Tsimane: IMR 1950 – UN World Population Prospects, IMR 2000–2010 - <http://unstats.un.org/unsd/demographic/products/socind/health.html>; Taiwan: LE - http://www.google.com/publicdata?ds=wb-wdi&met=sp_dyn_le00_in&idim=country, IMR 1950 - Griffith Feeney, Mortality and Fertility Decline, unpublished document; Taiwan IMR 2000–2010 - http://www.indexmundi.com/taiwan/infant_mortality_rate.html; Tsimane extrapolated from Gurven et al. 2007.

Table 3

(a) Percent of Sample Underweight, Obese, Stunted, with Anemia: Ages 50+								
	US	England	Mexico	Indonesia	Taiwan	China	Tsimane	
Males								
Underweight	1.04	0.60	2.46	19.90	2.40	7.53	1.24	
Obese	32.88	27.01	24.09	2.92	4.98	2.59	1.49	
Stunted	0.67	0.38	17.02	27.23	7.97	11.01	18.91	
Anemia	6.71	5.70	14.66	30.59	12.22	13.38	33.66	
Females								
Underweight	1.47	1.15	1.91	20.01	2.45	7.53	7.02	
Obese	35.54	30.67	36.73	7.20	9.86	6.35	12.57	
Stunted	0.17	0.60	9.51	12.09	1.75	23.93	2.05	
Anemia	6.49	6.32	14.54	35.63	11.41	14.58	19.02	

(b) Mean Lipid Levels, HbA1C ¹ , Pulse Pressure and Inflammation: Ages 50+								
	US	England	Mexico	Indonesia	Taiwan	China	Tsimane	
Males								
Total/HDL Ratio	4.41	4.24		5.52	4.53	4.13	3.73	
HbA1C ¹	5.77	5.65			6.18	110.57	5.63	
Pulse Pressure	58.04	60.02	57.77	59.91	59.18	55.80	50.37	
CRP	4.11	4.11		0.80	2.90	3.43	4.83	
Females								
Total/HDL Ratio	3.78	3.88		4.86	4.23	4.29	3.87	
HbA1C ¹	5.72	5.59			6.21	111.14	5.88	
Pulse Pressure	65.02	60.93	62.51	64.67	60.78	58.56	48.13	
CRP	5.33	4.39		0.64	2.62	2.69	11.62	

¹ Plasma Glucose for China

Table 4

Pearson Correlations of National Levels of Nutritional Status among 50–59 year olds and Current Life Expectancy and Infant Mortality in Childhood (N=7 or 8)

	Height	Stunting	Low Weight	Anemia	Obesity
Current LE	0.56	−0.30	−0.34	−0.90	0.52
IMR 50 years ago	−0.89	0.74	0.62	0.87	−0.74

Logistic Regression of Demographic and Social Indicators on Indicators of Childhood and Current Nutritional Status: Samples aged 50+, ORs [95% CI]

Table 5

	US	England	Mexico	Indonesia	Taiwan	China	Tsimane
Stunted (<=155cm for males, <=140cm for females)							
	n=6471	n=6683	n=2250	n=3045	n=1025	n=7945	n=116
Age	1.02* [1.02–1.02]	1.10* [1.07–1.13]	1.05* [1.04–1.07]	1.07* [1.06–1.08]	1.06* [1.02–1.09]	1.08* [1.07–1.09]	1.06 [0.98–1.15]
Female	0.26* [0.25–0.26]	1.17 [0.56–2.45]	0.53* [0.40–0.69]	0.27* [0.22–0.33]	0.20* [0.09–0.42]	2.64* [2.30–3.03]	0.01 [0.00–999]
Rural ⁸			2.51* [1.90–3.32]	1.55 [1.29–1.85]	1.65 [0.89–3.07]	1.69* [1.48–1.94]	0.94 [0.24–3.70]
Low Education ⁹	4.93* [4.89–4.97]	3.96 [0.98–16.00]	3.18* [1.39–7.56]	1.32 [1.09–1.61]	1.95 [0.84–4.57]	3.82* [2.52–5.80]	
Anemia (<130g/L for males; <120g/L for females)							
	n=6425	n=5331	n=2194	n=3017	n=1020	n=9152	n=118
Age	1.05* [1.05–1.05]	1.08* [1.07–1.09]	1.06* [1.05–1.07]	1.04* [1.03–1.05]	1.08* [1.05–1.10]	1.05* [1.04–1.06]	1.02 [0.97–1.07]
Female	0.88* [0.88–0.89]	0.92 [0.72–1.16]	1.14 [0.88–1.48]	1.24* [1.08–1.43]	0.95 [0.64–1.42]	1.09 [0.97–1.24]	0.62 [0.27–1.42]
Rural			1.00 [0.75–1.32]	1.15 [0.99–1.32]	0.93 [0.58–1.49]	1.02 [0.90–1.16]	0.65 [0.28–1.52]
Low Education	1.55* [1.54–1.55]	1.28 [0.97–1.70]	1.17 [0.72–1.89]	1.03 [0.88–1.21]	1.49 [0.84–2.64]	1.37* [1.10–1.70]	
Underweight (BMI<=18.5)							
	n=6384	n=6584	n=2234	n=3038	n=1024	n=7954	n=118
Age	1.02* [1.01–1.02]	1.04* [1.02–1.07]	1.05* [1.02–1.08]	1.06* [1.05–1.07]	1.08* [1.03–1.13]	0.97* [0.96–0.99]	0.99 [0.88–1.11]

	US	England	Mexico	Indonesia	Taiwan	China	Tsimane
Female	1.37* [1.37–1.38]	1.82* [1.02–3.26]	0.89 [0.47–1.66]	0.95 [0.79–1.14]	1.08 [0.48–2.47]	2.51* [1.96–3.22]	3.10 [0.31–30.98]
Rural			2.43* [1.30–4.54]	1.57* [1.32–1.88]	0.88 [0.33–2.39]	0.57* [0.46–0.72]	1.87 [0.18–19.41]
Low Education	0.98* [0.98–0.99]	0.53* [0.30–0.93]	4.98 [0.34–72.69]	1.34* [1.11–1.63]	1.18 [0.38–3.68]	1.08 [0.75–1.56]	
Obese (BMI>=30)							
	n=6384	n=6584	n=2234	n=3038	n=1024	n=7954	n=118
Age	0.98* [0.98–0.98]	0.98* [0.98–0.99]	0.97* [0.96–0.98]	0.94* [0.92–0.96]	0.98* [0.96–1.01]	0.97* [0.95–0.98]	0.98 [0.90–1.06]
Female	1.16* [1.16–1.17]	1.20* [1.07–1.34]	1.76* [1.45–2.15]	2.33* [1.75–3.12]	1.93* [1.17–3.17]	1.98* [1.53–2.55]	9.11* [1.10–75.66]
Rural			0.62* [0.50–0.77]	0.39* [0.29–0.54]	1.14 [0.66–1.97]	0.44* [0.32–0.59]	1.19 [0.26–5.34]
Low Education	0.91* [0.90–0.91]	1.43* [1.27–1.61]	1.60* [1.15–2.22]	0.76 [0.54–1.09]	1.62 [0.82–3.21]	2.47* [1.35–4.50]	

* p<.05

Rural: Tsimane – near town is not rural, all others rural

Low education: up to middle school (up to 8 years for US; up to 9 years for Taiwan; up to 11 years for England; up to middle school for China; up to 9 years for Mexico)

Table 6

OLS Regression Coefficients of Demographic and Social Indicators, and Indicators of Childhood and Current Nutrition on Indicators of Lipid Levels, HbA1c, Pulse pressure, Inflammation: Samples Aged 50+

a. Total/HDL Ratio						
	US	England	Mexico	Indonesia	Taiwan	China
Model 1						
	n=6323	n=5378		n=3004	n=1032	n=9235
Age	-0.02 *	-0.01 *		-0.01	-0.01	-0.01 *
Female	-0.60 *	-0.37 *		-0.73 *	-0.32 *	0.16 *
Rural				-0.35 *	-0.14	-0.37 *
Low Education	0.31 *	0.15 *		0.06	0.01	-0.03
R ²	0.064	0.049		0.020	0.022	0.015
Model 2						
	n=6048	n=5061		n=2992	n=1008	n=7618
Age	-0.01 *	-0.01 *		-0.00	-0.00	-0.00
Female	-0.61 *	-0.40 *		-0.72 *	-0.35 *	0.22 *
Rural				-0.30 *	-0.14	-0.30 *
Low Education	0.35 *	0.12 *		0.09	0.01	-0.05
Stunting	0.05	0.26		0.13	-0.06	-0.32 *
Underweight	-0.55 *	-0.60 *		-0.37 *	-0.82 *	-0.80 *
Obese	0.45 *	0.37 *		0.50 *	0.40 *	0.56 *
Anemia	-0.29 *	-0.15 *		-0.64 *	-0.26 *	-0.27 *
R ²	0.091	0.083		0.038	0.047	0.037
b. HbA1C (Plasma Glucose for China)						
	US	England	Mexico	Indonesia	Taiwan	Tsinane
Model 1						
	n=6471	n=5307			n=1032	n=8314
						n=55

b. HbA1C (Plasma Glucose for China)							
	US	England	Mexico	Indonesia	Taiwan	China	Tsimane
Age	0.00	0.01 *			-0.00	0.07	-0.02
Female	-0.05 *	-0.08 *			0.01	0.35	0.24
Rural					0.19	-2.26 *	-0.93 *
Low Education	0.27 *	0.07 *			0.16	0.76	
R ²	0.009	0.012			0.01	0.001	0.191
Model 2							
	n=6135	n=5066			n=1008	n=6955	n=45
Age	0.00 *	0.01 *			-0.00	0.12 *	-0.02
Female	-0.05 *	-0.10 *			-0.03	1.80 *	0.18
Rural					0.20 *	-1.86 *	-1.11 *
Low Education	0.29 *	0.06 *			0.15	1.88	
Stunting	-0.14	0.51 *			-0.24	-1.47	-0.22
Underweight	-0.21	-0.03			-0.21	-6.46 *	0.34
Obese	0.39 *	0.28 *			0.51 *	8.44 *	-0.55
Anemia	0.14 *	0.22 *			-0.04	-1.60	-0.29
R ²	0.050	0.046			0.020	0.008	0.218

c. Pulse Pressure							
	US	England	Mexico	Indonesia	Taiwan	China	Tsimane
Model 1							
	n=6271	n=6029	n=2184	n=3032	n=1025	n=8035	n=119
Age	1.11 *	0.68 *	0.56 *	0.76 *	0.73 *	0.70 *	0.45 *
Female	5.29 *	-0.75	5.66 *	3.68 *	2.16 *	2.69 *	-1.14
Rural			-2.29 *	-0.73	0.85	-0.88 *	0.03
Low Education	3.43 *	1.74 *	7.16 *	0.44	2.08	-0.47	
R ²	0.265	0.219	0.086	0.124	0.199	0.150	0.064
Model 2							

c. Pulse Pressure							
	US	England	Mexico	Indonesia	Taiwan	China	Tsimane
	n=5831	n=4520	n=2047	n=2989	n=997	n=7664	n=110
Age	1.09*	0.72*	0.58*	0.80*	0.73*	0.74*	0.66*
Female	5.02*	-1.12*	5.59*	3.38*	2.06*	2.24*	-1.94
Rural			-1.67	-0.39	1.23	-0.93*	2.56
Low Education	3.13*	1.50*	6.32*	0.72	1.82	-0.31	
Stunting	6.46	-1.23	-1.07	-0.06	-0.06	1.51*	-4.92
Underweight	-1.32	-3.64	-9.35*	-3.21*	-4.66	-3.00*	-19.75*
Obese	1.40*	1.52*	2.22*	4.87*	3.86*	2.79*	0.24
Anemia	6.50*	1.08	1.49	0.75	1.35	-0.52	-3.93
R ²	0.268	0.234	0.089	0.133	0.202	0.164	0.17

d. Inflammation (CRP)							
	US	England	Mexico	Indonesia	Taiwan	China	Tsimane
Model 1							
	n=6358	n=5378		n=1468	n=1032	n=9247	n=59
Age	0.00*	0.08*		0.01	0.04	0.05*	0.60
Female	0.12*	0.14		0.01	-0.46	-0.76*	5.99
Rural				-0.13*	0.23	0.10	5.72
Low Education	0.11*	1.02*		-0.05	1.47*	0.42	
R ²	0.008	0.013		0.005	0.016	0.005	0.087
Model 2							
	n=6079	n=5061		n=1461	n=1008	n=7628	n=57
Age	0.00	0.05*		0.01	0.02	0.05*	0.59
Female	0.13*	-0.17		-0.04	-0.61	-0.90*	2.96
Rural				-0.11	0.35	-0.11	2.91
Low Education	0.09*	0.91*		-0.08	1.40*	0.24	
Stunting	-0.18	-0.66		-0.15	-0.32	0.09	-2.43

d. Inflammation (CRP)							
	US	England	Mexico	Indonesia	Taiwan	China	Tsimane
Underweight	0.13	0.78		0.02	2.35	0.19	28.43
Obese	0.22*	2.01*		0.62*	-0.24	0.98*	-1.77
Anemia	0.36*	3.64*		0.18*	1.10	0.98*	-6.38
R ²	0.036	0.034		0.026	0.024	0.008	0.152

* p<.05