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Early-life conditions and older adult health in low- and middle-income countries: a review

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Abstract

Population aging and subsequent projected large increases in chronic conditions will be important health concerns in low- and middle-income countries. Although evidence is accumulating, little is known regarding the impact of poor early-life conditions on older adult (50 years and older) health in these settings. A systematic review of 1141 empirical studies was conducted to identify population-based and community studies in low- and middle-income countries, which examined associations between early-life conditions and older adult health. The resulting review of 20 studies revealed strong associations between (1) *in utero*/early infancy exposures (independent of other early life and adult conditions) and adult heart disease and diabetes; (2) poor nutrition during childhood and difficulties in adult cognition and diabetes; (3) specific childhood illnesses such as rheumatic fever and malaria and adult heart disease and mortality; (4) poor childhood health and adult functionality/disability and chronic diseases; (5) poor childhood socioeconomic status (SES) and adult mortality, functionality/disability and cognition; and (6) parental survival during childhood and adult functionality/disability and cognition. In several instances, associations remained strong even after controlling for adult SES and lifestyle. Although exact mechanisms cannot be identified, these studies reinforce to some extent the importance of early-life environment on health at older ages. Given the paucity of cohort data from the developing world to examine hypotheses of early-life conditions and older adult health, population-based studies are relevant in providing a broad perspective on the origins of adult health.

Keywords

adult health; early-life conditions; low- and middle-income countries; population aging

Introduction

Although several reviews summarize findings regarding the importance of early-life conditions and adult health in high-income countries,^{1–4} there have been no comprehensive reviews regarding associations between early-life conditions and older adult health (50 years and older) in low- and middle-income countries. This is partially due to the paucity of cohort data tracing individuals who have not yet reached older adult ages,^{5,6} thus limiting the examination of early-life conditions to younger adults in these settings.^{7–14} These studies of younger adults, in some instances, have produced evidence of the importance of early-life conditions on adult health and will be invaluable as individuals reach older adulthood. They do not yet provide answers to questions regarding how early-life conditions are associated

with adult health (chronic conditions, cognition and longevity) at much older ages. Although economic historians have produced several studies regarding early-life conditions and older adult health in the developed world based on the collection of extensive historical census or registration systems,^{15,16} these types of data are not often readily available in the developing world with some exceptions.¹⁷

There are, however, recent and numerous population-based surveys of older adults,^a which provide the opportunity to examine not only mortality but also morbidity. They have stimulated interest from the field of demography and population health resulting in several studies on early-life conditions and older adult health from the developed world and, more recently, from the developing world. Demographers and population health researchers have become increasingly interested not only in the social and behavioral but also in the biological mechanisms of early-life health. Much of their work is relevant to the developmental origins of disease framework.

Studies based on population surveys of older adults have focused on several mechanisms to explain early-life conditions and older adult health. These include direct mechanisms such as scarring (*in utero*/infancy, infectious diseases of childhood), acquired immunity, selection of the biologically robust and indirect mechanisms operating through adult socioeconomic conditions and lifestyle.¹⁸ How these mechanisms play out is closely related to socioeconomic conditions during early life. Socioeconomic conditions encompass the ability to provide proper nourishment and sanitary conditions, regular access to good medical care, educational opportunities and establish family norms and behavior, which set the foundation for good health over the life course.^{1,19–25}

Abundant evidence for those born in the late 19th or early 20th century in the developed world suggests that strong associations exist between early life and older adult health beginning before or at conception, continuing *in utero*/early infancy and extending through childhood.^{1,15,18–21,23–36} The critical timing of nutritional insults *in utero* or early infancy may contribute to the risk of adult chronic conditions such as heart disease, diabetes and hypertension,^{27,32} which are strongly associated with functionality/disability, disability and mortality.³⁵ Inflammation *in utero* may also have long term negative consequences for adult health.³¹ Biological gender differences *in utero* may place boys more at risk than girls.³⁷ Undernutrition in early life is also associated with poor adult cognition.^{38,39} It increases the risk of infection⁴⁰ leading to poor childhood health, which can have substantial impacts on adult health.^{1,23–25} Rheumatic fever, respiratory diseases and severe bouts of diarrhea during early infancy or childhood are clearly tied to older adult health such as heart disease, adult respiratory disease and cognition.¹ Childhood socioeconomic status (SES) can influence early growth and development and can have independent effects on later health and mortality.^{20,21,23} The formation of behaviors such as smoking, drinking and diet begin in early childhood, any of which may lead to greater risk of poor adult health.^{1,41} Family preferences for males may lead to differences in resource allocation in early life with long term consequences on older adult health.⁴²

^aExamples include but are not limited to the following studies. From Latin America there are the Mexican Health and Aging Study (MHAS), Puerto Rican Elderly: Health Conditions (PREHCO), Study of Aging Survey on Health and Well Being of Elders (SABE) and Costa Rican Study of Longevity and Healthy Aging (CRELES). From Asia there are the China Health and Nutrition Study (CHNS), Chinese Longitudinal Healthy Longevity Survey (CLHLS), Indonesia Family Life Survey (IFLS), Matlab Health and Socio-Economic Survey (MHSS), Study on Global Ageing and Adult Health in India (SAGE) and China (SAGE) and Social Environment and Biomarkers of Aging Study (SEBAS). From Africa there are the Study on Global Ageing and Adult Health in Ghana (SAGE) and South Africa (SAGE). From the developed world there are the Health and Retirement Study (HRS), Wisconsin Longitudinal Study (WLS), English Longitudinal Study of Ageing (ELSA) and Survey of Health, Ageing and Retirement (SHARE). A survey of older adults from the Study on Global Ageing and Adult Health in the Russian Federation (SAGE) is also available.

Clearly not all variation in older adult health originates from poor environmental conditions *in utero*, infancy or childhood. Older adult health can be an accumulation of adverse events or poor SES across the life course. Lower SES during childhood can translate into lower adult SES, which is associated with poor adult health.²⁰ Other intervening variables related to social environment may explain adult health.²² Strain during childhood to early adulthood (e.g. disease, poverty, low education or stressful working environment) increases the risk of early occurrence of chronic disease (e.g. cardiovascular disease), which in turn increases the risk of premature disability and mortality.^{35,42,43} Diet and exercise alone can dramatically reduce the risk of adult chronic conditions.⁴¹ Genetic predispositions and gene–environment interactions may determine adult health.^b Macro factors such as economic growth, healthcare systems and policy reforms can also affect health.³⁶ Interventions before the age of 5 to improve nutrition and household income can modify the effects of poor early-life conditions during the life course¹⁹ and social factors may also reduce the negative factors of poor early-life conditions.⁴⁴ Educational and economic opportunity during young adulthood can help mediate the effects of poor early-life conditions.^{34,45,46}

Findings on the importance of early-life exposures have particular significance in low- and middle-income countries not only for understanding the present but also making inferences about the future health of older adults who, on average, may have been more impacted by their early environments than their counterparts in high-income countries. Low- and middle-income countries are projected to experience large increases in the older adult population^{47,48} resulting in an increasing burden of disease in chronic conditions such as heart disease and diabetes.^{49–55} In many instances, increases will occur mostly in the context of lower standards of living and fragile institutional support.^{56–58} As a result, there are important ramifications for public policy.

The overwhelming poverty of most of the population in low- and middle-income countries during the early 20th century makes them different from the developed world of the early 20th century with its higher standard of living and economic growth. Much of the population experienced poor nutritional environments in early life followed by rapid changes in nutritional environment during adulthood, adopting a more Western diet high in saturated fat content.⁴¹ It is yet unclear how differences in environmental exposures, cohorts and culture may change the magnitude of the relationships in the developing world. The hypothesis of critical timing of nutritional insults *in utero* or early infancy becomes particularly relevant because the combination of poor early-life nutrition and later-life overnutrition may place older adults in low- and middle-income countries at higher risk of chronic conditions such as heart disease and diabetes.⁵⁹ Certain cohorts may also have greater susceptibility to the effects of poor early-life conditions at older ages,⁶⁰ and cultural differences in Western and non-Western populations may produce different patterns of older adult health.

Population-based data present an opportunity to examine early-life hypotheses and older adult health in the developing world. Survey data from population-based studies cover different aspects of the life course. However, recently published studies using population-based data in low- and middle-income countries are too diverse in outcomes, exposure and measures to, as of yet, make meaningful cross-national comparisons regarding specific effects of childhood conditions. The focus of this review is thus to examine broad patterns across countries and regions. The question of interest is in regards to how early-life conditions are associated with older adult health in low- and middle-income countries and what the associations may mean in regards to the literature on early-life conditions from the developed world. The review examines empirical evidence for any of the following early-life effects associated with adult chronic conditions, functionality/disability, cognition or

^bGenetic predispositions may be less important at a population level. See for example Case and Paxson.²⁸

mortality: (1) poor nutrition or undernutrition; (2) specific or groups of childhood illnesses; or (3) childhood SES. In reviewing the evidence, particular attention is paid to evidence pointing to attenuation of early life effects by adult conditions and lifestyle, critical periods and cumulative effects, gender differences in the manifestation of the effects of early-life conditions, the effects of undernutrition in early life with overnutrition in later life and cohort differences in the importance of childhood conditions in later life.

Methods

Criteria for selection and databases searched

An initial list of 14 published studies examining early-life conditions and older adults using major studies on aging in low- and middle-income countries was compiled from known work presented at demography, social science and public health conferences and then subsequently published.^c Two unpublished studies presented at these conferences were included because they were deemed sufficiently important to the review. To complement this list, a systematic review of PubMed was conducted limiting the search to empirical studies and adults 45 years and older. An initial search using the key words ‘early life conditions’ and ‘older adult health’ produced a listing of 426 studies and similar searches with variations of these words produced a total list of 1257 potential studies relating to early-life conditions and older adult health. When duplicates across searches and from the original list of identified studies were eliminated, the total number of potential empirical studies was reduced to 1079. We also conducted a review of the Public Library of Science’s (PLOS) online access publication PLoS ONE using similar key words and found an additional 62 potential empirical studies. Thus, there were a total of 1141 potential empirical studies on the general topic of early-life conditions and older adult health.

We selected studies from the list of potential studies that met the following criteria: (1) population-based or community study or birth cohort of adults in low- and middle-income countries as defined by the World Bank;⁶¹ (2) adults at least 50 years and older at the time of the survey who were born in the 20th century; (3) study whose main purpose was to examine early-life conditions and older adult health; (4) study that examined any of the following adult health outcomes: chronic conditions (heart disease, diabetes and hypertension), functionality/disability, cognition and mortality;^d (5) study that presented a viewpoint of demography and population sciences; (6) study published within the last 10 years; and (7) study published in English. From this review we found four additional relevant studies, which met the search criteria resulting in a total of 20 studies reflecting seven major population-based or community surveys and one birth cohort study of older adults. All studies were conducted in low- and middle-income countries with the exception of studies conducted in Puerto Rico, which was included because its setting shares many of the characteristics of low- and middle-income countries during the early 20th century.

Selected studies

The 20 selected studies (shown in Table 1) were carried out in China and Latin America (Mexico, Costa Rica, Puerto Rico, Brazil and major cities).^{60,62–80} Most studies were nationally or regionally representative of older adults with some exceptions. The data from major Latin American and Caribbean (LAC) cities are representative of older adults 60 years

^cMajor conferences attended by demographers and population science researchers include the Population Association of America (PAA), Social Science History Association (SSHA), American Sociological Association (ASA), Gerontological Society of America (GSA) and American Public Health Association (APHA).

^dThe review did not include self-reported health. Although a potent predictor of mortality on an individual country base, it has its limitations in cross-national comparisons because of how individuals in different cultural settings interpret the scaling of the self-reported health question.

and older in major cities of LAC. The Brazilian study⁷⁵ is based on a selection of elderly respondents from a low-income community setting in the city of Sao Paulo and two birth cohort studies from China.^{71,76} Chinese data were longitudinal surveys with more than two waves as compared with data from the Latin American region. The large sample sizes from China (8000–26,000) as compared with the smaller sample sizes obtained in Latin America reflect the larger population of China. The cohorts examined differ in that, in several Chinese studies, those selected were born in the very early 20th century or before, whereas the Latin America studies have a larger number born during the late 1920s and early 1940s.

Adult health outcomes included chronic conditions (heart disease, diabetes and hypertension), risk factors for cardiovascular disease, functionality/disability, cognition and adult mortality. Health outcomes were identified through respondent self-reports (heart disease and diabetes) or measured risk factors (blood pressure and cardiovascular risk factors), responses to a battery of questions (functionality/disability and cognition) or survey data in some cases combined with administrative records (mortality).

The selected studies incorporated to varying degrees measures of early life reflecting nutrition, childhood health and childhood SES, which were not necessarily comparable across all countries. Most studies used some measure of early-life nutrition (anthropometric measures, retrospective questions regarding experiencing hunger during childhood and/or season of birth) and early childhood measures of health. In the LAC region, self-reported malaria and rheumatic fever in childhood and groups of serious childhood illnesses were examined along with indicators of infectious disease load during the first year of life or during childhood (infant and child mortality rates). A few studies from LAC used a more generalized question asking respondents to rate their childhood health. Most studies used early-life measures of early childhood socioeconomic conditions or community setting. Some studies used multiple questions to reflect early life SES such as father occupation, birthplace, medical services, parental financial problems, wearing shoes as a child and sleeping arrangements. One study from China used family composition defined by sibling sex-composition as an indicator of family resource allocation. Studies from China used parental death as a measure of financial and emotional adversity in early childhood.

The studies differed in the inclusion of adult lifestyle and adult community setting. While all studies included adult SES, several controlled for adult lifestyle including self-reported smoking, drinking and exercise, although not all reported their effects. Obesity was included in model estimation only in studies from the LAC region.

Risk of bias

The selected studies were reviewed to ascertain how they addressed attrition, missing values, validation of measures of early-life conditions and underestimation of self-reported health outcomes. Attrition in mortality data was examined in a couple of ways in China and Costa Rica. Statistical testing was conducted to examine how the exclusion of Chinese respondents lost to follow-up influenced results.⁷⁹ Study deaths in Costa Rica were verified using a death index in addition to next of kin questionnaires⁸⁰ and statistical analyses of data were conducted on data quality.⁷² Studies in China, Puerto Rico and Mexico^{66–68,72,73,78} used imputation methods to address the presence of missing data from survey responses.⁸¹

Validation of early-life measures especially retrospective measures in population surveys in low- and middle-income countries is difficult. Obtaining a record of episodes of illnesses throughout childhood during the early 20th century is almost impossible for a large majority of older adults born in low- and middle-income countries due to the absence of quality medical records. Most of the studies reviewed did not test the validity of early-life measures with a couple of exceptions. The content and predictive validity of parental death in China

was examined by testing its association with seated adult height and a delayed 10-word recall score.⁷¹ In Puerto Rico the validity of season of birth was examined by comparing the prevalence of heart disease and diabetes across season in urban and rural areas and the validity of the retrospective rating childhood health was examined using respondent-identified childhood illnesses.⁶⁶

Most studies justified the use of early-life measures based on studies conducted in the developed world. Adult height has been associated with height at early ages in the developed world^{5,82} and has thus been used as a marker of early life net nutritional status, although the degree to which height reflects childhood or *in utero* exposures remains unclear especially among stunted populations.⁸³ There are also no clearly accepted international reference standards for adult height in low- and middle-income countries. Arm length, used in the China surveys, is believed to be a good marker of early-life nutritional environment.^{84–87} Waist–hip ratio is a risk factor for several metabolic disorders but the exact mechanism of influence is obscure. It may be affected by early-life malnutrition⁸ but it may also be a measure of current adiposity. Season of birth is a potentially viable broad indicator of early-life exposures and is easily obtained in most population studies of older adults. It has been shown to be a good indicator for early-life conditions *in utero* and early infancy that precipitates poor adult health in the developed world.^{11,29,30,88–91} It has also been shown to be independent of other life course factors such as socioeconomic conditions.³⁰

Retrospective measures of early childhood health have shown certain validity in the developed world as self-rating of childhood health by adult respondents has been associated with indicators of *in utero* growth.⁹² Other measures such as asking older adults if they ever went hungry as a child or household characteristics have not been thoroughly validated. Retrospective questions asked in surveys regarding parental SES have proven to have certain strong validity⁹³ but early SES measured by broad measures categorizing parents into agricultural v. non-agricultural occupations or asking respondents to rate their early SES do not permit a more granular understanding of the occupational status of their parents, which may be important in the agricultural societies of the early 20th century in low- and middle-income countries. Urban or rural residence may not be sufficiently precise to indicate SES differences because urban areas may have been worse than rural areas in terms of disease environment during certain periods.⁹⁴

Adult functionality/disability was measured using well-recognized measures of functionality/disability such as activities of daily living (ADLs)⁹⁵ and the Nagi⁹⁶ functionality/disability items. Functionality measures were tested to ensure they were culturally relevant for China.⁷² Studies of adult cognition used recognized measures of cognition,⁹⁷ adapting them to reflect cultural and socioeconomic conditions relevant to Chinese and Latin American older adults.^{72,76,78} The Brazilian study used a battery of validated cognitive assessment tools, which were combined to identify respondents with dementia.⁷⁵ Self-reported questions for chronic conditions (heart disease and diabetes) were based on whether the respondent was diagnosed by a medical professional. Although chronic conditions may be underestimated and only one study used biomarkers to test the validity of self-reported chronic conditions,⁶⁵ there is evidence that self-reports do in some circumstances show good validity with more objective measures such as biomarkers,^{98,99} even in the context of a developing country.⁶⁵

Analysis

Studies were reviewed and summarized according to adult health outcome using the most complete model estimation reported. The net effects of childhood nutrition, health and SES were identified, showing where feasible the effects of adult lifestyle (exercise, smoking, drinking and leisure activities). Variables used as controls in model estimation are not

shown but in some instances described in the table notes. Results are described by health outcome and then according to country-specific results in relation to early-life nutrition, childhood health and childhood SES.

Results

Chronic conditions

Studies reporting results for early-life conditions and chronic conditions came from the LAC region with the exception of one study from China reporting on cardiovascular risk factors.⁷¹ The results were mixed using anthropometric measures of early-life nutrition. Being in the lowest quartile of knee height increased the odds of adult diabetes by about 20% in Puerto Ricans.⁶⁴ Yet, there was no association with knee height and adult diabetes in older adult Costa Ricans⁶⁵ or in most major cities of the LAC region nor was there an association with knee height and adult heart disease in the LAC region and in Puerto Rico.^{60,64} There was also no association between being stunted and reporting hypertension in Mexico,⁷⁰ or being taller and having hypertension or reporting heart disease, diabetes, stroke or cancer in Mexico.⁶² There were very strong associations between waist-hip ratio and diabetes in LAC and Puerto Rico. Being in the highest quartile of waist-hip ratio increased the odds of diabetes by almost 2.5 in some instances as compared with those in lower quartiles.^{60,64}

The effects of season of birth on older adult Puerto Rican health were remarkably strong, robust and in the expected direction, especially for heart disease.^{66–68} Being born at the end of the lean season increased the odds of adult heart disease by almost 90% and being born during the lean season increased the odds of adult diabetes by about 80%.⁶⁶ Season of birth was not associated with any other predictor variable (e.g. childhood health, childhood SES, low knee height, low height, education, age or gender), nor did competing hypotheses appear to explain the results (e.g. family planning, breast feeding or timing of mother working). Strong effects of season of birth on adult health appeared in a related study and appeared strong even after controlling for adult smoking (results not shown).⁶⁷ The risk of onset of heart disease was 65% higher among those born during the lean season as compared with those born during the harvest, controlling for other childhood and adult conditions (results not shown).⁶⁸

Having had rheumatic fever as a child increased the odds of adult heart disease by about 2–3 times in the LAC region and Puerto Rico.^{60,64,66–68} Reporting poor childhood health increased the odds of adult heart disease among Puerto Ricans by 40%.⁶⁶ The combination of poor childhood health (hepatitis, tuberculosis, rheumatic fever, chronic bronchitis, nephritis, hepatitis, typhus fever, polio, malaria, dengue, pneumonia and/or asthma) and poor childhood SES was associated with a higher prevalence of chronic conditions in adulthood in LAC.⁶⁰ A similar question among Mexicans showed that those who had a serious health problem before the age of 10 had a 17% higher odds of diabetes than those who did not have such a problem.⁶³ Having a toilet inside the house as a child decreased the odds of diabetes by about 20% among some Mexican older adults⁶³ but was not significant among another group of older adult Mexicans.⁷⁰ Going to bed hungry increased the odds of diabetes by almost 90% among Mexican females.⁶³

A general question rating childhood SES produced no significant effects in the LAC region or Puerto Rico.^{60,64,66–68} Overall, there were no significant effects between having been born in a region with high child mortality and diabetes for older adults in Costa Rica.⁶⁵ The effects of being born in the lean season were very strong for Puerto Ricans with heart disease and diabetes and born in a year when infant mortality (IMR) was lower but there were no significant effects for those born in a year when IMR was higher suggesting that

season of birth is a meaningful measure of early-life exposure under restricted conditions (results not shown).⁶⁸

Other measures of early life SES such as place of birth, going to bed hungry and having a toilet in the home during childhood showed mixed or puzzling results as in the case of Mexico where wearing shoes as a child increased the odds of diabetes by almost 30%.⁶³ In a study from China, emotional adversity in childhood using parental death during childhood was negatively associated with cardiovascular risk factors such as blood pressure, fasting glucose and cholesterol in older adults, particularly in men.⁷¹ Having a family member with diabetes increased the odds of diabetes more than four times as compared with those without a family member with diabetes,^{66–68} although it is not possible to identify the exact social or genetic mechanisms.

Smoking and drinking were not significant predictors of chronic conditions in Costa Rica⁶⁵ and Puerto Rico^{66–68} but they reduced the odds of hypertension by about 40% in Mexico.⁶² However, there were no significant associations between smoking and hypertension in other studies from Latin America.^{62,65–68} Exercising as an adult decreased the odds of diabetes by about 35% in Costa Rica but not in Puerto Rico⁶⁵ (Table 2).

Functionality/disability

In Mexico taller height was associated with less functional difficulty.⁶² Going to bed hungry increased the odds of poor adult functionality/disability by almost 50% among older adult Mexicans. Having at least one identified serious health problem (tuberculosis, rheumatic fever, polio, typhoid fever or a serious blow to the head that made the respondent faint) during childhood increased the odds of problems with functionality/disability in adulthood by almost 30% in Mexico.⁷³ Mother's educational level was a strong predictor of poor health at older ages. Having a mother with an elementary school education or higher reduced the odds of having functional limitations as an adult by about 10–30%.⁷³ Being born in a high migration state to the United States reduced the odds of difficulty with functionality/disability by about 17%⁷³ implying that the family benefited from remittances and work in the United States improved their economic conditions. The effects of going to bed hungry is greatly attenuated after adding adult lifestyle but the effects of serious health problems and being born in a high migration state remain strong.⁷³ In another study from Mexico,⁶² the effects of height on adult functionality/disability remain even after controlling for adult lifestyle. Having ever smoked increased the odds of difficulty with functionality/disability in Mexico by about 12–45%.⁷³ Heavy drinking increased the odds of poor functionality/disability in Mexico by almost three times.⁶²

In the major cities of LAC, older adults reporting both poor childhood health and childhood SES showed high odds of having difficulty with at least one ADL for musculoskeletal and mental categories of disease although those reporting good early conditions curiously also showed strong odds of poor functionality/disability across several categories of disease (results not shown).⁶⁹

Those Chinese respondents who reported parental death (associated with poorer health) had very high odds of problems with functionality/disability in adulthood.⁷² Exercise in both male and female Chinese respondents reduced the odds of difficulty with functionality/disability by about 27–35%.⁷² The effects of early-life conditions (father's occupation, birthplace, survival status of parents and education of respondent) disappear after adult lifestyle is added in China.⁷² However, survival status of parents, health problems and health services in childhood remain strong predictors of adult functionality/disability. Curiously, there were strong protective effects of smoking on adult functionality/disability for Chinese men.⁷² Heavy drinking had a protective effect in Chinese males, reducing the odds by about

30%.⁷² Having both parents alive at age 10 reduced the odds of functionality/disability difficulties by almost 20%, whereas living in an urban area during childhood increased the odds by 22%.⁷⁴ Participation in leisure activities reduced the odds by about 22% and there were no significant effects from adult smoking or drinking behavior (Table 3).

Cognition

Taller older adults living in the major cities of LAC showed better cognition in both men and women, whereas taller knee height was associated with better adult cognition in women.⁷⁷ In contrast, being in excellent health and never being hungry were not associated with adult cognition, whereas being in a good economic situation was marginally associated with poor adult cognition in women.⁷⁷ In Brazil, longer leg length and larger head circumference reduced the odds of adult dementia by over 25% in baseline models (results not shown) and did not mediate the association between poor early SES and dementia.⁷⁵ In contrast, in the same study being illiterate increased the odds of dementia by about 64–83% (results not shown) and these associations were partially mediated by adult SES. The prevalence of dementia was strongly associated with increasing number of unfavorable risks factors across the life course.

In China, being in the lowest 10th percentile of arm length increased the odds of poor adult cognition by 62% for males and 38% for females among the same age group.⁷⁸ Being in the lowest 10th percentile of knee height in China increased the odds of problems with cognition in women by 24%.⁷⁸ Survival status of parents, health problems and health services in childhood remain strong predictors of adult cognition even after adding adult lifestyle. Going to bed hungry, low knee height, arm length and education all remain important predictors of adult cognition after adjusting for adult lifestyle, which did not show strong associations with adult cognition.⁷⁸ In another study from China,⁷² infrequently going to bed hungry decreased the odds of poor cognition by 11% for females but not for males. Those who did not report parental death (missing) had very high odds of poor cognition in adulthood. Exercise reduced the odds of cognitive impairment in both males and females by 42–46%. Curiously, there were strong protective effects of smoking on cognition for Chinese men. Participation in leisure activities decreased the odds of poor cognition by 20%.⁷⁴ In another study from China prenatal factors reflected by head circumference, ponderal index, placental weight, birth order and maternal age at birth were significant in unadjusted models but the effects disappeared after adding adult factors (results not shown).⁷⁶ In contrast, early life SES factors such as better father occupation, drinking milk in childhood and being taller were associated with better adult cognition even after controlling for adult factors (Table 4).

Mortality (overall and cause specific)

There were strong effects of poor early-life conditions on adult mortality in Costa Rica even after controlling for adult lifestyle, economic conditions and health. Being a childhood malaria survivor increased the hazard of dying due to stroke by over 4–7 times.⁸⁰ Older adults born in regions with high child mortality in Costa Rica had almost three times greater risk of dying at younger ages, and curiously Costa Rican older adults with lower knee height lived longer than taller adults as the relative risk of dying decreased by more than 50% for those in the lowest quartile of knee height.⁶⁵

In the case of China, longer arm length reduced the relative mortality hazard by about 21% among Chinese respondents 80 years and old but became marginally significant after adding adult lifestyle,⁷⁹ and in another study from China reduced it by about 11–15% (results not shown), which then disappeared after controlling for previous health conditions.⁷⁴ Never or rarely having suffered from severe sickness in childhood decreased the odds of problems

with adult functionality/disability and cognition by almost 30% but had no effect on adult mortality suggesting that functionality/disability or cognition may mediate the effects of early-life conditions.⁷² Father's occupation did not appear to be largely associated with older adult health, although it is marginally significant in baseline models predicting old-age mortality among Chinese 80 years and older (results not shown).^{72,79} Being a single child increased the hazard of dying by 18% in Chinese 80 years and older possibly reflecting the consequences of illness or death of a parent.⁷⁹ Being male living in a household with all male siblings increased the hazard of dying by 52% possibly reflecting increased competition for resources among all male siblings.⁷⁹ While adult lifestyle (smoking, drinking and exercise) showed strong effects on adult health, in some instances it did not attenuate the effects of early-life conditions. Exercise reduced the odds of dying by about 26% and having ever smoked increased the odds of mortality by about 11%. However, the effects of arm length became marginal after adding adult smoking, drinking and exercise, while the effects of family composition remained strong.⁷⁹ The significant effects of early-life conditions (father's occupation, birthplace, survival status of parents and education of respondent) in baseline models disappear after adult lifestyle is added.⁷² Participation in leisure activities reduced the odds by about 14% but has little effect on the importance of having economic independence in adulthood, which reduces the hazard of dying⁷⁴ (Table 5).

Discussion

Twenty articles reviewed from major population-based studies of aging in low- and middle-income countries showed strong associations between early-life conditions and adult health outcomes such as chronic conditions, functionality/disability, cognition and mortality. Strong associations emerged: (1) *in utero*/early infancy exposures (independent of other early life and adult conditions) and adult heart disease and diabetes; (2) poor nutrition during childhood and adult mortality, difficulties in adult cognition and diabetes; (3) specific childhood illnesses such as rheumatic fever in childhood and adult heart disease, and malaria and adult mortality due to stroke; (4) serious childhood illnesses and adult functionality/disability and chronic disease; (5) poor childhood SES and adult mortality, functionality/disability and cognition; and (6) parental survival during childhood and adult functionality/disability and cognition. There was a very clear pattern that exercise had a protective effect on older adult health as exercising decreased the odds of several health outcomes by about 20–46%.

The results are specific to a handful of countries, cities or communities (China, Costa Rica, Mexico, Puerto Rico, Brazil and major cities in the LAC region). However, taken as a whole the results confirm previous studies from the developed world as to the importance of early-life conditions across several adult health outcomes.^{1,15,18–21,23–36} There is evidence to support the importance of a critical period *in utero*/early infancy in adult heart disease and diabetes but there is also evidence to support the idea of a cumulative effect of adversity on conditions such as adult dementia. Yet, there is insufficient information to understand the reasons why in some settings the effects of early life on older adult health have a similar magnitude as adult lifestyle with little attenuation of effects after adding adult lifestyle and community settings but in other settings the effects of early life disappear or weaken as adult lifestyle is added. Differences between males and females appeared but there is insufficient information to understand the differences. There were no studies that explicitly tested the degree to which undernutrition in early life is compounded by overnutrition in later life to produce disease but differences in older adult health due to cohort or cultural differences in at least one study point to the importance of examining more carefully the possibility that such differences exist.

To some degree, cross-national comparisons obscure the richness and comprehensive nature of the published studies. Until better data on early-life conditions become available, different measures and modeling approaches make comparability regarding effects of specific childhood conditions across countries difficult. The reviewed studies are thus better viewed as interesting case studies from which associations between early-life conditions and older adult health have emerged not only for adult mortality but also for different aspects of adult morbidity.

Nevertheless, many questions remain. The puzzling results of height and knee height, unexpected patterns of associations (e.g. wearing shoes associated with adult health in Mexico, the protective effect of smoking in China or drinking in Mexico) or mixed results from similar measures such as going to bed hungry requires more examination as does the meaning of waist-hip ratio as a potential measure of early-life nutrition. There are differences between adult diabetes and heart disease in terms of the importance of early nutrition but the measures of nutrition are too broad to discern the differences. The very strong association between having a family member with diabetes and being diagnosed with diabetes may reflect genetics or family background and behavior but there is insufficient information to disentangle its meaning. Childhood malaria, rheumatic fever and serious health problems or illness in childhood are associated with adult health although it is not possible to tease apart effects of individual illnesses. There are strong associations between country-specific child mortality and adult mortality but having household child mortality would provide a more direct tie with respondent's early-life conditions. Gender differences may exist in early life as shown by the results of family composition and older adult health in China but more information on early life family environment is needed to fully understand them. The generality of the question on parental SES in relation to the mostly agricultural societies of the 20th century may explain the reason why parental SES is not significant in many cases.

Admittedly, the measures of early-life conditions are broad and imprecise and exact mechanisms cannot be determined. Measures of childhood health are largely untested and not validated and rely on retrospective questions asked of older adults. Reference standards for anthropometric measures are based mostly on the developed world and in some instances may not be appropriate for low- and middle-income countries. The number of countries examined is too small to discern the uniqueness of the findings for particular countries and the need for more data harmonization for more meaningful cross-national comparisons is apparent. Events between early life and older adult health often cannot often be bridged with available survey data. Linking other types of data (administrative, historical censuses, vital statistics or information on nutritional conditions) with survey data to address the data limitations of surveys of older adult health holds promise in complementing older adult surveys to enhance analyses of early-life conditions. Although this approach is feasible in the developed world,¹⁰⁰ it is often not a realistic option given the quality of data sources in low- and middle-income countries in the early 20th century. It is not yet possible to discern the conditions under which the results are observed. Questions remain such as the interaction between early life and older adult health and differences between cohort and the degree the determinants of adult heart disease differs between Western and non-Western countries.

In spite of these limitations, the topic of health determinants for older adults in these settings continues to be one of recognized importance for public health and those studying aging populations in these settings.^{47,101,102} One may question the wisdom of recreating dose in terms of using season of birth as an indicator of *in utero*/early infancy exposures or using retrospective questions asked of older adults regarding their childhood. However, given the paucity of cohort data from the developing world to examine hypotheses of early-life

conditions and older adult health, population-based studies are relevant in providing a broad perspective on the origins of adult health. Understanding the determinants of older adult health will lead to better interventions and more effective health policy for older adults in low- and middle-income countries, although knowing how to best translate research on early-life exposures and older adult health into relevant public policy guidelines in low- and middle-income countries remains a challenge.

Demographers and population researchers are already working with biomedical researchers as they incorporate more biomarkers into population surveys.¹⁰³ There are relevant instances of this collaboration between social science and biomedical researchers in the developing world.^{14,65} Bio-markers will improve the measurement of adult health outcomes in population studies and address concerns regarding the underestimation of adult chronic conditions using self-reported measures. Improving the measurement of early-life conditions in population-based studies in low- and middle-income countries will be a difficult task especially for older adults born in the early to mid-20th century. However, just as demographers are in the position to interpret social and behavioral aspects discovered in population-based studies, biomedical researchers hold the key to illuminating their biological aspects and to understanding different environmental settings and population-specific risk factors. More collaborative research efforts within the framework of the developmental origins of life combining population-based surveys with biomedical research approaches has the potential to more fully illuminate the complexity of how early-life conditions impact older adult health.

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Table 1

Selected studies according to adult (50 years and older) health outcomes^a

Authors, publication year, country	n	Age (years)	Early-life conditions			Adult life
			Nutrition	Health	SES	
Chronic conditions						
Crimmins <i>et al.</i> , 2005, ⁶² Mexico	2265	60+	Height			Smoke Drink
Kohler and Soldo, 2005, ⁶³ Mexico	6423	50+	Hunger	Serious illnesses Toilet location	Mother education Father education Sibling education Worse shoes Sleeping location Financial problems	
Palloni <i>et al.</i> , 2005, 2006, ^{60,64} PR, LAC	4291, 10,602	60+	Knee height WHR	Poor health Rheumatic fever	Poor childhood SES	Obesity
Brenes, 2008, ⁶⁵ Costa Rica	4000	55+	Knee height	Child mortality		Smoke Drink Exercise
McEniry <i>et al.</i> , 2008, 2010, 2011, ⁶⁶⁻⁶⁸ PR	1434	60–74	Knee height Season of birth	Poor health Rheumatic fever	Poor childhood SES	Smoke Obesity
Monteverde <i>et al.</i> , 2009, ⁶⁹ LAC, PR	10,602, 4293	60+		Serious illnesses plus SES conditions		Smoke
Beltrán-Sánchez <i>et al.</i> , 2011, ⁷⁰ Mexico	2099	60+	Height	Toilet location	Birthplace	
Schooling <i>et al.</i> , 2011, ⁷¹ China	26,820	50+	Leg length		Father occupation	Smoke
Functionality/disability						
Crimmins <i>et al.</i> , 2005, ⁶² Mexico	2265	60+	Height			Smoke Drink
Yi <i>et al.</i> , 2007, ⁷² China	13,294	80+	Arm length Hunger	Severe illnesses	Father occupation Birthplace Parental survival Medical services Education	Smoke Drink Exercise
Monteverde <i>et al.</i> , 2009, ⁶⁹ LAC, PR	10,602, 4293	60+		Serious illnesses plus SES conditions		Smoke
Huang <i>et al.</i> , 2011, ⁷³ Mexico	7364	50+	Hunger	Serious illnesses	Mother education Father occupation Birthplace	Smoke
Wen and Gu, 2011, ⁷⁴ China	8099	65+	Arm length Hunger		Father occupation Parental survival Medical services Birthplace	Smoke Drink Exercise
Cognitive functioning						

Authors, publication year, country	n	Age (years)	Early-life conditions			Adult life
			Nutrition	Health	SES	
Yi <i>et al.</i> , 2007, ⁷² China	13,294	80+	Arm length Hunger	Severe illnesses	Father occupation Birthplace Parental survival Medical services Education	Smoke Drink Exercise
Sczufca <i>et al.</i> , 2008, ⁷⁵ Brazil	2005	65+	Leg length Head circumference		Illiteracy Birthplace	Smoke
Zhang <i>et al.</i> , 2009, ⁷⁶ China	2062	50–82	Head circumference Height Drank milk as a child		Father occupation	
Maurer, 2010, ⁷⁷ LAC	7894	60+	Height		Good childhood SES	
Zhang <i>et al.</i> , 2010, ⁷⁸ China	15,444	80+	Arm length Knee height		Birthplace Education	Smoke
Wen and Gu, 2011, ⁷⁴ China	8099	65+	Arm length Hunger		Father occupation Parental survival Medical services Birthplace	Smoke Drink Exercise
Mortality						
Zeng <i>et al.</i> , 2007, ⁷² China	13,294	80+	Hunger	Severe illnesses	Father occupation Birthplace Parental survival Medical services Education	Smoke Drink Exercise
Brenes, 2008, ⁶⁵ Costa Rica	4000	55+	Knee height	Child mortality		Smoke Drink Exercise
Huang and Elo, 2009, ⁷⁹ China	8099	80+	Arm length		Father occupation Sibling composition Place of birth	Smoke Drink Exercise
Brenes and Palloni, 2011, ⁸⁰ Costa Rica	2827	60+		Malaria		<i>b</i>
Wen and Gu, 2011, ⁷⁴ China	13,802	65+	Arm length Hunger		Father occupation Parental survival Medical services Birthplace	SES (adult, community)

SES, socioeconomic status; PR, Puerto Rico; LAC, Latin American and Caribbean major cities; WHR, waist–hip ratio.

^aThe above studies are based on eight major studies on aging populations in low- and middle-income countries: Chinese Longitudinal Healthy Longevity Survey (CLHLS)^{72, 74, 78, 79}; Costa Rican Study of Longevity and Healthy Aging (CRELES)^{65, 80}; Mexican Health and Aging Study (MHAS)^{62, 63, 70, 73}; Study of Aging Survey on Health and Well Being of Elders (SABE)^{60, 69, 77}; Puerto Rican Elderly: Health Conditions (PREHCO)^{64, 66–68}; Guangzhou Biobank Cohort Study (GBCS)⁷¹; the Sao Paulo Ageing & Health Study (SPAH)⁷⁵; and a birth cohort from Peking Union Medical College Hospital (PUMCH)⁷⁶.

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^bBrenes and Palloni⁸⁰ did not control for adult lifestyle but did control for several adult variables related to income, health insurance and baseline prevalence of certain health conditions.

Table 2

Effects of early-life conditions on adult chronic conditions

Outcome ^a	Predictors ^b	Category	Effects	Country
Diabetes	Went to bed hungry	Child Health	0.71 ***	Mexico ⁶³
	Female × hungry	Child Health	1.86 ***	
	Health problem before age 10	Child Health	1.17 *	
	Toilet inside house	Child Health	0.80 *	
	More education for mother	Child Health and Nutrition	1.00 – none	
			1.00 – some	
			0.74 * – completed	
	More education for father	Child SES	0.54 ** – more than	
			1.00 – none	
			1.02 – some	
			1.20 – completed	
			1.22 – more than	
	Some schooling	Child SES	1.14	
	Wore shoes regularly	Child SES	1.30 ***	
	Slept in cooking room	Child SES	0.96	
	Help with financial problems	Child SES	0.89	
Diabetes	Low knee height	Child Nutrition	1.21 *	PR ⁶⁴
	Low height	Child Nutrition	0.95	
	High WHR	Child Nutrition	1.68 ***	
	Poor child health	Child Health	1.44, 1.47 *	
	Poor child SES	Child SES	0.96–0.97	
Diabetes	Low knee height	Child Nutrition	0.88–1.67 ^c	LAC ^{60,d}
	Low height	Child Nutrition	0.62–1.19 ^c	
	High WHR	Child Nutrition	1.40–2.47 ^c	
	Poor child health	Child Health	0.94–1.65	
	Poor child SES	Child SES	0.53–1.42 ^e	
Diabetes	Low knee height	Child Nutrition	1.18	Costa Rica ⁶⁵
	High child mortality	Child Environment	0.84	
	Ever smoked	Adult Lifestyle	0.91–1.03	
	Drinks	Adult Lifestyle	0.83–1.09	
	Exercises now	Adult Lifestyle	0.65 **	
Diabetes	Low knee height	Child Nutrition	1.29	PR ^{66–68,f}
	Born in lean season	Child Nutrition, Infection	1.78 *	
	Lean season × family member with diabetes	Child Nutrition	0.57 *	
	Poor child health	Child Health	1.20	
	Poor childhood SES	Child SES	0.56–1.28	

Outcome ^a	Predictors ^b	Category	Effects	Country
Heart disease	Family member with diabetes	Child SES	3.94 ^{***}	PR ⁶⁴
	Ever smoked	Adult Lifestyle	1.14	
	Exercises now	Adult Lifestyle	0.85	
	Low knee height	Child Nutrition	0.90	
	Low height	Child Nutrition	0.90–0.94	
	High WHR	Child Nutrition	1.10–1.12	
	Poor child health	Child Health	1.60 [*]	
	Disease group	Child Health	1.93 ^{***}	
			1.66 ^{***g}	
	Rheumatic fever	Child Health	1.82 [*]	
Heart disease	Poor childhood SES	Child SES	1.18	LAC ^{60,d}
	Low knee height	Child Nutrition	0.74–1.68 ^h	
	Low height	Child Nutrition	0.68–1.20 ^h	
	High WHR	Child Nutrition	0.65–1.39 ^h	
	Poor child health	Child Health	4.29–4.41 ^{***j}	
	Poor childhood SES	Child SES	0.66–1.43 ⁱ	
Heart disease	Low knee height	Child Nutrition	1.04	PR ^{66–68,f}
	Born at end of lean season	Child Nutrition	1.89 ^{***}	
	Poor child health	Child Health	1.40 [*]	
	Rheumatic fever	Child Health	3.44 ^{***}	
Hypertension	Poor childhood SES	Child SES	1.11	Mexico ⁷⁰
	Stunted	Child Nutrition	0.84 (m), 1.07 (f)	
	Toilet at age 12	Child Health	1.18 (m), 0.73 (f)	
	Born in city	Child SES, Environment	1.45 (m), 3.08 ^{***} (f)	
Risk factors for cardiovascular disease	Parental death	Child SES	See note ^j	China ^{71,k}
		Ref: none 1 death 2 deaths		
Several ^l	Low height	Child Nutrition	0.99–1.01	Mexico ⁶²
	Ever smoked	Adult Lifestyle	0.37–0.75 C	
			0.60 ^{**} HT	
	Drinks	Adult Lifestyle	0.49–0.71 C	
Several ^l			0.59 [*] HT	LAC ⁶⁹
	Child health problems + poor child SES	Child Health, SES	1.30–3.90 ^{**}	
Several ^l	Child health problems + poor child SES	Child Health, SES	1.56–5.37 ^{**}	PR ⁶⁹

×, interaction between two variables; SES, socioeconomic status; None, no formal education; Some, 1–5 years of education; Completed, 6 years of education; More than, completed 7 years or more of education; PR, Puerto Rico; WHR, waist–hip ratio; LAC, Latin American and Caribbean major cities; Separate models for gender noted by: m, males; f, females; C, chronic conditions such as heart disease, diabetes, stroke, cancer; HT, hypertension; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Notes: Shown are odds ratios that reflect net effects after controlling for covariates, which varied from study to study but in most instances included age, gender and education. Two studies^{69, 71} controlled for adult lifestyle but did not report the results.

^aDiabetes and heart disease are based on self-reported survey questions asking if the respondent was ever diagnosed with these conditions. Hypertension was based on measured blood pressure or if the respondent reported taking medication for blood pressure. Risk factors for cardiovascular disease included in Schooling *et al.*⁷¹ were blood pressure, LDL-cholesterol, HDL-cholesterol, fasting glucose, triglycerides and adiposity and inflammation.

^bMeasures for nutrition, health, SES and lifestyle were defined slightly differently from country to country.

Measures of childhood nutrition were defined in the following manner: (1) low knee height (lowest quartile);^{60, 64, 65, 66–68} (2) low height [continuous (cm)];^{60, 62, 64} (3) WHR (highest quartile);^{60, 64} (4) season of birth (reference group was harvest season for diabetes and fourth quarter for heart disease);^{66–68} (5) stunting [yes (no) using US NHANES cutoff point];⁷⁰ and (5) being born in the lean season and having a family member with diabetes.^{66–68}

Measures of childhood health were self-reported and defined in the following manner: (1) poor childhood health [yes (no)];^{60, 64, 66–68} (2) childhood health problems including poor general childhood health, hepatitis, tuberculosis, rheumatic fever, chronic bronchitis and nephritis + poor childhood SES [yes (no)];⁶⁹ (3) went to bed hungry as a child [yes (no)];⁶³ (4) female and going hungry as a child;⁶³ (5) had a health problem before the age of 10 [yes (no)];⁶³ (6) disease group including typhoid, hepatitis, tuberculosis, polio and/or rheumatic fever [yes (no)];⁶⁴ (7) rheumatic fever [yes (no)];⁶⁴ (8) toilet inside the house [yes (no)];^{63, 70} and (9) mother's education [no school (reference group), some elementary, completed elementary, more than elementary].⁶³ Some of these measures can be interpreted as measures of childhood SES (e.g. went to bed hungry and toilet inside the house). For example, Mexico⁷⁰ viewed having a toilet at the age of 12 as both an indicator of childhood SES and exposure to disease in childhood.

Measures of childhood SES were self-reported and defined in the following manner: (1) poor childhood SES [yes (no)];^{60, 64, 66–68} (2) family member with diabetes [yes (no)];^{66–68} (3) father's education [no school (reference group), some elementary, completed elementary, more than elementary];⁶³ (4) some education (respondent or sibling dropped out of school because of financial problems) [yes (no)];⁶³ (5) wore shoes regularly [yes (no)];⁶³ (6) slept in the same room as was used for cooking [yes (no)];⁶³ (7) received financial help [yes (no)];⁶³ (8) was born in a city [yes (no)];⁷⁰ and (9) parental death [no deaths (reference group), one death, two deaths].⁷¹ Some measures shown in the table can also be interpreted as measures of childhood health but are shown here because the authors of the studies identified them as being indicators of childhood SES.

Measures of early-life environment were defined in the following manner: (1) child mortality (ln child mortality index).⁶⁵

Measures of adult lifestyle were defined in the following manner: (1) smoking: current smoker [yes (no)];⁶² never smoked (reference group), former smoker, current smoker;^{65, 68} ever smoked;⁶⁷ (2) drinking: heavy drinker (reports 5+ drinks per day in the past year);⁶² never drank (reference group), past alcoholic drinker, current alcoholic drinker;⁶⁵ and (3) exercising (exercises regularly [yes (no)]).^{65, 67, 68}

^cHeight was not significant across all countries, though it was marginally significant in Brazil [0.62 ($P=0.090$)]. Knee height was significant in Chile (OR 1.67*) and Mexico (OR 1.51*). WHR was significant in 5 of the 6 countries: Barbados (OR 2.47***), Brazil (OR 2.40***), Cuba (OR 1.60*), Mexico (OR 1.50*) and Uruguay (OR 1.72*).

^dCountry-specific models were estimated to examine the association between markers of nutritional status, childhood health and childhood SES with adult diabetes and heart disease controlling for age, gender, education and obesity.

^eChildhood SES had a curiously protective effect on diabetes in Uruguay (OR 0.56* controlling for height, OR 0.53* controlling for knee height, OR 0.57* controlling for WHR). In Brazil, childhood SES was marginally significant [OR 1.39 ($P=0.077$) controlling for height, OR 1.42 ($P=0.060$) controlling for knee height].

^fFor early-life conditions PR results are shown for McEniry *et al.* 2008⁶⁶ and these results were similar to results obtained in related studies.^{67, 68} Adult lifestyle effects come from related studies.^{67, 68}

^gThe OR 1.93 occurred when the disease group included rheumatic fever. When rheumatic fever was removed, the OR decreased to 1.66.

^hHeight was not significant across all countries, though it was marginally significant in Cuba [0.68 ($P=0.085$)]. Knee height was only marginally significant in Mexico [OR 1.68 ($P=0.070$)]. WHR was only marginally significant in Brazil [OR 1.39 ($P=0.062$)] and Chile [OR 0.65 ($P=0.070$)].

ⁱThe effects of childhood health on adult health was significant only in the case of Mexico. These effects were very strong and are reported in the table. Childhood health was marginally significant in Brazil [OR 0.47 ($P=0.074$) when controlling for height, OR 0.47 ($P=0.69$) when controlling for knee height, OR 0.48 ($P=0.082$) when controlling for WHR] and Chile [OR 1.66 ($P=0.078$) when controlling for height, OR 1.69 ($P=0.071$)

when controlling for knee height]. Childhood SES was only marginally significant in Barbados [OR 0.66 ($P=0.079$) when controlling for height] and Brazil [OR 1.43 ($P=0.052$) when controlling for height, OR 1.42 ($P=0.060$) when controlling for knee height, OR 1.40 ($P=0.070$) when controlling for WHR].

^jSpace does not permit showing the numerous results showing associations between cardiovascular risk factors (systolic/diastolic blood pressure, fasting plasma, cholesterol, triglycerides, body mass index, WHR, white blood cell count, seated height and delayed 10-word recall) and parental death. Significant negative associations were obtained between parental death and triglycerides, body mass index, delayed 10-word recall score and seated height.

^kSchooling *et al.*⁷¹ controlled for leg length but its effects were not reported.

^lChildhood health and several chronic conditions were examined in LAC⁶⁹ including poor general childhood health, hepatitis, tuberculosis, rheumatic fever, chronic bronchitis or nephritis, and in PR⁶⁹ including poor general childhood health, was often sick or often had activities restricted, hepatitis, tuberculosis, rheumatic fever, chronic bronchitis, typhus fever, polio, malaria, dengue, pneumonia or asthma.

*
 $P<0.05$;

**
 $P<0.01$;

 $P<0.001$.

Table 3

Effects of early-life conditions on adult functionality/disability

Outcome ^a	Measure ^b	Category	Effects	Country
At least one ADL	Height (continuous)	Child Nutrition	0.96 ^{**}	Mexico ⁶²
	Current smoking	Adult Lifestyle	1.07	
	Heavy drinking	Adult Lifestyle	2.64 ^{**}	
At least one ADL	Never/rarely suffered from severe sickness	Child Health	0.70 ^{***} (m), 0.74 ^{***} (f)	China ⁷²
		Child SES	0.82 [*] (m), 0.78 ^{***} (f)	
	Adequate medical service for childhood illnesses	Child SES	0.90 (m), 1.17 (f)	
		Child SES		
	Father's occupation professional	Ref: at least one	1.00	
	Survival status of parents at age 10	Both parents alive	1.06 (m), 1.01 (f)	
		Missing	1.51 ^{***} (m), 1.29 ^{**} (f)	
		Child SES	0.96 (m), 1.03 (f)	
		Child SES	1.01 (m), 1.02 (f)	
	Currently smokes	Adult Lifestyle	0.72 ^{***} (m), 1.01 (f)	
At least one ADL	Currently drinks heavily	Adult Lifestyle	0.67 ^{***} (m), 1.05 (f)	LAC ⁶⁹
		Adult Lifestyle	0.65 ^{***} (m), 0.73 ^{***} (f)	
	Currently exercises regularly	Adult Lifestyle		
	Child health problems + poor child SES	Child Health, SES	2.46–7.54 ^{**}	
	Child health problems + poor child SES	Child Health, SES	2.36–10.18 ^{**}	
	Had both parents alive at age 10	Child Health	0.82 ^{**}	
	Lived in urban area	Child SES	1.22 [*]	
	Leisure activity index	Adult Lifestyle	0.78 ^{***}	
	Smoked in the past 5 years	Adult Lifestyle	0.95	
	Alcoholic use in the past 5 years	Adult Lifestyle	1.00	
Number of lower body limitations	Regular exercise in the past 5 years	Adult Lifestyle	1.08	Mexico ⁷³
		Child Nutrition	1.45 ^{**}	
	Went to bed hungry ^d	Child Health	1.28 ^{**}	
	Health problems ^e	Child Health, Nutrition	1.00 – none	
	Mother's education			

Outcome ^a	Measure ^b	Category	Effects	Country
	Father's occupation	Child SES	0.89 [*] – elementary 0.69 [*] – Junior high+ 1.00 – agriculture 0.82 – office/professional 0.90 – other non-agricultural	
			1.21 [*] – other (child care, occupation not in questionnaire, or did not work)	
	Born high migration state	Child SES	0.90 – had no father 0.83 ^{**}	
	Smoking	Child and Adult Lifestyle	1.45 ^{**} – start <age 16 1.12 [*] – start age 16+	

ADL, activities of daily living; Gender models noted by: m, males; f, females; SES, socioeconomic status; LAC, Latin American and Caribbean major cities; PR, Puerto Rico.

Notes: Shown are odds ratios that reflect net effects after controlling for covariates that varied from study to study but in most instances included age, gender and education. One study⁶⁹ controlled for adult lifestyle but did not report the results.

^aFunctionality was defined using either ADLs⁹⁵ or the Nagi⁹⁶ items.

Huang *et al.*⁷³ included eight Nagi items to measure functional performance: difficulty with running a mile, walking several blocks, walking one block, climbing several flights of stairs, climbing one flight of stairs, sitting for two hours, getting up from a chair after sitting for long periods and stooping, kneeling and crouching.

Studies that used ADLs to define functionality differed slightly in the items that comprised ADLs. The Yi *et al.*⁷² measured functionality using eating, dressing, indoor transferring, using the toilet, bathing and incontinence. Wen and Gu⁷⁴ measured functionality using bathing, dressing, eating, indoor transferring, toileting and incontinence. The LAC⁶⁹ measured functionality using going across the room, dressing, bathing, eating, getting up and laying down in bed and going to the bathroom.

^bMeasures for nutrition, health, SES and lifestyle were defined slightly differently from country to country.

Measures of childhood nutrition were defined in the following manner: (1) height [continuous (cm)];⁶² and (2) went to bed hungry [yes (no)].⁷³

Measures of childhood health were defined in the following manner: (1) childhood health problems + poor childhood SES [yes (no)];⁶⁹ (2) health problems [yes (no)];⁷³ (3) never/rarely suffered from a severe illness [yes (no)];⁷² and (4) mother's education [no school (reference group), some elementary, completed elementary, more than elementary].⁷³

Measures of childhood SES were defined in the following manner: (1) poor childhood SES [yes (no)];⁶⁹ (2) adequate medical service for childhood illnesses [yes (no)];⁷² (3) father's occupation professional [yes (no)];⁷² (4) father's occupation [agricultural (reference group), professional, other non-agricultural, housework/other];⁷³ (5) survival status of parents at respondent's age 10 [at least one parent died (reference group), both living, missing];⁷² (6) had both parents alive at age 10 [yes (no)];⁷⁴ (7) some schooling [yes (no)];⁷² (8) place of birth – urban [yes (no)];^{72, 74} and (9) born in high migration state [yes (no)].⁷³

Measures of adult lifestyle were defined in the following manner: (1) smoking: current smoker [yes (no)];^{62, 72} never smoked (reference group), started smoking before age 16, started smoking at age 16 or older;⁷³ smoked in the past 5 years [yes (no)];⁷⁴ (2) drinking: heavy drinker (reports 5+ drinks per day in the past year);⁶² drinks heavily [defined as 400 g of beer per day (yes (no))];⁷² drank in the

past 5 years [yes (no)];⁷⁴ (3) exercising: exercises regularly [yes (no)];⁷² regularly exercised in the past 5 years [yes (no)];⁷⁴ and (4) leisure activity index (an index developed to encompass a range of activities shown to impact health conditions at older ages including gardening, raising pets, outdoor activities, reading, playing cards, listening to radio, watching television and social activities).⁷⁴

^cOnly select variables were included from Wen and Gu⁷⁴ due to space constraints.

^dSome measures shown in the table can also be interpreted as measures of childhood SES. Mexico⁷³ interpreted health problems and went to bed hungry as indicators of childhood nutritional deprivation and poor health.

^eHealth problems in Huang *et al.*⁷³ included at least one of the following: tuberculosis, rheumatic fever, polio, typhoid fever or a serious blow to the head that made the respondent faint.

* $P < 0.05$;

** $P < 0.01$;

*** $P < 0.001$.

Table 4

Effects of early-life conditions on adult cognition

Outcome ^a	Measures ^b	Category	Effects	Country
Cognitive tests	Small head circumference	Child Nutrition	1.05	China ^{76, c}
	Large head circumference	Child Nutrition	0.83	
	Taller height	Child Nutrition	0.66 *	
	Drank milk	Child Nutrition	0.65 *	
	Father occupation	Child SES	1.00 – professional 1.01 – administrator 1.24 – service 1.75 * – laborer	
Dementia	Leg length	Child Nutrition	0.82	Brazil ^{75, d}
	Head circumference	Child Nutrition	0.80	
	Illiteracy	Child SES	1.18	
	Place of birth	Child SES	1.22 – town 1.23 – rural	
MMSE	Adult smoking	Adult Lifestyle	0.73	China ⁷²
	Infrequently went to bed hungry	Child Nutrition	0.89 (m), 0.89 * (f) ^e	
	Never/rarely suffered from severe sickness	Child Health	0.74 *** (m), 0.75 *** (f)	
	Adequate medical service for childhood illnesses	Child Health	0.67 *** (m), 0.77 *** (f)	
	Father's occupation professional	Child SES	0.89 (m), 1.01 (f)	
	Some schooling	Child SES	0.64 *** (m), 0.63 *** (f)	
	Survival status of parents at age 10	Child SES		
		Ref: at least one	1.00 (m), 1.00 (f)	
		Both parents alive	1.03 (m), 0.88 (f)	
		Missing	2.28 *** (m), 1.84 *** (f)	
	Place of birth (urban)	Child SES	0.66 *** (m), 0.75 *** (f)	
	Currently smokes	Adult Lifestyle	0.79 ** (m), 1.00 (f)	
	Currently drinks heavily	Adult Lifestyle	0.84 (m), 1.12 (f) ^e	
	Currently exercises regularly	Adult Lifestyle	0.54 *** (m), 0.58 *** (f)	
MMSE score (0–19) height	Height	Child Nutrition	0.01 ** (m), 0.03 *** (f)	LAC ⁷⁷
	Excellent health	Child Health	0.05 (m), 0.14 (f)	
	Never hungry	Child Nutrition	0.08 (m), 0.12 (f)	
	Good economic situation	Child SES	20.08 (m), 20.22 * (f)	
MMSE score (0–19) knee height	Height	Child Nutrition	20.00 (m), 0.04 * (f)	
	Excellent health	Child Health	0.05 (m), 0.14 (f)	
	Never hungry	Child Nutrition	0.09 (m), 0.12 (f)	
	Good economic situation	Child SES	20.07 (m), 20.22 * (f)	
MMSE	Low knee height	Child Nutrition	1.08 (m), 1.24 * (f)	China ⁷⁸

Outcome ^a	Measures ^b	Category	Effects	Country
MMSE –impaired or not	Arm length	Child Nutrition	1.62 ** (m), 1.38 ** (f)	China ^{74f}
	Went to bed hungry	Child Nutrition	1.12 (m), 1.27 ** (f)	
	Education	Child SES		
		Ref: 7 years +	1.00	
		1–6 years	1.59 ** (m), 1.44 (f)	
		0 years	2.64 ** (m), 2.05 ** (f)	
	Place of birth (rural)	Child SES	1.10 (m), 0.96 (f)	
	Current smoker	Adult Lifestyle	0.94 (m), 0.95 (f)	
	Had both parents alive at age 10	Child SES	0.94	
	Born in urban area	Child SES	0.83	
	Leisure activity index	Adult Lifestyle	0.80 ***	
	Smoked in the past 5 years	Adult Lifestyle	1.02	
	Alcoholic use in the past 5 years	Adult Lifestyle	1.04	
	Regular exercise in the past 5 years	Adult Lifestyle	1.02	

SES, socioeconomic status; MMSE, Mini Mental State Examination; Gender models noted by: m, males; f, females.

Notes: Shown are odds ratios with the exception of Maurer and Height⁷⁷ from the LAC region, which are results from linear regressions. The numbers reported reflect net effects after controlling for covariates, which varied from study to study but in most instances included age, gender and education along with other covariates.

^aIn several studies, cognitive impairment was defined using the MMSE.⁹⁷ Higher numbers indicate better cognition.

Yi *et al.*⁷² used the Chinese version of the MMSE; it tests orientation, registration, attention, calculation, recall and language. Any respondent scoring between 24 and 30 (a perfect score) has ‘normal cognitive functioning’ and anything below 24 is considered ‘impaired’.

Zhang *et al.*⁷⁸ used the Chinese version of the MMSE; it tests orientation, calculation, recall and language. A perfect score is 30 and lower scores indicate poor cognitive ability.

Maurer⁷⁷ used an abbreviated MMSE exam and minimized low literacy bias and measured cognition based on a series of orientation, memory and executive functioning tests. The resulting MMSE score ranged from 0–19 points, and tended to be left-skewed.

Wen and Gu⁷⁴ used the Chinese version of the MMSE; it tests orientation, registration, copy and design, calculation, recall, naming and language.

Scazufca *et al.* and Zhang *et al.*^{75, 76} used a battery of validated assessments of cognitive functioning.

^bMeasures for nutrition, health, SES and lifestyle were defined slightly differently from country to country.

Measures of childhood nutrition were defined in the following manner: (1) low knee height (lowest 10th percentile);⁷⁸ (2) height [continuous (cm)];⁷⁷ (3) height (m), taller (1 SD);⁷⁶ (4) arm length (lowest 10th percentile);⁷⁸ (5) leg length [continuous (cm)];⁷⁵ (6) head circumference: (cm), small (<1 SD), large (1 SD);⁷⁶ continuous (cm);⁷⁵ (7) went to bed hungry [yes (no)];^{72, 78} (8) never hungry [time of lack of food resulting in hunger (yes (no))];⁷⁷ and (9) drinking milk daily in childhood [yes (no)].⁷⁶ Some measures shown in the table can also be interpreted as measures of childhood SES such as went to bed hungry.

Measures of childhood health were defined in the following manner: (1) excellent health [yes (no)];⁷⁷ (2) never/rarely suffered from a severe sickness [yes (no)];⁷² and (3) adequate medical for childhood illnesses [yes (no)].⁷²

Measures of childhood SES were defined in the following manner: (1) father’s occupation [professional (reference group), laborer, administrator, service];⁷⁶ (2) father’s occupation professional [yes (no)];⁷² (3) some schooling [yes (no)];⁷² (4) education [7+ years (reference group), 1–6 years, 0 years];⁷⁸ (5) literacy [yes (no)];⁷⁵ (6) survival status of parents at the age of 10 [at least one parent died (reference group), both living, missing];⁷² (7) had both parents alive at age 10 [yes (no)];⁷⁴ (8) good economic situation [good economic circumstances of the family (good (average/poor))];⁷⁷ and (9) birthplace: place of birth – urban [yes (no)];^{72, 74} place of birth – rural [yes (no)];⁷⁸ place of birth [city (reference group), town, rural].⁷⁵

Measures of adult lifestyle were defined in the following manner: (1) smoking: current smoker [yes (no)];^{72, 78} smoked in the past 5 years [yes (no)];⁷⁴ ever smoked [no (yes)];⁷⁵ (2) drinking: drinks heavily [defined as 400 g of beer per day (yes (no))];⁷² drank in the past 5 years [yes (no)];⁷⁴ (3) exercising: exercises regularly [yes (no)];⁷² regularly exercised in the past 5 years [yes (no)];⁷⁴ and (4) leisure activity index (an index developed to encompass a range of activities shown to impact health conditions at older ages including gardening, raising pets, outdoor activities, reading, playing cards, listening to radio, watching television and social activities).⁷⁴

^cThe significance levels reflect the reporting of 95% confidence intervals. The full models reported in this study included other prenatal factors but did not report their effects in the full model.

^dIn baseline models (results not shown), the effects of leg length and head circumference were significant. In the final model reported in the table these effects disappear. In a model with exposure adjusted for age and gender, the effects of leg length and head circumference remain strong even after adjusting for adult SES and lifestyle.

^eYi *et al.*⁷² reported effects that were of marginal significance ($P < 0.10$). The odds ratios for males who infrequently went to bed hungry as well as that for females who currently drink heavily were marginally significant.

^fOnly select variables were included from Wen and Gu⁷⁴ due to space constraints.

* $P < 0.05$;

** $P < 0.01$;

*** $P < 0.001$.

Table 5

Effects of early-life conditions on adult mortality

Measures ^a	Category	Effects	Country
Infrequently went to bed hungry	Child Nutrition	1.02 (m), 1.06 (f)	China ⁷²
Never/rarely suffered from severe sickness	Child Health	1.03 (m), 1.01 (f)	
Adequate medical service for childhood illnesses	Child SES	1.00 (m), 1.06 (f)	
Father's occupation professional	Child SES	0.86 (m), 0.97 (f)	
Some schooling	Child SES	1.02 (m), 0.96 (f)	
Survival status of parents at age 10	Child SES		
	Ref: at least one	1.00	
	Both parents alive	0.96 (m), 0.94 (f)	
	Missing	1.11 (m), 0.96 (f)	
Place of birth (urban)	Child SES	0.95 (m), 0.94 (f)	
Currently smokes	Adult Lifestyle	1.09 (m), 1.08 (f) ^b	
Currently drinks	Adult Lifestyle	0.96 (m), 1.19 [*] (f)	
Currently exercises regularly	Adult Lifestyle	0.80 ^{***} (m), 0.81 [*] (f)	
Knee height (lowest quartile)	Child Nutrition	0.54 [*]	Costa Rica ⁶⁵
Child mortality	Child Health	2.73 ^{**}	
Current smoker	Adult Lifestyle	1.12	
Past smoker	Adult Lifestyle	0.74	
Never smoked (ref)	Adult Lifestyle	1.00	
Current alcoholic drinker	Adult Lifestyle	0.64	
Past alcoholic drinker	Adult Lifestyle	1.05	
Never an alcoholic (ref)	Adult Lifestyle	1.00	
Arm length (logged cm)	Child Nutrition	0.79 ^b	China ⁷⁹
Father's occupation	Child SES	1.00 – agricultural	
		1.02 – professional	
		0.96 – other non-agricultural	
		0.98 – housework/other	
Sibling sex-composition	Child SES	1.00 – multiple children, mixed sex	
		1.18 [*] – single child	
		0.76 ^{**} – multiple, single sex	
		0.94 – male × single child	
		1.52 ^{**} – males × single sex	
Place of birth (urban)	Child SES	1.02	
Ever smoked	Adult Lifestyle	1.11 ^{**}	
Ever drinks	Adult Lifestyle	0.98	
Ever exercises	Adult Lifestyle	0.74 ^{**}	
Malaria as a child	Child Health	4.35 ^{**}	Costa Rica ⁸⁰
		6.68 ^{**c}	

Measures ^a	Category	Effects	Country
Arm length among top 90%	Child Nutrition	0.92 ^d	China ^{74e}
Had both parents alive at age 10	Child SES	0.94 ^d	
Born in urban area	Child SES	1.13 [*]	
Leisure activity index	Adult Lifestyle	0.86 ^{***}	
Smoked in the past 5 years	Adult Lifestyle	1.05	
Alcoholic use in the past 5 years	Adult Lifestyle	0.98	
Regular exercise in the past 5 years	Adult Lifestyle	0.90 ^{**}	

SES, socioeconomic status; Gender models noted by: m, males; f, females; ADL, activities of daily living.

Notes: Numbers shown are relative hazard ratios reflecting net effects after controlling for covariates, which varied from study to study but in most instances included age, gender and education.

^a Measures for nutrition, health, SES and lifestyle were defined slightly differently from country to country.

Measures of childhood nutrition were defined in the following manner: (1) knee height (quartiles and reference group was the third quartile);⁶⁵ (2) arm length [logged (cm)];⁷⁹ (3) arm length (90th percentile);⁷⁴ and (4) infrequently went to bed hungry [yes (no)].⁷²

Measures of childhood health were defined in the following manner: (1) never/rarely suffered from a severe illness [(yes (no))];⁷² (2) malaria as a child [yes (no)];⁸⁰ and (3) child mortality (ln index).⁶⁵

Measures of childhood SES were defined in the following manner: (1) adequate medical services for childhood illnesses [yes (no)];⁷² (2) father's occupation professional [yes (no)];⁷² (3) father's occupation [agricultural (reference group), professional, other non-agricultural, housework/other];⁷⁹ (4) some schooling [yes (no)];⁷² (5) survival status of parents at age 10 [at least one dead (reference group), both living, missing];⁷² (6) sibling sex-composition [multiple children, mixed sex (reference group); single child; multiple children, single sex; male, single child; male, single sex];⁷⁹ (7) place of birth – urban [yes (no)];^{72, 74, 79} and (8) had both parents alive at age 10.⁷⁴

Measures of adult lifestyle were defined in the following manner: (1) smoking: never smoked (reference group), former smoker, current smoker;⁶⁵ current smoker [yes (no)];⁷² smoked in the past 5 years [yes (no)];⁷⁴ never smoked (reference group), ever smoked;⁷⁹ (2) drinking: never drank (reference group), past alcoholic drinker, current alcoholic drinker;⁶⁵ drinks heavily [defined as 400 g of beer per day (yes (no))];⁷² drank in the past 5 years [yes (no)];⁷⁴ never drank (reference group), ever drinks;⁷⁹ (3) exercising: exercises regularly [yes (no)];^{72, 79} regularly exercised in the past 5 years [yes (no)];⁷⁴ and (4) leisure activity index (an index developed to encompass a range of activities shown to impact health conditions at older ages including gardening, raising pets, outdoor activities, reading, playing cards, listening to radio, watching television, and social activities).⁷⁴

^b Yi *et al.* and Huang^{72, 79} reported effects that were marginally significant ($P < 0.10$). The odds ratio for males who currently smoke in Yi *et al.*⁷² and the odds ratio for arm length in Huang⁷⁹ were marginally significant.

^c Brenes and Palloni⁸⁰ used both a simple (HR 4.35**) and complex (HR 6.68**) equation. The simple equation had only malaria as a covariate. The complex equation included the following covariates: sex, place of residence, education, living alone status, income, self-reported financial situation, health insurance, public subsidies, and baseline prevalence of hypertension, hypercholesterolemia, diabetes mellitus, lung disease, heart attack, cancer, osteoporosis, arthritis and geriatric falls.

^d Both arm length and having both parents alive at age 10 were found to be significant in baseline models but significant effects disappeared when adding if respondent had cognitive impairment, ADL disability or poor self-rated health in 2002.

^e Only select variables were included from Wen and Gu⁷⁴ due to space constraints.

* $P < 0.05$;

** $P < 0.01$;

*** $P < 0.001$