Early-Life Origins of Adult Disease: National Longitudinal Population-Based Study of the United States

Rucker C. Johnson, PhD, and Robert F. Schoeni, PhD

Objectives. We examined the relation between low birth weight and childhood family and neighborhood socioeconomic disadvantage and disease onset in adulthood.

Methods. Using US nationally representative longitudinal data, we estimated hazard models of the onset of asthma, hypertension, diabetes, and stroke, heart attack, or heart disease. The sample contained 4387 children who were members of the Panel Study of Income Dynamics in 1968; they were followed up to 2007, when they were aged 39 to 56 years. Our research design included sibling comparisons of disease onset among siblings with different birth weights.

Results. The odds ratios of having asthma, hypertension, diabetes, and stroke, heart attack, or heart disease by age 50 years for low–birth weight babies vs others were 1.64 ($P<.01$), 1.51 ($P<.01$), 2.09 ($P<.01$), and 2.16 ($P<.01$), respectively. Adult disease prevalence differed substantially by childhood socioeconomic status (SES). After accounting for childhood socioeconomic factors, we found a substantial hazard ratio of disease onset associated with low birth weight, which persisted for sibling comparisons.

Conclusions. Childhood SES is strongly associated with the onset of chronic disease in adulthood. Low birth weight plays an important role in disease onset; this relation persists after an array of childhood socioeconomic factors is accounted for. (*Am J Public Health.* 2011;101:2317–2324. doi:10.2105/AJPH.2011.300252)

The fetal origins hypothesis, developed by David Barker,[1] proposes that when nutritional intake of a fetus is limited, the body's physiology and metabolism are changed fundamentally, and some of the consequences of these changes become apparent much later in life. Health insults in utero may lead to greater physiological deterioration of metabolic and immune systems. Early-life health may influence a broad range of subsequent disease risks over the life cycle. Over the past 2 decades, a voluminous empirical literature has documented associations between early-life health outcomes—most often, but not exclusively, low birth weight—and adult mortality and disease onset.[1–5] The fetal origins hypothesis provides an explanation of why there may be important interactions between parental health status and parental economic status in their children's subsequent risk of onset of disease in adulthood.

At the same time, evidence from human and animal studies highlights the importance of other early-life factors that set in place the structures that shape future health outcomes.[6] Specifically, limited parental resources and childhood poverty can reduce investments in children's health and learning, shape the neurobiology of the developing child, and lead to worse health later in life.[7–10] Lack of health insurance for childhood can discourage the use of medical care, particularly in the early and more treatable stages of a health problem. High levels of neighborhood poverty and associated stressors can limit development and lead to poor health, and they can also compound and amplify the neurobiological disadvantages that many poor children already face.[11]

These various factors in early life—health status (e.g., low birth weight may serve as a marker for poor infant health), familial socioeconomic disadvantage, health insurance coverage, and neighborhood disadvantage—are highly correlated in most populations; children living in poor families disproportionately live in poor neighborhoods, lack high-quality health care, and have poor health. As a result, the typically estimated statistical association between birth weight and adult health status may be spurious and instead reflect the lasting influence of hereditary risk factors and childhood family and neighborhood socioeconomic disadvantage, which are correlated with both low birth weight and onset of chronic disease. The evidence to date remains inconclusive in distinguishing between these competing explanations, and there is ongoing debate regarding the source of reported associations between low birth weight and risks of chronic diseases later in life.[12–15] Assessing the relative importance of these competing explanations has implications for our understanding of the early-life origins of adult disease.

We examined the long-term consequences of low birth weight and childhood socioeconomic disadvantage on the onset of fatal chronic conditions in adulthood in the United States. We used nationally representative longitudinal data from the United States spanning nearly 4 decades to estimate the onset of chronic health conditions that are among the leading causes of mortality and disability.

METHODS

We used data from the Panel Study of Income Dynamics (PSID), which is the longest-running nationally representative household survey in the world. It began in 1968 with interviews of 4802 families in the United States that included 18 230 individuals of all ages. The PSID included an oversample of low-income and Black families so that issues of poverty and race could be examined. Sample weights account for oversampling and make the weighted sample nationally representative, and these weights are used in all analyses. PSID families and their descendents were reinterviewed each year through 1997, when interviewing became biennial.

All persons in PSID families in 1968 are considered sample members, which means

they are followed in subsequent years. In addition, anyone born to or adopted by a PSID sample member becomes a sample member and is therefore followed. When PSID sample members leave their parents' homes, they become their own PSID "family unit" and are interviewed in each wave. This sample of new adults has been found to be nationally representative.[16] Moreover, the genealogical design implies that the PSID sample today includes numerous adult sibling groupings that have been members of PSID-interviewed families for nearly 40 years (1968–2007). The PSID maintains wave-to-wave response rates of 95% to 98%.

The subsample chosen for this study consists of PSID sample members who were children when the study began. Specifically, we selected non-Hispanic Black and non-Hispanic White PSID sample members born between 1951 and 1968 who were aged birth to 17 years in the first wave of interviewing in 1968. We then combined all available information on these individuals for each wave (1968–2007). By 2007, the oldest person in the sample was 56 years and the youngest was 39 years. There were 4387 individuals in this subsample, who were members of 1872 different families in 1968. This sample, which we call the mortality sample, was used to examine annual mortality between 1968 and 2007. We used data on chronic disease that were collected from 1999 through 2007. Of the 4387 children aged birth to 17 years in 1968, a total of 2171 (who were members of 1157 different families in 1968) remained in the study until 1999 and were therefore examined in analyses of disease onset, which also took into account the competing risk of mortality; we call this the disease sample.

Most previous studies of the connection between early-life factors and adult health have relied on health surveys that contain limited socioeconomic data. The PSID, one of the world's premier economic surveys, also collects significant detail on health. As a result, it can more fully account for the broad set of early-life family and neighborhood socioeconomic factors that may lead to onset of disease in adulthood. The PSID has the additional unique feature of allowing analyses of siblings with differing birth weights and comparing their subsequent risk of disease onset in adulthood. This allowed us to account for additional unmeasured background characteristics that siblings have in common, leading to improved estimates of the influence of birth weight.

Outcome Measures

Diseases were assessed through the following question: "Has a doctor or health professional ever told you that you have had ——?" The specific diseases measured by the survey included stroke; heart attack; coronary heart disease, angina, and congestive heart failure; high blood pressure and hypertension; asthma; and diabetes and high blood sugar. Individuals who had had a disease were then asked how old they were when it was first diagnosed, and we used this information to determine age of onset. We grouped together stroke, heart attack, and coronary heart disease, angina, and congestive heart failure because of the relatively low prevalence of these individual diseases in young adulthood; we call this grouping stroke, heart attack, and heart disease. We chose these diseases on the basis of existing theory and empirical evidence relating early-life factors to adult onset of these diseases.[17] Hypertension, diabetes, and stroke, heart attack, and heart disease are among the most common causes of mortality in the United States.[18] Asthma prevalence has been increasing over recent decades; more than 23 million Americans had the disease in 2008.[19]

Key Risk Factors

The key explanatory variable was an indicator for whether the child's birth weight (as reported by a parent, typically the mother) was less than 5.5 pounds. Validation studies have demonstrated high rates of correspondence between birth weight reported by the mother and vital records.[20,21] Childhood poverty is a 0–1 indicator variable for whether the average of the parent's income when the child was aged 13 to 16 years was below the poverty threshold for their family as determined by the US government. Three categories of the father's and mother's education were identified: high school dropouts, high school graduates, and those with at least some college.

We divided childhood health insurance coverage for the years 1968 through 1972 into 3 categories: continuous private health insurance coverage during the 5-year period, intermittent private coverage during those years, and lack of private health insurance coverage in all of these years.

We defined the census tract where the child lived in 1968 as the neighborhood of upbringing. On average, two thirds of childhood years were spent in the 1968 neighborhood. By our definition, a child lived in a high-poverty neighborhood if more than 30% of the people who lived in the neighborhood were in poverty. Medium-poverty neighborhoods were neighborhoods in which 10% to 30% of the residents lived in poverty. All other neighborhoods were defined as low-poverty neighborhoods. We obtained census tract–level poverty information by linking the PSID individual data to US census data for each census tract. Additional neighborhood characteristics were based on parental reports of neighborhood quality in terms of crime, connectedness to informal sources of help, plumbing problems, and housing insulation problems in the homes in the neighborhood.

Parental smoking was measured in the PSID from self-reports of whether the parents smoked cigarettes at any time from 1968 through 1972. To determine childhood general health status as retrospectively reported in adulthood on the basis of self-rated general health status, participants were asked the following: "Consider your health while you were growing up, before you were 17 years old. Would you say that your health during that time was excellent, very good, good, fair, or poor?" The accuracy of retrospective reports of childhood health have been examined and found to be reliable.[22] Descriptive statistics of the key childhood risk factors are reported in Table 1.

Statistical Analyses

We examined mortality and the onset of each of 4 chronic conditions. The first analysis estimated cumulative hazard rates of disease onset using the disease sample. The estimated hazard models allow a fully flexible functional form of disease onset with age for each of the key childhood risk factors: low birth weight, family poverty, parental education, lack of health insurance, neighborhood poverty, and parental smoking. These estimates were based on the Nelson-Aalen cumulative integrated hazard function for each disease. On the basis of these models, we present estimates of the

TABLE 1—Proportion of Study Sample With Selected Childhood Risk Factors: Panel Study of Income Dynamics, 1968–2007

Childhood Risk Factor	Mortality Sample (n = 4387)	Disease-Onset Sample (n = 2171)
Low birth weight (< 5.5 lb)	0.07	0.07
Health status in childhood		
Excellent or very good	0.84	0.83
Good	0.13	0.13
Fair or poor	0.03	0.03
Grew up in poverty	0.11	0.09
Parental education[a]		
High school dropout	0.41	0.36
High school graduate	0.31	0.32
At least some college	0.28	0.32
Childhood health insurance, 1968–1972		
Private health insurance coverage in all years	0.59	0.66
No private health insurance coverage	0.10	0.07
Intermittent private health insurance coverage	0.30	0.26
Childhood neighborhood poverty[b]		
Lived in low-poverty neighborhood	0.78	0.82
Lived in medium-poverty neighborhood	0.18	0.14
Lived in high-poverty neighborhood	0.05	0.04
Additional childhood neighborhood factors[c]		
High-crime neighborhood	0.16	0.14
Connectedness to informal sources of help (mean of index)	6.09	6.14
Plumbing problems	0.14	0.15
Housing insulation problems	0.14	0.14
Parent smoked	0.73	0.71

Note. All statistics are sample weighted to produce nationally representative estimates. The number of individuals who died by 2007 is 174 for the mortality sample and 47 for the disease-onset sample.
[a]The father's education if he is present; the mother's education if she is head of the household.
[b]Childhood neighborhood defined as the census tract where the child lived in 1968. High-poverty = > 30% of the people who lived in the neighborhood were in poverty; medium-poverty = 10%–30%; low-poverty = < 10%. We obtained census tract–level poverty information by linking the PSID individual data to US census data for each census tract.
[c]Based on parental report.

proportion of the population with a given disease at age 50 years (Table 2).

For the second analysis, we estimated multivariate competing-risks proportional hazard models of disease onset using the disease sample separately for each disease; these models took into account the competing risk of mortality.[23] They included as explanatory variables birth weight and each of the key childhood family and neighborhood characteristics simultaneously, except childhood health during ages birth to 17 years (Table 3). Additional factors that were accounted for and included in the models but left out of Table 3 because of space considerations were gender, race/ethnicity, birth order, mother's age at birth, whether born into a 2-parent family, birth year, region of birth, proportion of the parent's life between ages 50 and 59 years (ages chosen to maximize sample size) that was spent in fair or poor health, and an index representing parental rates of time preference, which were based on parental reports of the extent to which they planned ahead, saved for the future, thought a lot about things that might happen in the future, and other matters related to planning for the future, as expressed by the parents in the period 1968 to 1972.

In the third analysis, using the disease sample, we employed sibling models to account for unmeasured time-invariant factors in common among siblings. For this analysis, we used the approach developed by Chamberlain[24] and Lancaster.[25] These unmeasured factors could include, among other factors, parental health behaviors, quality of childhood medical care, and parental healthy lifestyle orientation, as well as shared genetic factors. Estimates in the first column for each disease in Table 4 are from models that included the same set of risk factors as the models generating the estimates in Table 3, except for the risk factors that did not differ among siblings. The second column for each disease in Table 4 reports estimates from models that added as controls childhood health status from birth to age 17 years. We estimated these models to determine the extent to which the effect of birth weight on adult disease onset was accounted for by birth weight's effect on childhood heath broadly defined.

The next set of analyses considered mortality rates. In a similar manner, we report cumulative hazard rates of mortality that allow a fully flexible, functional form of mortality risk with age for key childhood risk factors. We display these descriptive results graphically in Figure A (available as a supplement to the online version of this article at http://www.ajph.org), with the cumulative mortality hazard estimates by age reported separately by low birth weight and childhood socioeconomic conditions.

A final set of regression analyses investigated the extent to which low birth weight and childhood economic disadvantage interact to create especially elevated rates of mortality risk and adult disease onset (controlling for the same set of other childhood risk factors). A family's ability to respond to a health shock, such as low birth weight, may mitigate the lasting effect of the shock. We investigated this hypothesis by testing for differential impacts of low birth weight by childhood family poverty status in both the hazard model specifications with and those without sibling fixed effects (Table A, available as a supplement to the online version of this article at http://www.ajph.org).

In all multivariate models, standard errors were clustered at the neighborhood level.

RESULTS

Children with low birth weight had much higher prevalence of each of the 4 diseases in

TABLE 2—Disease Prevalence at Age 50 Years, by Birth Weight and Childhood Socioeconomic Conditions: Panel Study of Income Dynamics, 1968–2007

	Asthma		Hypertension		Diabetes		Stroke, Heart Attack, or Heart Disease	
Condition	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)
Birth weight								
Low (<5.5 lb)	25.7	1.64 (1.55, 1.72)	68.6	1.51 (1.44, 1.58)	23.0	2.09 (1.97, 2.23)	25.8	2.16 (2.01, 2.32)
Not low (Ref)	15.7	1.00	45.5	1.00	11.0	1.00	11.9	1.00
Childhood family poverty								
Grew up in poverty	25.1	1.47 (1.40, 1.55)	74.3	1.71 (1.66, 1.77)	21.2	1.86 (1.78, 1.94)	19.6	1.71 (1.63, 1.78)
Did not grow up in poverty (Ref)	17.1	1.00	43.4	1.00	11.4	1.00	11.5	1.00
Parental education[a]								
High school dropout	21.3	1.39 (1.38, 1.40)	64.6	1.66 (1.66, 1.66)	16.3	1.65 (1.65, 1.65)	17.8	1.59 (1.58, 1.59)
High school graduate or more (Ref)	15.3	1.00	38.9	1.00	9.9	1.00	11.2	1.00
Childhood health insurance								
No health insurance	27.0	1.60 (1.54, 1.67)	68.5	1.48 (1.44, 1.53)	19.0	1.63 (1.55, 1.72)	24.8	1.98 (1.89, 2.07)
Had health insurance (Ref)	16.8	1.00	46.1	1.00	11.6	1.00	12.5	1.00
Childhood neighborhood poverty[b]								
Lived in high-poverty neighborhood	35.5	2.05 (1.90, 2.22)	82.9	1.80 (1.68, 1.92)	21.7	1.72 (1.52, 1.94)	29.6	2.14 (1.93, 2.37)
Did not live in high-poverty neighborhood (Ref)	17.3	1.00	46.1	1.00	12.6	1.00	13.9	1.00
Parental smoking								
Smoker	18.8	1.28 (1.26, 1.31)	49.6	1.14 (1.13, 1.16)	13.4	1.43 (1.38, 1.48)	15.3	1.62 (1.57, 1.67)
Nonsmoker (Ref)	14.6	1.00	43.5	1.00	9.4	1.00	9.5	1.00

Note. CI = confidence interval; OR = odds ratio. All statistics are sample weighted to produce nationally representative estimates.
[a]The father's education if he was present; the mother's education if she was head of the household.
[b]Childhood neighborhood defined as the census tract where the child lived in 1968. High-poverty = > 30% of the people who lived in the neighborhood were in poverty; medium-poverty = 10%–30%; low-poverty = < 10%. We obtained census tract–level poverty information by linking the PSID individual data to US census data for each census tract.

adulthood (Table 2). The prevalence of asthma at age 50 years was 25.7% for those with low birth weight and only 15.7% for those with higher birth weight (odds ratio [OR]=1.64; 95% confidence interval [CI]= 1.55, 1.72). The gaps for hypertension, diabetes, and for stroke, heart attack, and heart disease were also large at age 50 years, with odds ratios of 1.51 (95% CI=1.44, 1.58), 2.09 (95% CI=1.97, 2.23), and 2.16 (95% CI=2.01, 2.32), respectively.

By age 50 years, relative to children who did not grow up in poverty, children who did grow up in poverty were more likely to have asthma (OR=1.47), hypertension (OR=1.71), diabetes (OR=1.86), or stroke, heart attack, and heart disease (OR=1.71).

Each of the remaining measures of childhood background (Tables 1–2) was strongly related to disease prevalence in adulthood. All of the gaps as measured by odds ratio (range=1.14–2.14) were statistically significant.

Multivariate Analysis of Disease Onset in Adulthood

Even after controlling for all dimensions of childhood family and neighborhood background (Table 3), the hazard ratio of each disease was statistically significantly higher for babies with low birth weight: 2.09 for asthma ($P<.01$), 1.74 for hypertension ($P<.01$), 1.88 for diabetes ($P<.05$), and 1.94 for stroke, heart attack, and heart disease ($P<.05$).

The childhood family and neighborhood background measures as a whole were highly significant in the multivariate models ($P<.01$). At the same time, some individual childhood family and neighborhood background variables became insignificant. For example, childhood family poverty was not statistically significantly associated with the onset of asthma or of stroke, heart attack, and heart disease; however, other measures of family and neighborhood background were. Specifically for asthma, parental education was important (hazard ratio=0.43; $P<.01$ for father being a high school graduate vs a high school dropout). For stroke, heart attack, and heart disease, not having private health insurance coverage in childhood relative to having continuous private health insurance coverage was associated with a hazard ratio of 1.95 ($P<.1$).

For hypertension and diabetes, several childhood family and neighborhood background factors continued to be strongly related even in the multivariate models. Specifically, childhood poverty status, parental education, intermittent health insurance coverage (for hypertension only), and some dimensions of childhood neighborhood setting were all statistically significant.

Sibling Models of Disease Onset in Adulthood

In Table 4, the estimates in the first column for each disease indicate that even within families, siblings with low birth weight had an elevated hazard rate of disease onset relative to siblings with higher birth weight. The hazard rates associated with low birth weight were 2.0

TABLE 3—Effects of Low Birth Weight and Childhood Socioeconomic Factors on Disease Onset: Panel Study of Income Dynamics, 1968–2007

Risk Factor	Asthma, HR (95% CI)	Hypertension, HR (95% CI)	Diabetes, HR (95% CI)	Stroke, Heart Attack, or Heart Disease, HR (95% CI)
Low birth weight (<5.5 lb)	2.09*** (1.22, 3.57)	1.74*** (1.22, 2.49)	1.88** (1.13, 3.11)	1.94** (1.03, 3.67)
Grew up in poverty	0.91 (0.55, 1.49)	1.31* (0.97, 1.78)	1.47* (0.96, 2.23)	0.64 (0.38, 1.08)
Father's education				
High school dropout (Ref)	1.00	1.00	1.00	1.00
High school degree	0.43*** (0.27, 0.70)	0.89 (0.65, 1.22)	1.04 (0.70, 1.56)	0.84 (0.51, 1.40)
At least some college	0.80 (0.49, 1.28)	0.62** (0.42, 0.91)	0.53** (0.29, 0.95)	0.74 (0.39, 1.37)
Mother's education				
High school dropout (Ref)	1.00	1.00	1.00	1.00
High school degree	1.49 (0.98, 2.26)	0.91 (0.66, 1.24)	0.68* (0.47, 1.00)	1.14 (0.65, 1.99)
At least some college	1.31 (0.71, 2.43)	1.15 (0.73, 1.82)	0.89 (0.49, 1.61)	1.62 (0.83, 3.17)
Childhood health insurance, 1968–1972				
Private health insurance in all years (Ref)	1.00	1.00	1.00	1.00
No private health insurance	0.70 (0.38, 1.29)	1.17 (0.79, 1.74)	1.11 (0.65, 1.88)	1.95* (0.97, 3.94)
Intermittent private health insurance	0.91 (0.60, 1.39)	1.36** (1.05, 1.76)	1.12 (0.78, 1.62)	1.37* (0.85, 2.22)
Childhood neighborhood poverty[a]				
Lived in low-poverty neighborhood (Ref)	1.00	1.00	1.00	1.00
Lived in medium-poverty neighborhood	1.32 (0.74, 2.38)	1.17 (0.79, 1.72)	1.70** (1.07, 2.70)	1.24 (0.62, 2.47)
Lived in high-poverty neighborhood	1.31 (0.57, 3.01)	1.00 (0.61, 1.62)	0.97 (0.52, 1.83)	0.81 (0.38, 1.73)
Additional childhood neighborhood factors[b]				
High-crime neighborhood	1.18 (0.81, 1.72)	1.22* (0.94, 1.58)	0.92 (0.63, 1.33)	0.76 (0.46, 1.26)
Connectedness to informal sources of help	0.98 (0.88, 1.10)	1.06 (0.96, 1.16)	1.11* (0.98, 1.25)	0.99 (0.86, 1.14)
Plumbing problems	1.07 (0.66, 1.73)	0.89 (0.61, 1.30)	1.88*** (1.18, 3.01)	1.06 (0.56, 1.99)
Housing insulation problems	1.26 (0.76, 2.08)	1.01 (0.71, 1.45)	1.11 (0.67, 1.84)	1.30 (0.71, 2.38)
Parent smoked	1.31* (0.92, 1.87)	1.13 (0.86, 1.48)	1.21 (0.80, 1.84)	1.19 (0.77, 1.84)

Note. CI = confidence interval; HR = hazard ratio. All regressions are estimated as competing-risk Cox proportional hazard models to explicitly take into account the competing risk of mortality. All models include controls for gender, race/ethnicity, birth order, mother's age at birth, whether born into 2-parent family, birth year, region of birth, proportion of parent's life between ages 50 and 59 years spent in fair or poor health, parental rate of time preference, and a dummy indicator for missing education of father (coefficients omitted to conserve space). Sample weights are used, and standard errors are clustered at the neighborhood level. For all conditions, the number of families was 1157 and the number of individuals was 2171. The number of person-year observations was as follows: for asthma, 91 259; for hypertension, 90 884; for diabetes, 95 896; for stroke, heart attack, or heart disease, 95 503.

[a]Childhood neighborhood defined as the census tract where the child lived in 1968. High-poverty = > 30% of the people who lived in the neighborhood were in poverty; medium-poverty = 10%–30%; low-poverty = < 10%. We obtained census tract–level poverty information by linking the PSID individual data to US census data for each census tract.

[b]Based on parental report.

*P < .1; **P < .05; ***P < .01.

for asthma (P<.05), 1.45 for hypertension (P<.1), and 6.82 for stroke, heart attack, and heart disease (P<.01), but only 0.80 for diabetes.

Self-reported childhood health status was an independent predictor of disease onset, even in the sibling models. For asthma in adulthood, siblings reported to be in fair or poor health in childhood had a hazard ratio of 2.31 (P<.01) compared with siblings reported to be in excellent or very good health in childhood. The estimate hazard ratios for hypertension, diabetes, and stroke, heart attack, and heart disease were 2.11 (P<.01), 1.96 (P<.1), and 6.83 (P<.05), respectively.

Although self-reported childhood health status was a significant predictor of disease onset, it did not account for the effect of low birth weight on the onset of asthma, hypertension, or stroke, heart attack, and heart disease. The hazard ratio associated with low birth weight remained statistically significant and changed very little after control for self-reported childhood health status.

Adult Mortality, Birth Weight, and Childhood Poverty

The cumulative mortality hazard functions displayed gaps in mortality across the life course by child background (Figure A). Mortality was especially high for low–birth weight children in poor families. Differences in mortality by child neighborhood poverty increased with age.

The final set of models examined the interaction between low birth weight and childhood socioeconomic deprivation in determining adult mortality (Table A). Although statistically significant interactions for disease onset were not found, we did find significant interactions between low birth weight and socioeconomic disadvantage for mortality using the mortality sample. The first model reported the effects of low birth weight on adult

TABLE 4—Sibling Models of the Effect of Low Birth Weight and Childhood Health Status on Disease Onset: Panel Study of Income Dynamics, 1968–2007

	Asthma, HR (95% CI)		Hypertension, HR (95% CI)		Diabetes, HR (95% CI)		Stroke, Heart Attack, or Heart Disease, Hazard Ratio (95% CI)	
	Without Controls for Child Health	With Controls for Child Health	Without Controls for Child Health	With Controls for Child Health	Without Controls for Child Health	With Controls for Child Health	Without Controls for Child Health	With Controls for Child Health
Low birth weight (< 5.5 lb)	2.00** (1.17, 3.41)	2.05** (1.19, 3.55)	1.45* (0.95, 2.21)	1.43* (0.93, 2.18)	0.80 (0.45, 1.43)	0.81 (0.44, 1.51)	6.82*** (1.92, 24.18)	7.21*** (2.18, 23.82)
Health status in childhood[a]								
Excellent or very good (Ref)		1.00		1.00		1.00		1.00
Good		1.30* (0.97, 1.76)		1.03 (0.78, 1.36)		1.34 (0.84, 2.13)		2.35*** (1.26, 4.40)
Fair or poor		2.31*** (1.29, 4.11)		2.11*** (1.33, 3.34)		1.96* (0.98, 3.92)		6.83** (1.30, 35.93)

Note. CI = confidence interval; HR = hazard ratio. All regressions are estimated as competing-risk Cox proportional hazard models to explicitly take into account the competing risk of mortality. All models include controls for childhood poverty, gender, race/ethnicity, birth order, mother's age at birth, whether born into 2-parent family, birth year, and region of birth (coefficients omitted to conserve space). Sample weights are used, and robust standard errors are clustered at the neighborhood level. Sibling fixed effects were present for all conditions. For all conditions, the number of families was 1157 and the number of individuals was 2171. The number of person-year observations was as follows: for asthma, 91 259; for hypertension, 90 884; for diabetes, 95 896; for stroke, heart attack, or heart disease, 95 503.

[a]Based on retrospective self-report.

*P < .1; **P < .05; ***P < .01.

mortality for all children. The second model was identical to the first model, except it included only children from poor families. Models 3 and 4 were identical to models 1 and 2, respectively, except that they accounted for sibling fixed effects. For the full sample of all children in the mortality sample, low birth weight substantially increased the hazard ratio for mortality with and without sibling models (2.13 and 1.79, respectively), although it was not statistically significant. Among children from poor families, however, the hazard ratio was much larger and statistically significant (6.33 [P<.05] and 7.02 [P<.05] with and without sibling models, respectively).

DISCUSSION

To our knowledge, this study produced the first nationally representative estimates of adult chronic disease onset by birth weight and by childhood family and neighborhood socioeconomic disadvantage in the United States. We found that low birth weight significantly increased the likelihood of asthma, hypertension, and stroke, heart attack, and heart disease; this finding was still robust when we included extensive controls for childhood socioeconomic disadvantage as well as comparisons among siblings. For diabetes, the strong association existed in the multivariate models but was not statistically significant in the sibling models. This finding was most likely due to the fact that there was little variation in the occurrence of diabetes within pairs of siblings in these data.

We found that general health status in childhood had large, significant effects on the onset of asthma, hypertension, diabetes, and of stroke, heart attack, and heart disease. Moreover, the effects of low birth weight on disease onset in adulthood persisted even after adjustment for general health status in childhood. This evidence is consistent with the fetal origins hypothesis.[3]

As an extension to further our understanding of the life course pattern of the effects of low birth weight on disease risk, we estimated models identical to those reported in Table 3 but allowed the effects of low birth weight on the risk of disease to become more or less pronounced with age. The results indicated that low birth weight became more strongly related to elevated risks of onset of hypertension and diabetes at older ages (Figure B, available as a supplement to the online version of this article at http://www.ajph.org), which is consistent with the hypothesis that the effects of birth weight may not be fully visible until later in life.[26]

The most convincing identification strategy for estimating long-term health consequences of adverse conditions in utero and poor fetal health requires variation in early health conditions that is not confounded by other factors, such as childhood socioeconomic conditions and family background, that might also affect adult health outcomes. A methodological strength of the empirical approach is the model's inclusion of an extensive array of well-measured dimensions of childhood family and neighborhood background. The unusually rich set of family and child-specific control variables included in the models reduced potential omitted variable bias, providing stronger evidence on whether the estimated effects of low birth weight and childhood socioeconomic disadvantage on disease onset in adulthood were causal. In addition, the socioeconomic factors in this study were measured more accurately and comprehensively than in other surveys used to examine the impact of childhood factors on health in adulthood because the assessment of these factors has been a primary focus of the PSID.

Parental investments in children, the quality of parenting received, parents' resources, and children's abilities, personality traits, and genetic characteristics may be correlated with both early-life health and subsequent disease onset and mortality risks. These childhood factors are often unobserved and are potential sources of bias in traditional ordinary least squares models that examine long-run consequences of poor infant health. To the extent these characteristics are family specific, our sibling design enabled us to control for these sources of unobserved heterogeneity.

A strength of the PSID is its genealogical design, which allowed comparison of siblings throughout nearly 40 years of their lives. This feature allowed adjustment for additional risk factors—specifically, unmeasured risk factors that siblings shared in common—thus improving the estimated effects of low birth weight on disease onset in adulthood. The sibling models

led to the same qualitative conclusion for 3 of the 4 diseases: low birth weight leads to accelerated onset of chronic disease in adulthood.

We have shown that low birth weight is a strong predictor of onset of disease over the life cycle and remains so even for sibling comparisons. The results provide strong support for a causal role of poor infant health (which interacts with parental socioeconomic status) on the onset of later-life health conditions and mortality.

Longitudinal data that include information on initial health conditions and later-life health are rare, which has limited efforts to estimate long-term effects of conditions in utero and during childhood. Few studies follow individuals from birth through middle age. Although sibling models have been used in previous studies, they have not been frequently used to study the lasting impact of early-life events on adult health outcomes because sibling data have not been available. This study makes contributions to the literature along these lines.

Study Limitations

Disease onset was based on self-reported measures, and a patient's knowledge of disease presence could have been affected by differential access to and interaction with the health care system. People in poor families have lower levels of health care utilization than does the general population and are less likely to have a disease diagnosed. The disparities in self-reported disease prevalence observed in our study are therefore probably smaller than disparities in true disease prevalence, making our estimates of these disparities conservative.

Selective attrition is a potential source of bias in longitudinal analyses. We addressed 3 types of attrition and found no evidence that attrition was different for individuals with low birth weight and for those with normal birth weight. In the first type of attrition, children born between 1951 and 1968 (the birth cohorts we examined) may have been less likely to survive until 1968, when their families were first interviewed, if they had low birth weight. Because PSID mothers reported the weight of all births and not just the births surviving until 1968, we investigated this issue and found no evidence that this type of attrition had occurred. In the second type, low–birth weight babies may have been lost through attrition from the PSID at differential rates after 1968. However, models of attrition did not find low birth weight as predictive. In the third type, because the information on disease was not collected before 1999, selective attrition before 1999 may have biased parameter estimates. We also found no evidence that estimates suffered significant bias from attrition before 1999 among individuals with low birth weight. Furthermore, studies have examined the representativeness of the PSID over the years and concluded that the sample remains representative.[15,27]

Our sibling models eliminated confounding from shared unobserved family background characteristics and attempted to restrict the identifying variation to prenatal shocks that induced low birth weight but did not appear to persist into the postnatal environment. Sibling differences in prenatal environmental conditions (with low–birth weight status as a marker) that are positively correlated with sibling differences in postnatal parental investments in children's health and learning are a potential source of bias; we minimized this potential with the inclusion of sibling-specific controls for early-life factors such as mother's marital status at birth, maternal age at birth, birth order, and childhood stage-specific parental income measures.

Although sibling models explicitly control for all persistent parental family background factors, they are unable to account for possible effects of unshared genetic factors, which studies of monozygotic twins can.[13] Full biological siblings share on average 50% of their genetic makeup, so genetic differences between nonidentical siblings remain and can be a source of bias. All of the siblings in our sample grew up together with the same mother, and most of them were fully biologically related.

Conclusions and Policy Implications

Our findings suggest that the seeds of vulnerability to chronic health conditions are planted early in life. Birth weight and childhood socioeconomic disadvantage accelerate the onset of chronic diseases in the United States.

Future work is needed to identify and measure the mechanisms along the causal chain linking poor infant health and childhood economic disadvantage to disease onset later in life. This research may enable more effective policy interventions to be implemented to ameliorate the burden of disease and the economic burden to the health care system.

Interventions and policies that promote early childhood health and reduce childhood socioeconomic disadvantage generate immediate gains in well-being that can justify their existence. Moreover, as shown in this study, additional benefits from these interventions can arise across the entire life course because improvements in early-life conditions reduce disease onset, improve health, and reduce mortality. These lifelong benefits should be factored into decisions about the adoption of early-life investments. ■

About the Authors

Rucker C. Johnson is with the Goldman School of Public Policy, University of California, Berkeley. Robert F. Schoeni is with the Ford School of Public Policy, Institute for Social Research, and the Department of Economics, University of Michigan, Ann Arbor.

Correspondence should be sent to Rucker C. Johnson, University of California, Berkeley, Goldman School of Public Policy, 2607 Hearst Ave, Mail Code 7320, Berkeley, CA 94720-7320 (e-mail: ruckerj@berkeley.edu). Reprints can be ordered at http://www.ajph.org by clicking the "Reprints/Eprints" link.

This article was accepted April 11, 2011.

Contributors

Both authors were involved in designing the study, interpreting the data, and writing the article. R.C. Johnson, who created the data extract and executed the statistical analyses with consultation from R.F. Schoeni, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Acknowledgments

This study was supported by a grant from the National Institute on Aging.

Human Participant Protection

The data collection was reviewed and approved by the University of Michigan institutional review board. All participants gave oral informed consent.

References

1. Barker DJP. *Fetal Origins of Cardiovascular and Lung Disease.* New York, NY: Marcel Dekker Inc; 2001.

2. Barker DJP. Maternal nutrition, fetal nutrition, and disease in later life. *Nutrition.* 1997;13(9):807–813.

3. Barker DJP. *Mothers, Babies and Health and Later Life.* Edinburgh, UK: Churchill Livingstone; 1998.

4. Victora C, Adair L, Fall C, Hallal P, Martorell R, Richter L. Maternal and child undernutrition:

consequences for adult health and human capital. *Lancet.* 2008;371(9609):340–357.

5. Hack M, Flannery DJ, Schluchter M, Cartar L, Borawski E, Klein N. Outcomes in young adulthood for very-low-birth-weight infants. *N Engl J Med.* 2002; 346(3):149–157.

6. Shonkoff J, Phillips D. *From Neurons to Neighborhoods: The Science of Early Childhood Development.* Washington, DC: National Academy Press; 2000.

7. Lawlor D, Ebrahim S, Davey Smith G, British Women's Heart and Health Study. Socioeconomic position in childhood and adulthood and insulin resistance: cross-sectional survey using data from British Women's Heart and Health Study. *BMJ.* 2002;325(7368):805.

8. Smith GD, Hart C, Blane D, Gillis C, Hawthorne V. Lifetime socioeconomic position and mortality: prospective observational study. *BMJ.* 1997;314(7080):547–552.

9. Smith GD, Hart C, Blane D, Hole D. Adverse social economic conditions in childhood and cause specific adult mortality: prospective observational study. *BMJ.* 1998;360(7145):1631–1635.

10. Kuh D, Hardy R, Langenberg C, Richards M, Wadsworth M. Mortality in adults aged 26–54 years related to socioeconomic conditions in childhood and adulthood: post war birth cohort study. *BMJ.* 2002; 325(7372):1076–1080.

11. Duncan G, Kalil A, Ziol-Guest K. Economic costs of early childhood poverty. Pew Charitable Trusts Research Report. 2008. Available at: http://www.partnershipforsuccess.org/docs/researchproject_duncan_200802_paper.pdf. Accessed August 17, 2011.

12. Huxley R, Neil A, Collins R. Unraveling the fetal origins hypothesis: is there really an inverse association between birth weight and subsequent blood pressure? *Lancet.* 2002;360(9394):659–665.

13. Christensen K, Stovring H, McGue M. Do genetic factors contribute to the association between birth weight and blood pressure? *J Epidemiol Community Health.* 2001;55(8):583–587.

14. Joseph K, Kramer M. Review of the evidence on fetal and early childhood antecedents of adult chronic disease. *Epidemiol Rev.* 1996;18(2):158–174.

15. Koupilova I, Leon DA, Vagero D. Can confounding by socioeconomic and behavioural factors explain the association between size at birth and blood pressure at age 50 in Sweden? *J Epidemiol Community Health.* 1997;51(1):14–18.

16. Fitzgerald J, Gottschalk P, Moffitt R. An analysis of the impact of sample attrition on the second generation of respondents in the Michigan panel study of income dynamics. *J Hum Resour.* 1998;33(2):300–344.

17. Gluckman P, Hanson M. *The Fetal Matrix: Evolution, Development and Disease.* Cambridge, UK: Cambridge University press; 2005.

18. Heron MP. Deaths: leading causes for 2004. *Natl Vital Stat Rep.* 2007;56(5):1–95.

19. Center for Disease Control and Prevention. FastStats: Asthma. 2009. Available at: http://www.cdc.gov/nchs/FASTATS/asthma.htm. Accessed August 17, 2011.

20. Klebanoff MA, Graubard BI. How well do mothers recall the birth weights of their children? *Am J Epidemiol.* 1986;124:535.

21. Baker PC, Keck CK, Mott FL, Quinlan SV. *NLSY Child Handbook.* Columbus, OH: Center for Human Resource Research; 1993.

22. Haas SA. The long-term effects of poor childhood health. *Demography.* 2007;44(1):113–135.

23. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc.* 1999;94(446):496–509.

24. Chamberlain G. Heterogeneity, omitted variable bias, and duration dependence. In: Heckman JJ, Singer B, eds. *Longitudinal Analysis of Labor Market Data.* Cambridge, UK: Cambridge University Press; 1985:3–38.

25. Lancaster T. *The Econometric Analysis of Transition Data.* Cambridge, UK: Cambridge University Press; 1990.

26. Leon D, Koupilova I. Birth weight, blood pressure, and hypertension: epidemiological studies. In: Barker DJP, ed. *Fetal Origins of Cardiovascular and Lung Disease.* New York, NY: Marcel Dekker; 2001:23–48.

27. Andreski P, McGonagle K, Schoeni RF. *An Analysis of the Quality of the Health Data in the Panel Study of Income Dynamics.* Ann Arbor: University of Michigan; 2009. PSID Technical Paper Series 09-02.