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Chapter 5

A Global Perspective on Physiological Change with Age

Eileen Crimmins, Felicia Wheaton, Sarinnapha Vasunilashorn, Hiram Beltrán-Sánchez, Lu Zhang and Jung Ki Kim

In Western countries, we think of certain physiological changes as part of normal "ageing." The idea that the levels of blood pressure and cholesterol rise, that weight increases, that functioning decreases is viewed as part of the ageing process. These physiological changes are monitored by physicians and health systems, and are associated with a significant portion of the use of prescription drugs. Physiological changes associated with age not only contribute to chronic disease, but also lead to disability, diminished quality of life and ultimately, mortality. Yet while ageing is inevitable, it is necessary to question whether the physiological changes we associate with ageing are the result of innate human biology and to what extent physiological age changes are shaped by the social environments in which we live.

In this chapter, we examine global differences in a number of markers of ageing to show that there are many patterns of physiological differences with age depending on environmental, cultural, economic, medical and historical circumstances. The observed differences highlight that what we regard as the ageing process is not consistent across countries and is very influenced by environmental circumstances. The differences that we observe suggest that these processes may be changing rapidly in much of the world and that much of what we have assumed to be normal physiological changes with ageing may reflect the environmental circumstances in modern Western or American society. These societies have undergone demographic and economic revolutions that are now ongoing in the rest of the world where newly ageing populations have lived through the entire economic and demographic transition.

Recently, a number of nationally representative surveys of ageing populations have added biomarkers to their data collections. The inclusion of measured physiology in social surveys allows for the comparison of markers of health which cannot be reported accurately by respondents in many circumstances. The ability to compare these measured indicators across societies allows us to make generalizations about ageing that have, heretofore, not been possible. To investigate whether physiological changes with age are universal, we examine age differences in a number of markers of physiological dysregulation associated with ageing across a range of populations including Japan, the United States (US), England, Taiwan, two provinces in China, Mexico, Indonesia and the Tsimane of

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Bolivia. The synthesis of findings from different countries can lead to a deeper understanding of how physiological changes are shaped by social, economic and epidemiological factors. Different environmental contexts can serve as natural laboratories to explore how different combinations of macro-level and micro-level factors influence health in later life.

Data and Methods

Data Sources

We use data on measured biomarkers from recent surveys of national populations or extensive national sub populations to examine current age- and gender-specific patterns of blood pressure, body mass index, cholesterol and glycosylated hemoglobin (HbA1c). Data sets include the US National Health and Nutrition Examination Survey (NHANES) 2001–2006, the English Longitudinal Study of Ageing (ELSA 2004), the China Health and Retirement Longitudinal Pilot Study of two provinces Gansu and Zhejiang (CHARLS 2008), the Social Environment Biomarkers of Aging Study (SEBAS) in Taiwan (2000), the Indonesian Family Life Survey (IFLS 2007–2008), the Mexican Family Life Survey (MxFLS 2002), Mexico- National Health and Nutrition Survey (ENSANUT 2006),[1] Japanese National Health and Nutrition Survey (2004) and the Tsimane Health and Life History Project (2003–2007). For most populations, we have measures on adults age 20 and over, with the exception of China, England and Taiwan, where the sample includes individuals over age 50.

Our set of studies includes information from a wide range of countries at different stages of their demographic transitions; from the world's longest lived population – the Japanese – to a pretransitional short-lived foraging population in Bolivia – the Tsimane. In 2005, Japanese males and females lived on average 79 years and 85.7 years, respectively (Figure 5.1). At the other end of the continuum, the Tsimane are forager-farmers of the Bolivian Amazon with short adult life expectancy (42.6 years, estimated from 1950–1989) relative to other countries (Gurven et al. 2008). They represent a model for ageing in preindustrial human populations due to their high infectious morbidity and natural fertility (Walker et al. 2008), variable energy balance with high workloads and short life expectancies. After Japan, England has the next highest life expectancy. While life expectancy in Taiwan is now similar to that of the US (76 and 81 years for males and females, respectively), Taiwan has undergone a much more recent and rapid epidemiological and demographic transition. Mexico, China and Indonesia are countries that are in the process of rapid changes in nutrition and income accompanied by increases in life expectancy.

1 Figures 5.2, 5.2, 5.3, 5.4 and 5.5 use data from the MxFLS. Figures 5.6, 5.7 and 5.8 use data from ENSANUT.

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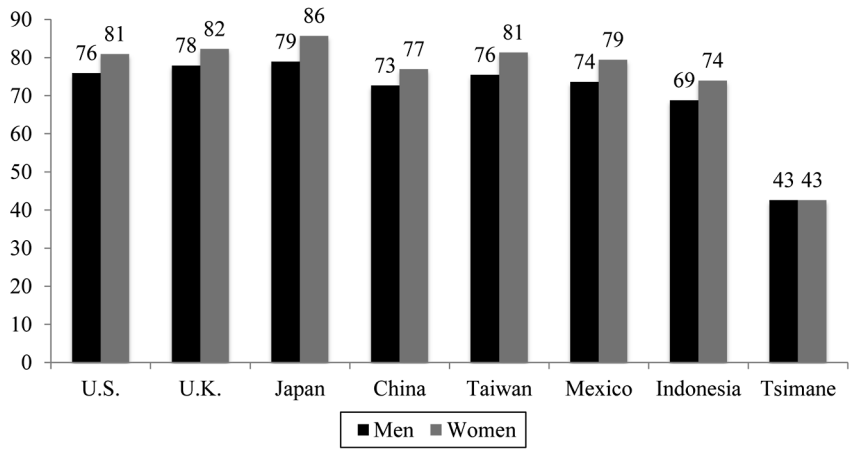

Figure 5.1 Life expectancy at birth, 2011
Note: Data from 1950–1989 calculated by Gurven et al. 2008.
Source: World Factbook, 2011 by CIA.

Measurement of Physiological Status

In large-scale population studies, the commonly collected biomarkers related to physiological ageing usually reflect cardiovascular functioning and metabolic indicators. The surveys we use have collected measured anthropometric indicators of height and weight, measured blood pressure from which we can elicit systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse pressure (PP), which is the difference between SBP and DBP. Pulse pressure reflects stiffness and inflammation in the blood vessels and some research has suggested that pulse pressure is a better indicator than either SBP or DBP of cardiovascular risk among the old (Blacher et al. 2000, Crimmins et al. 2008, Franklin et al. 2001).

Many studies that have collected blood samples have indicators of lipid levels including total cholesterol and high-density lipoprotein (HDL) cholesterol. Because most of these population samples do not have the subjects fast before collection, low-density lipoprotein (LDL) cholesterol is not recorded. We also examine the ratio of total cholesterol to HDL cholesterol as some research has suggested it is the ratio of the two, rather than the independent levels, that is important (Crimmins et al. 2008). A limited number of countries have information on HbA1c, which is an indicator of blood glucose concentration over the past few months. This can serve as an indicator of the presence of diabetes, prediabetes, or the control of diabetes among diabetics.

In each country, we examine the average level of markers or the percent (prevalence) of the population above the clinically determined level for defining risk for age-sex groups within a population (See Figures for definitions). For the

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measure of pulse pressure and the ratio measure of total/HDL cholesterol we show levels by age rather than percent elevated. We also examine the links between prevalence of risk levels of these markers and life expectancy, urbanization and per capita gross domestic product in these populations.

Age Differences in Physiological Markers

While we are interested in physiological change with age, we examine cross-sectional differences in physiological markers by age. Longitudinal data, which in most cases we do not have, would be required to look at individual change with age. We are cognizant that while age differences may be due to changes in physiology with age, they could also result from cohort differences in physiology or to differential survival of the most physiologically healthy into the oldest ages. Many physiological measures change in a predictable manner with age, others are less predictable; some biomarkers increase or decrease with age, while others follow a U-shaped pattern with respect to age differences (Glei et al. 2011). In the following sections we examine each set of markers in turn; first the cardiovascular markers and then the metabolic indicators.

Blood Pressure

Normal arterial ageing, including thickening and stiffening of arterial walls, leads to an increase in systolic blood pressure with age, even in the absence of cardiovascular disease (Finch 2007). Between age 20 and 80, systolic blood pressure has been shown to increase by about 22% (O'Rourke and Nichols 2005); however, not all research indicates that blood pressure increases in populations throughout the age range. Examination of age differences in SBP in the US population shows that increases in SBP occur in middle age but that in old age the level of SBP in the population plateaus (Crimmins et al. 2006). A longitudinal study by Glei and colleagues (2011), studying people age 45 and over in Taiwan, found little age-related increase in SBP over 6 years, which they attribute to the period effect of increased use of anti-hypertensive medication.

In contrast, diastolic blood pressure is thought to follow an inverse U-shape with age (Franklin et al. 1997). Diastolic blood pressure has been observed to increase until age 55 and then decrease after age 60 (Yashin et al. 2006). As DBP decreases at older ages and SBP continues to increase, there is generally an age-related increase in the prevalence of high pulse pressure (Skumick, Aladjem and Aviv 2010). The age changes may not be the same among all groups in the population; at the younger years DBP among women is lower than that of men, but it increases more rapidly with age (Yashin et al. 2006) and in the US high blood pressure among older adults over age 70 is greater among women than men (Kim et al. 2006). Average pulse pressure has been shown to more than double between age 20 and 80 (O'Rourke and Nichols 2005).

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Blood pressure varies across countries and has been shown to change over time within countries. Generally, in comparison to industrialized populations, traditional populations and less urbanized societies have lower levels of blood pressure, less increase in blood pressure with age and lower rates of hypertension (Gurven et al. 2009, Ostfeld and D'Atri 1977, Page 1976, Pavan et al. 1997, Poulter and Sever 1994, Waldron et al. 1982). It is clear, however, that a number of characteristics contribute to variability in blood pressure across populations including salt intake and culture (Waldron et al. 1982). It has been suggested that the link between industrialization and blood pressure may result from changes in social organization and structure that accompany industrialization (Carvalho et al. 1985, Cassel 1975, Epstein and Eckoff 1967, Lowenstein 1961, Marmot 1980, McGarvey and Baker 1979, Patrick et al. 1983, Prior and Stanhope 1980, Waldron et al. 1982). Overall levels of blood pressure and its increase with age, have been shown to be higher in people with more involvement in money economy, greater economic competition and more contact with individuals of different beliefs and cultures (Cooper et al. 1997, Waldron et al. 1982).

Figures 5.2 and 5.3 show the prevalence of men and women with hypertensive levels of SBP and DBP. Mexico, Indonesia and Japan have the highest prevalence of hypertension, while the US has relatively low hypertension, which is at least partly related to extensive use of medication to control blood pressure in the US (Crimmins et al. 2010). The Tsimane have almost no high systolic blood pressure even at older ages. More generally it has been reported that arterial disease is much lower in the Tsimane than among US adults (Gurven et al. 2009, Vasunilashorn et al. 2010). Countries with higher prevalence of high SBP (Figure 5.2) also have a higher prevalence of high DBP (Figure 5.3). High-risk levels of DBP are more common in Mexico, Indonesia, Japan and Taiwan than in the US or England or among the Tsimane (Figure 5.3).

If we did not include the Tsimane in our comparison, we might conclude that the substantial increase in high SBP was universal. However, the fact that high blood pressure is rare among the Tsimane suggests that contextual, social and dietary factors also play an important role. Also, some of the highest prevalences of high systolic and diastolic blood pressure in both sexes are observed in Mexico and Indonesia, countries with relatively low levels of income compared to the US, Japan and England. Both countries have undergone rapid epidemiologic and nutrition transitions in the past several decades and these risk factors seem to be more prevalent at younger ages than in more developed countries. Finally, there appears to be variation between countries not only in the absolute prevalence of high systolic and diastolic blood pressure at a given age, but also substantial variation in the shape and inflection points of the age trends.

Mean pulse pressure with age increases in all countries and the pattern of increase with age are quite similar across countries (Figure 5.4). At the younger ages, the differences across countries are quite small but they increase with age and are quite large at the oldest ages. The countries with high pulse pressure include Indonesia and Mexico; on the other hand, the Tsimane have relatively low pulse pressure.

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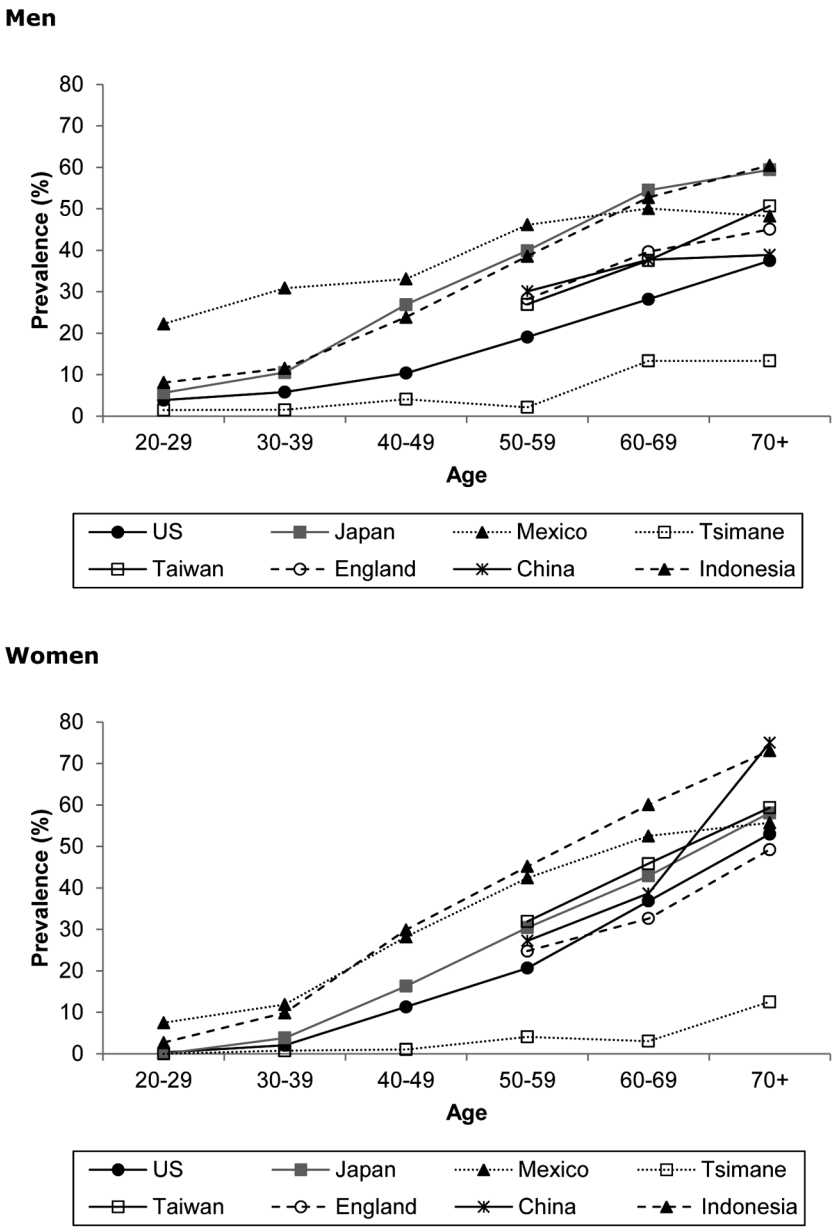

Figure 5.2 Percent with high systolic blood pressure (≥ 140 mm Hg) by country and sex

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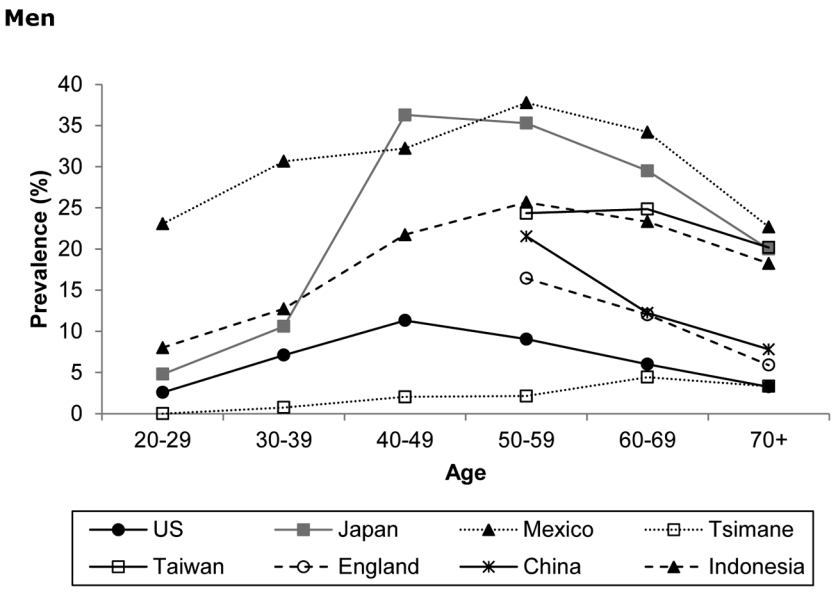

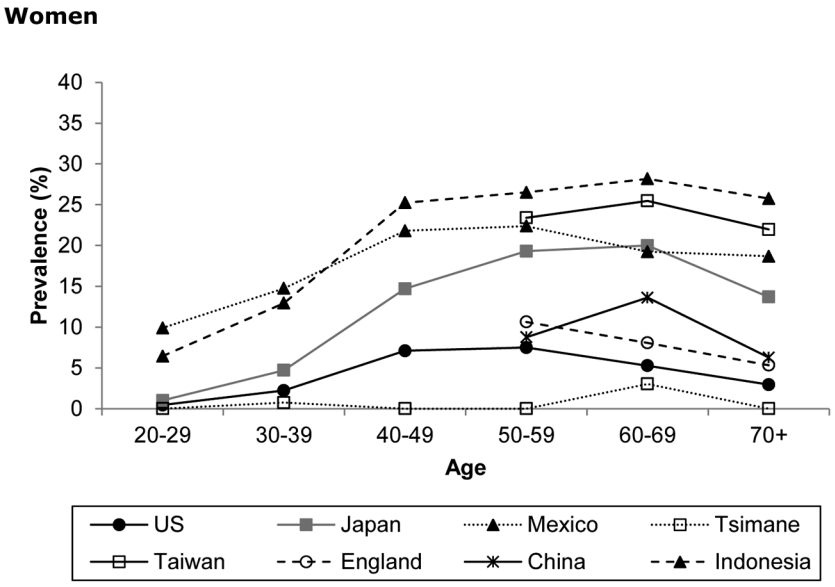

Figure 5.3 Percent with diastolic blood pressure (≥ 90 mm Hg) by country and sex

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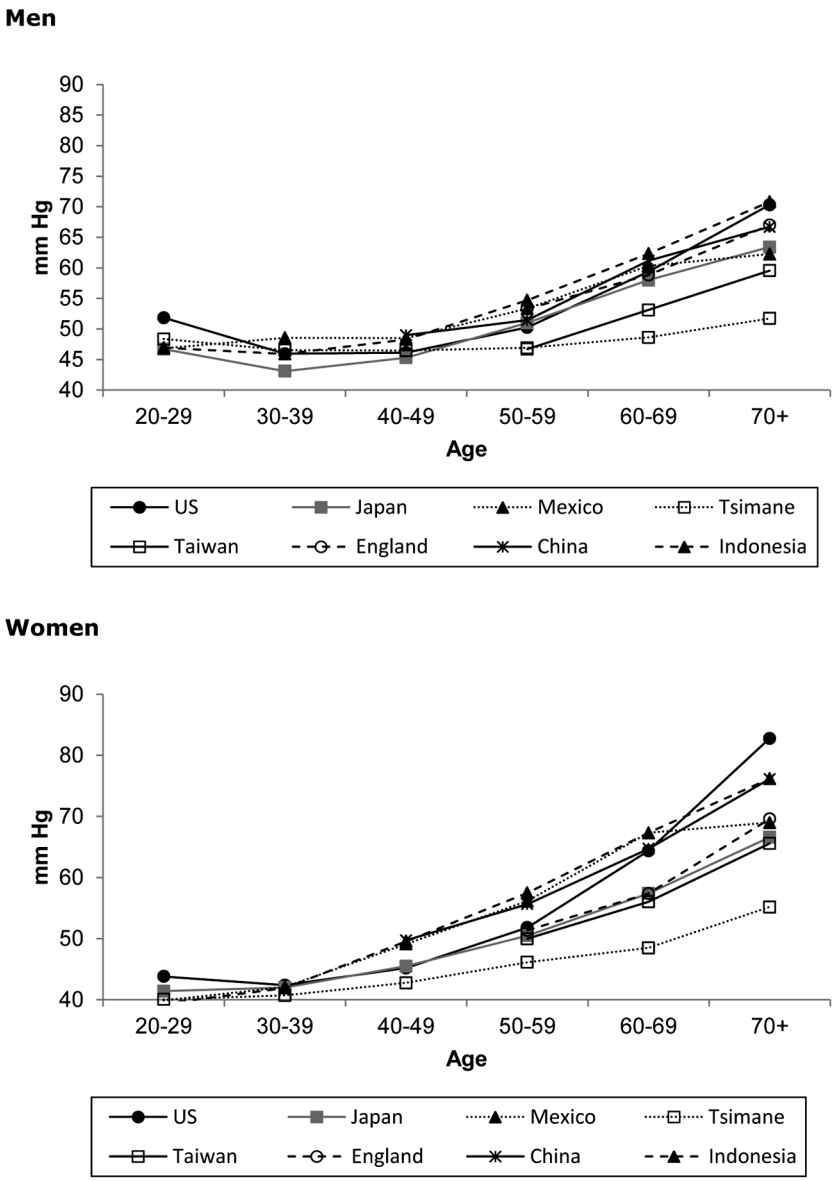

Figure 5.4 Mean pulse pressure by country and sex

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Body Mass Index

In general, body mass index (BMI) and the prevalence of overweight and obesity in populations have been found to increase until about 60 years of age, after which weight tends to decline (Seidell et al. 2000). Most studies on BMI changes with age are cross-sectional and therefore, while this pattern may be due to age changes, cohort differences in BMI and selective survival of those with lower BMI could also explain the observed lower BMI level at older ages. Several studies have in fact documented that later cohorts have a higher BMI at a given age compared to older cohorts at the same age (Juhaeri et al. 2003, Nooyens et al. 2008, Sheehan et al. 2003). There is also evidence that links obesity in early and mid life to earlier mortality (Lewis et al. 2009). For example, results from a life-table analysis of data from the Framingham Heart Study show that at age 40, obese non-smokers had a life expectancy of about 6 to 7 years shorter than those who were not obese (Peters et al. 2003). Lower survival among the obese could help explain the suggestion that cross-sectional studies underestimate the association between BMI and mortality (Nooyens et al. 2008).

BMI has been shown to be lower in traditional than in industrialized populations and to increase with gross domestic product (GDP) (Pavan et al. 1997, Strauss and Thomas 2007). It has also been shown to have increased over time in most countries. Many studies, from Africa and Asia to the Americas and Europe, have observed increasing numbers of overweight and obese individuals. These increases have been associated with dietary changes occurring across geography, culture and stage of development (Galal 2002, Kosulwat 2002, McHiza and Steyn 2011, Misra et al. 2011, Misra, Singhai and Khurana 2010, Pomerleau et al. 2003, Popkin 2010, Rivera et al. 2002, Neila et al. 2011). The rise in urban living, international trade and global economic integration has brought wide availability of cheap processed food, fast food, sweeteners and edible oils. Concurrent improvements in standard of living and household income, especially among rapidly developing nations, have resulted in personal dietary changes including the reduction of vegetable and fruit consumption and the increase in animal-sourced foods (Misra et al. 2011, Popkin 2001, 2008, Popkin, Lu and Zhai 2002).

The prevalence of overweight (BMI[3] 25kg/m^2) by age group, sex and country is shown in Figure 5.5. In most country populations, it appears that BMI increases until middle age, i.e. about age 45 and then decreases later in life. There are clearly two groups of countries in Figure 5.5. People in Mexico, the US and England are far more likely to be overweight than in the other countries. On the other hand, the prevalence of overweight is relatively low in the Asian countries and among the Tsimane. Japanese women are particularly unlikely to be overweight although the prevalence has a faster increase with age than in any other country. Among men, Indonesians are the least likely to be overweight across all ages.

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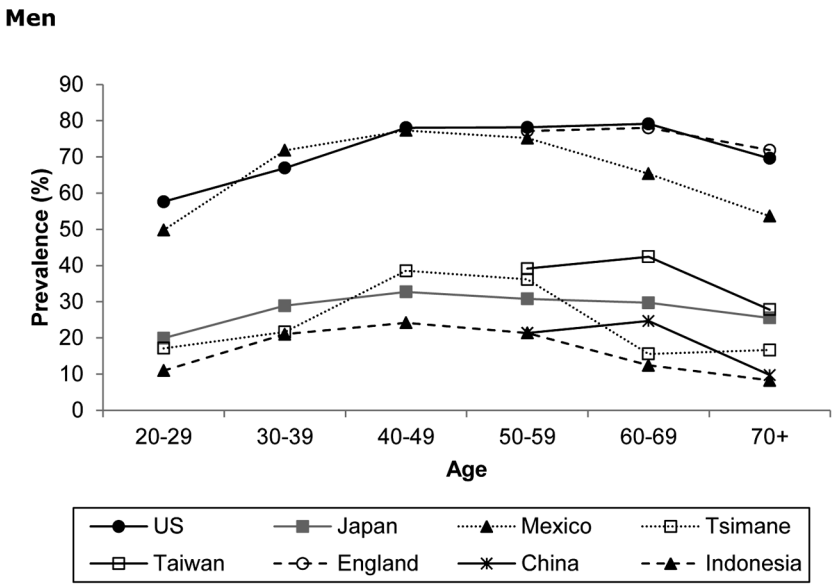

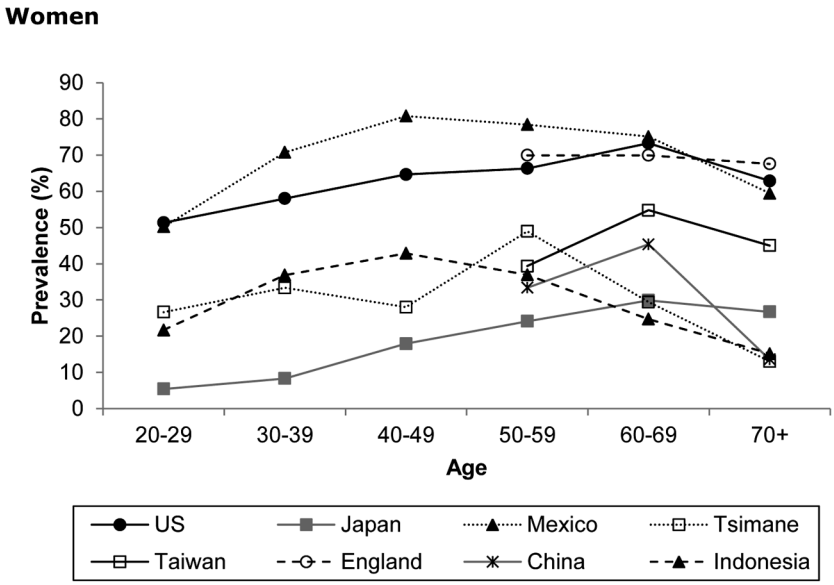

Figure 5.5 Percent overweight (body mass index ≥ 25 kg/m^2) by country and sex

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Cholesterol

Total cholesterol has been recognized as having an inverted U pattern with age in both cross-sectional and longitudinal studies. Studies based on the US show that total cholesterol tends to increase until approximately age 50 among men and age 60 among women (Schubert et al. 2005). In women, total cholesterol then plateaus until about age 70 after which it declines, while in men, total cholesterol begins to decline at age 50 and declines at an accelerating rate after age 70 (Yashin et al. 2006).

National differences in total cholesterol may be linked to both diet and epidemiological conditions. Increases in calorie intake, particularly intake of saturated fats, have been associated with higher cholesterol levels (Clarke et al. 1997, Mattson, Erikson and Kligman 1972). In subsistence populations, where food containing high saturated fats is less available than in modern societies, cholesterol levels are lower (Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults 2001, Gurven et al. 2009, Lindeberg et al. 2003, Pauletto et al. 1996, Pavan et al. 1997). While in general, cholesterol levels among the global ageing population are rising, this escalation is most drastic among rapidly developing nations due to increases in high-fat diets. Less developed nations are experiencing growing cholesterol levels in highly urbanized areas, while these levels have general stabilized or dropped in developed nations due to greater health education and awareness of the effects of diet (Deaton et al. 2011, Levenson, Skerret and Gaziano 2002). The Tsimane, who still have high levels of infection in their population, should have relatively low levels of cholesterol as infection typically lowers both total cholesterol and high density lipoprotein (HDL) cholesterol (Finch 2007, Vasunilashorn et al. 2010).

Measured high total cholesterol is highest among English men and Chinese and English women (Figure 5.6). It is exceptionally low, or almost non-existent, among the Tsimane. The other countries have roughly similar levels although Indonesia and Taiwan are on the low side. The US has moderate values; however, it is important to note that the US is the country where measured cholesterol is most likely to be reduced by the use of drugs. Young Japanese women have very low levels of high cholesterol but the increase with age is sharp in this group. For men, most of the increase with age in total cholesterol occurs before age 40–49; for women, the increase continues to older years as shown in earlier literature (Kim et al. 2006).

National differences in low HDL cholesterol are not the same for women and men (Figure 5.7). In Indonesia, men have very high prevalence of low HDL cholesterol; Japan, China and England have low levels. Among women, Mexico, Indonesia and the Tsimane are quite high in adverse levels of HDL. HDL is the lipid we expect to be more related to infection and this may be more true for women than for men. Among women, adverse levels of HDL cholesterol are low in the US, Japan and China. There is no pattern of increase with age in adverse levels of HDL cholesterol in any of the countries.

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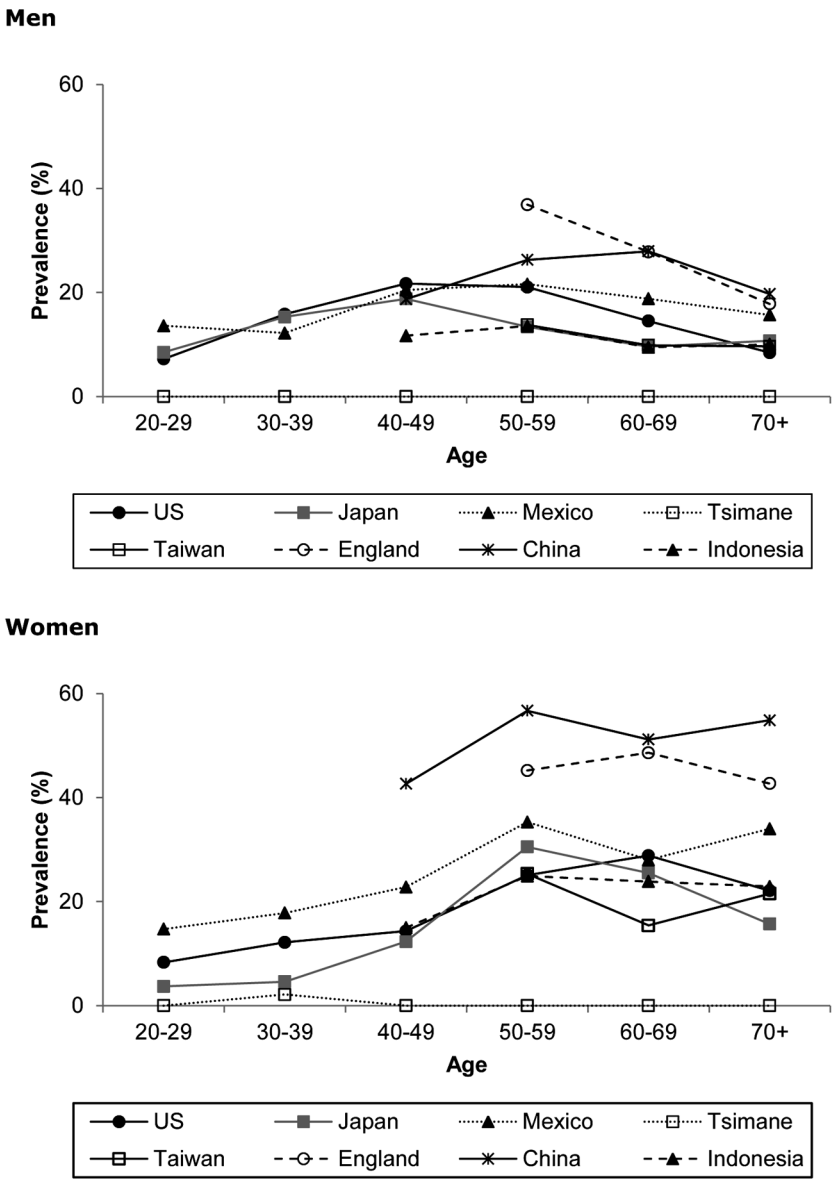

Figure 5.6 Percent with high total cholesterol (≥ 240 mg/dl) by country and sex

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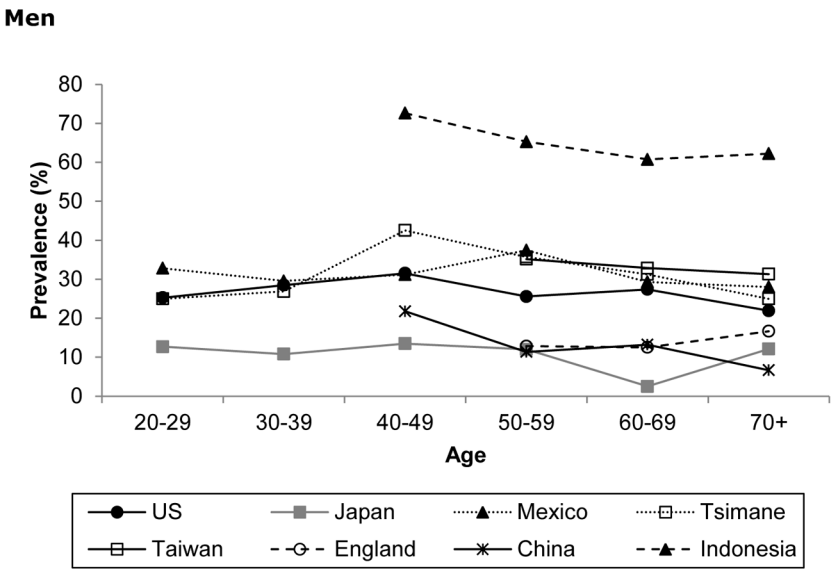

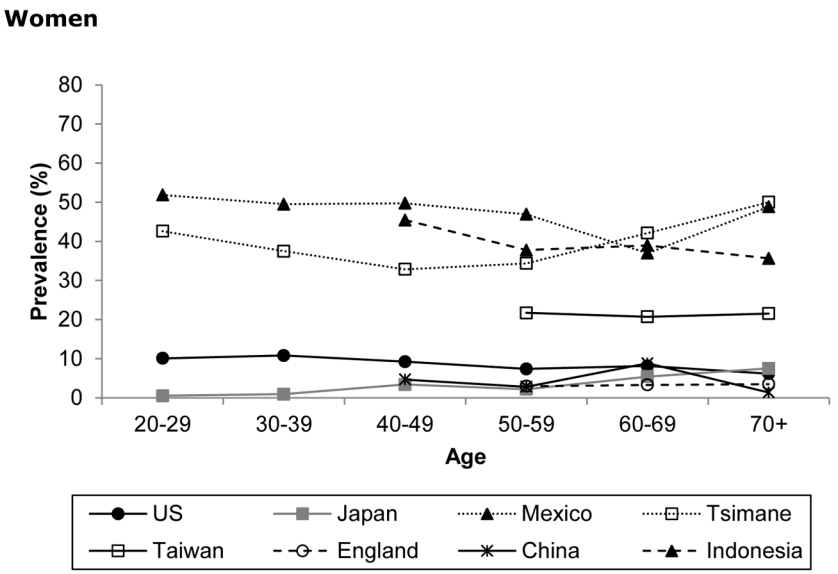

Figure 5.7 Percent with low HDL cholesterol (< 40 mg/dl) by country and sex

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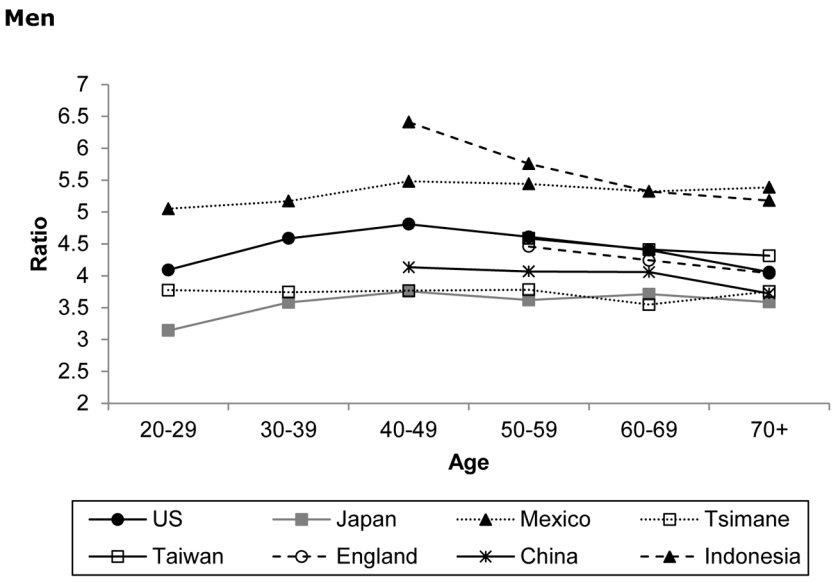

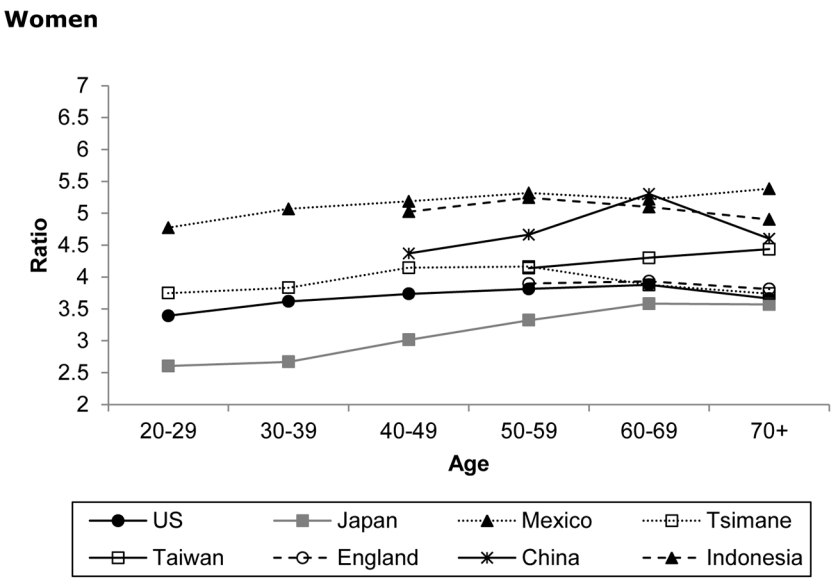

Figure 5.8 Mean total/HDL cholesterol (mg/dl) ratio by country and sex

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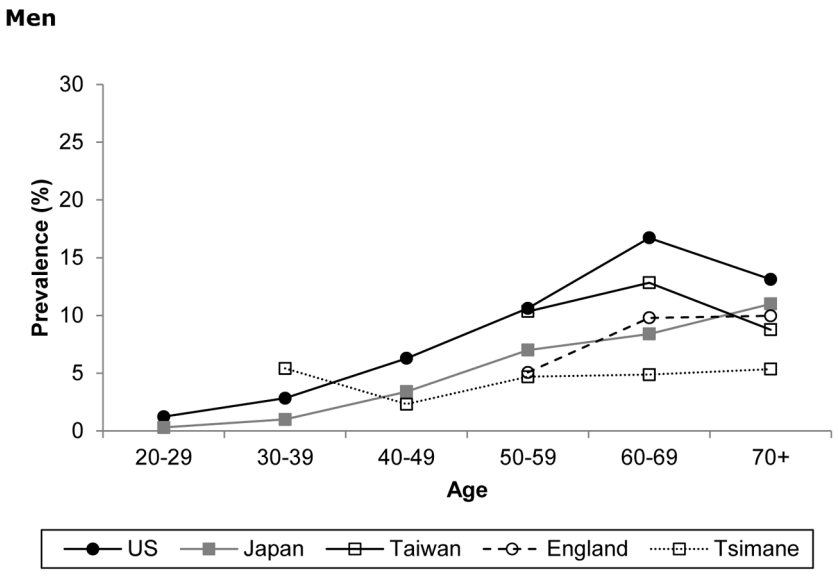

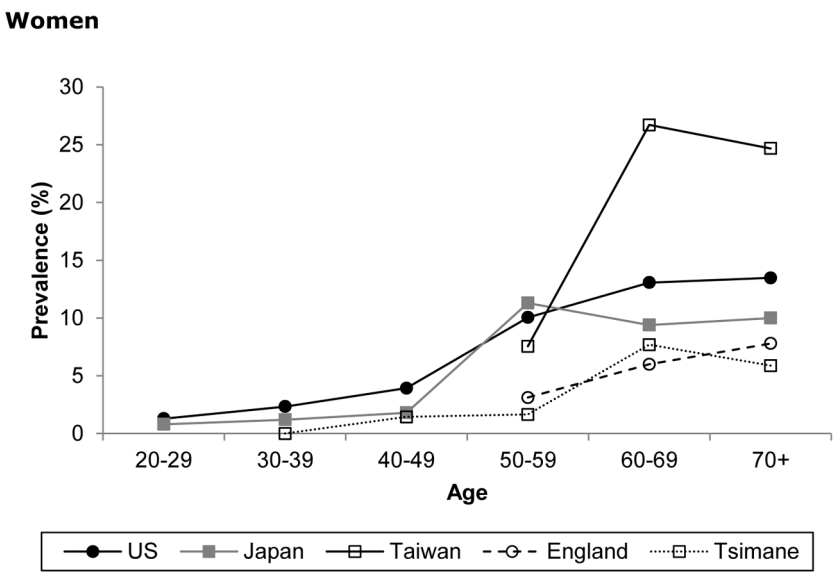

Figure 5.9 Percent with high glycosylated hemoglobin (≥ 6.4%) by country and sex

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We also present the ratio of total to HDL cholesterol (Figure 5.8). There is little pattern of age change in this ratio, except among Japanese women. The age pattern for total/HDL cholesterol is more similar across all countries than the patterns observed for the independent measures of total cholesterol (Figure 5.6) and HDL cholesterol (Figure 5.7). The ratio is, however, particularly high among Indonesians and Mexicans.

Glycosylated Hemoglobin (HbA1c)

The prevalence of diabetes mellitus increases with age, at least up to the older ages, and many studies find a positive association between age and blood glucose and HbA1c (Chiu, Martinez and Chu 2005, Pani et al. 2008, Yashin et al. 2006). National differences in insulin regulation may also arise from diet and weight differences. Insulin regulation may be affected by increasing weight and increasing food consumption. Increases in diabetes have been noted in many countries undergoing industrialization (Zheng et al. 2009). The prevalence of type 2 diabetes has surged across older populations worldwide (Jia et al. 2002, Misra, Singhai and Khurana 2010, Rivera et al. 2002).

We have information on HbA1c from only five populations: the US, Japan, Taiwan, England and the Tsimane. The Tsimane generally have very low prevalence of elevated HbA1c (Figure 5.9). English women also have relatively low levels. Countries with high adverse levels of HbA1c also differ for men and women. The United States and Taiwan are high for men; among women, Taiwan is exceptionally high particularly at older ages.

Social Indicators

We hypothesized that physiological changes with age are not only the result of biological ageing, but are also influenced by social processes that vary considerably across countries. We examine correlations between country-level indicators of social and economic development and the average prevalence or level of each of the biomarkers discussed above for the 50–59 age group by sex. We choose to examine the rates for those aged 50 to 59 because biological risk at these ages tends to have risen from values found among younger age groups, yet selective mortality is not as extensive as that which has occurred among older age groups. Correlations were not calculated for the prevalence of high HbA1c because this measure was only collected in five of the eight studies. The Tsimane were excluded from the correlations because they are an extreme outlier in terms of life expectancy and data are not available on the other social indicators.

To examine the association between social factors and biological measures in the fifth decade, we employ the following country-level indicators: life expectancy,

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per capita gross domestic product and percent urban (CIA 2011). Higher levels of these indicators signify greater development and a later stage in demographic and epidemiologic transition.

In general, the correlations in Table 5.1 suggest that life expectancy is negatively associated with most measures of biological risk, although the relationship appears stronger for some measures than others. For instance, there is a fairly high negative correlation between life expectancy and the prevalence of low HDL cholesterol, particularly in men (r = -0.77) and the ratio of total to HDL cholesterol in both men and women (r = -0.74 and r = -0.85, respectively). Among women, mean pulse pressure and prevalence of high SBP are negatively correlated with life expectancy, but this relationship is much weaker among men. The exception to the negative relationships is the positive relationship between life expectancy and the percent overweight among men (r = 0.42).

Table 5.1 Correlations between social indicators and biological measures

	Life expectancy	**GDP**	**Urban**
Men			
Prevalence of high SBP	-0.25	-0.62	-0.23
Prevalence of high DBP	-0.07	-0.45	-0.17
Mean pulse pressure	-0.41	-0.58	-0.31
Prevalence of overweight	0.42	0.53	0.93
Prevalence of high total cholesterol	0.26	0.08	0.38
Prevalence of low HDL cholesterol	-0.77	-0.44	-0.36
Ratio of total/HDL cholesterol	-0.74	-0.47	-0.12
Prevalence of high SBP or medication	**0.07**	**-0.12**	**0.31**
N	**7**	**7**	**6**
Women			
Prevalence of high SBP	-0.52	-0.72	-0.43
Prevalence of high DBP	-0.21	-0.39	-0.33
Mean pulse pressure	-0.87	-0.90	-0.63
Prevalence of overweight	0.02	0.22	0.76
Prevalence of high total cholesterol	-0.11	-0.36	-0.20
Prevalence of low HDL cholesterol	-0.52	-0.52	-0.11
Ratio of total/HDL cholesterol	-0.85	-0.84	-0.43
Prevalence of high SBP or medication	**-0.36**	**-0.18**	**0.06**
N	**7**	**7**	**6**

Note: GDP = gross domestic product; % Urban = percent living in an urban area; SBP = systolic blood pressure; DBP = diastolic blood pressure; PP = pulse pressure; HDL = high density lipoprotein.

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Most markers of cardiovascular and metabolic dysfunction are also negatively correlated with per capita GDP and proportion of the population that is urban, with the exception of prevalence of overweight, which is positively associated with all country-level social indicators. In particular, higher GDP is associated with a lower prevalence of high SBP and lower mean pulse pressure and ratio of total to HDL cholesterol. In general, the correlations between urbanization and most measures are weaker than those found for GDP. However, greater urbanization is strongly correlated with higher prevalence of overweight.

It is interesting that the percent urban relates to the biological indicators somewhat differently than the other measures. Overweight, hypertension, high cholesterol, diabetes and other risk factors appear to be more prevalent in urban settings, at least in developing countries (Beltrán-Sánchez et al. 2011, Njelekela et al. 2003, Sobngwi et al. 2004, Yang et al. 2010). The association between urbanization, globalization and health is thought to be, at least in part, due to changes in diet and physical activity (Popkin 1999, Rivera 2002, 2004). The rapid urbanization now occurring with increasing life expectancy may be changing the links between the epidemiological transition and the rise in overweight.

Health Care Systems

Health care system features likely contribute to differences in physiological ageing across countries due to differences in treatment and control of some biological risk factors. In contexts where infectious diseases are still highly prevalent, health care systems may be more oriented toward treating infectious disease than toward the prevention and management of chronic conditions. In the face of rising chronic disease prevalence, health care systems in many lower-income countries are financially and structurally poorly equipped to meet the health needs of a rapidly ageing population. Substantial variation exists between countries in rates of awareness, treatment and control of chronic conditions. These tend to be higher in more developed countries (Ong et al. 2007, 2008) compared with less developed countries (Blondin and Lewis 2007, Porapakkham, Pattaraarchachai and Aekplakorn 2008, Rampal et al. 2008).

Awareness, treatment and control of biological risk factors depend in part on access to health care. In countries with national health systems or universal coverage, fewer barriers exist for health care services such as blood pressure and cholesterol screenings. In other countries, access to care is often conditional on having health insurance due to the high costs of out-of-pocket care. In Mexico, for example, health insurance coverage was highly associated with medication use for hypertension (Maurer 2008). In the US, compared with insured individuals, uninsured diabetics and those with high cholesterol were significantly less likely to have been diagnosed and uninsured individuals with hypertension were less likely to achieve control of their high blood pressure (Wilper et al. 2009). Globally, there are high proportions of those with elevated risk factors who are unaware of their condition, even in developed countries. Thus, health care systems that facilitate

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access to health services and emphasize preventative care and screenings can help reduce the levels of biological risk.

This is true in the countries we investigate here. There are three countries for which we have information on the use of medication to control hypertension: the US, England and Japan. If we define hypertension as either measured high or using medication and recompute the correlations between the percent having high SBP among those aged 50–59 and the life expectancy, GDP and percent urban, the size of the correlations is considerably reduced, indicating that much of the relationship came from the differences caused by the use of drugs to control measured hypertension in rich countries. In rich countries, people have their hypertension diagnosed and treated so the measured levels are lower than they would be otherwise.

Conclusion

This analysis provides, for the first time, an examination of the age differences in multiple bio-indicators across a number of countries, which span the range of development and life expectancy. The availability of harmonized data has made this type of cross-country comparison possible. Of particular significance in this study is the use of measured risk factors such as weight, blood pressure and cholesterol, which provide more accurate assessments of the underlying physiological status of the population than self-reported indicators. It becomes apparent that there is considerable heterogeneity in the pattern of age-related physiological changes between countries and across indicators. Some indicators, such as high systolic and diastolic blood pressure, mean pulse pressure and high glycosylated hemoglobin, show a clear pattern of differences across ages that imply change with age.

The prevalence of high SBP increases with age, while high DBP increases until middle-age and levels off or decreases. The exceptions to these patterns are the Tsimane of Bolivia, who show little change in either measure with age, calling into question whether age changes in blood pressure are universal. At any given age, countries also differ considerably in the prevalence of high blood pressure, suggesting that non-age related factors such as diet, economic conditions, level of development and access to health care and antihypertensives may be more important than age per se. Mean pulse pressure appears to rise with age and shows less variation between countries. Glycosylated hemoglobin also rises with age, particularly in the United States.

On the other hand, several biomarkers do not appear to change with age in any regular pattern. Cholesterol levels and overweight levels are not strongly related to age in most of these countries. Certainly there are higher levels of risk for these measures after the beginning of adulthood but these occur long before what one would consider old age. Large differences in levels of risk at any given age, however, suggest that environmental factors are of greater importance than age.

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The variability in level of physiological dysregulation across countries is not random. For example, the Tsimane have minimal levels of risk from all of these indicators. Japan and Taiwan have low levels of overweight but high prevalence of high systolic and diastolic blood pressure. Mexico and Indonesia have a high prevalence of high systolic and diastolic blood pressure, high total cholesterol, low HDL cholesterol and high mean total/HDL ratio. However, Mexico has a much higher prevalence of overweight compared to Indonesia. England and the US have very high prevalence of overweight but appear to do fairly well in terms of blood pressure, HDL cholesterol and the ratio of total/HDL cholesterol, which may be due to the widespread use of medications for these risk factors. However, these countries differ in the prevalence of high total cholesterol, which is much more common in England and high glycosylated hemoglobin, which is more prevalent in the US. Meanwhile, China appears to have intermediate levels of most biomarkers. These differences seem to be patterned in part by the economic status and level of urbanization of each country.

Some of the biomarkers vary with economic status but not all markers vary in the same way. Countries with high levels of SBP and pulse pressure, and low levels of HDL cholesterol appear to be poorer, with lower life expectancy and lower GDP. On the other hand, overweight and high cholesterol tend to be more common in more urban societies. Further studies that examine longitudinal change with age will more clearly illustrate the individual biological changes with age across these very different populations and better clarify the links between change in biomarkers and individual and community level factors.

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