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Infant mortality, season of birth and the health of older Puerto Rican adults

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Abstract

The increasing prevalence of heart disease and diabetes among aging populations in low and middle income countries leads to questions regarding the degree to which endogenous early life exposures (exposures *in utero*) are important determinants of these health conditions. We devised a test using infant mortality (IMR) to verify if season of birth is a good indicator of early life (*in utero*) conditions that precipitate adult onset of disease. We linked annual infant mortality (IMR) at the municipality (*municipio*) level from the late 1920s-early 1940s with individual birth year and place using a representative sample of older Puerto Rican adults (n=1447) from the Puerto Rican Elderly: Health Conditions (PREHCO) study. We then estimated the effects of season of birth on adult heart disease and diabetes for all respondents and then for respondents according to whether they were born when IMR was lower or higher, controlling for age, gender, obesity, respondent's educational level, adult behavior (smoking and exercise) and other early life exposures (childhood health, knee height and childhood socioeconomic status (SES)). The pattern of effects suggests that season of birth reflects endogenous causes: (1) odds of heart disease and diabetes were strong and significant for those born during the lean season in years when IMR was lower; (2) effects remained consistent even after controlling for other childhood conditions and adult behavior; but (3) no seasonality effects on adult health for adults born when IMR was higher. We conclude that in this population of older Puerto Rican adults there is continued support that the timing of adverse endogenous (*in utero*) conditions such as poor nutrition and infectious diseases may be associated with adult heart disease and diabetes. It will be important to test the validity of these findings in other similar populations in the developing world.

Keywords

Puerto Rico; early life conditions; season of birth; infant mortality; aging; adults; in utero conditions; heart disease; diabetes

Introduction

Aging populations are increasing in the developing world (Kinsella & Velkoff, 2001) resulting in a growing prevalence of chronic conditions among older adults. Heart disease is already one of the leading causes of death in the developing world and several countries with larger population sizes are projected to see a significant increase in cardiovascular disease and some will soon rank among the top ten countries in the world in terms of

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numbers of adults with diabetes (Murray & Lopez, 1996; Amos et al., 1997). Obesity, an important risk factor for diabetes and heart disease, is also rapidly increasing in these settings (WHO, 2000). Still, little is known about the determinants of older adult health in low and middle income countries.

The possibility that the increasing prevalence of heart disease and diabetes may originate at least partially in early life has yet to be fully examined in the developing world. Any number of pathways and mechanisms are possible beginning with endogenous factors *in utero* or early infancy (Barker, 1998; Finch & Crimmins, 2004; Catalano & Bruckner, 2006), and continuing with later conditions during childhood such as poor socioeconomic status (SES) and health (Lundberg, 1991; Hertzman, 1994; Wadsworth et al., 2002; Wadsworth & Kuh, 1997; Davey Smith et al., 1998; Davey Smith & Lynch, 2004; Elo & Preston, 1992; Bengtsson & Mineau, 2009). Hypotheses regarding the importance of endogenous factors such as early nutrition during critical periods of pregnancy (Barker, 1998), infection leading to inflammation over the life course (Finch & Crimmins, 2004) or stressors *in utero* triggering a culling effect (Catalano & Bruckner, 2006) are particularly relevant to the developing world. Maternal undernutrition is still very pervasive and poor maternal nutrition has been linked with poor health in young adults in these settings (Victora et al., 2008). Severe infectious diseases such as malaria and tuberculosis are also still important health concerns (Murray & Lopez, 1996) and exposure to infectious diseases in early life have been linked with mortality in young adulthood (Moore et al., 1999). Yet even if any of these conditions in early life are important to later adult health, disentangling their effects is difficult. In addition, other important life course factors such as SES could confound the effects of early life on adult health (Huxley, Neil, & Collins, 2002; Joseph & Kramer, 1996).

The aim in this paper is to examine the degree to which conditions *in utero* or early infancy are associated with older adult heart disease and diabetes in Puerto Rico. In previous work (McEniry et al., 2008; McEniry & Palloni, 2010), we showed a strong association between season of birth and adult heart disease and diabetes among older Puerto Ricans who lived in the countryside during childhood, suggesting the importance of the timing of adverse early life exposures for older adult health. In this article, we use season of birth but also infant mortality rates (IMR) to further examine the strength of these effects. There have been few studies in the Latin American and Caribbean region which have examined the effects of early life (*in utero*/infancy) on older adult health and few studies in the developing world which have used both season of birth and infant mortality as indicators of early life exposures. This paper contributes to expand knowledge in both areas.

One difficulty with testing any of the hypotheses regarding early life conditions and older adult health using population studies is that for the most part there are limited indicators of early life exposures *in utero* or early infancy in survey data of older adults. However, season of birth has been shown to be a good proxy for very early life conditions *in utero* and early infancy that precipitates poor adult health in the developed world. Being born at the end of the harvest season has been associated with better adult health (Doblhammer, 2004; Costa, 2005; Gavrilov & Gavrilova, 2005; Moore et al., 1999; Muñoz-Tuduri & García-Moro, 2008; McEniry et al., 2008; McEniry & Palloni, 2010; Mazumder et al., 2009). These results have been attributed to the importance of the timing of nutritional insults during late gestation (Doblhammer, 2004) which provides support for interpretations such as the Barker (1998) hypothesis. Because season of birth also has been shown to be independent of other life course factors such as socioeconomic conditions (Doblhammer, 2004), it is a potential viable indicator of early life exposures. It may capture very early life exposures such as nutritional status or increased risks of infectious and parasitic diseases affecting mother and fetus alike. In decades past there were important seasonal differences in the supply of food (quantity, variety and freshness) and infectious disease environment which could potentially

influence intrauterine growth depending on the month of gestation. Certainly as health and nutritional conditions improved throughout the twentieth century, the influence of seasonal differences weakened in the developed world (Kevan, 1979; Gavrilov & Gavrilova, 2005; Costa, 2005) and thus season of birth became less relevant as an indicator of early life exposures. However, nutritional status and infectious diseases still follow strong seasonal patterns in developing countries, especially around the rainy and dry seasons in tropical regions (Trowbridge & Newton, 1979; Tomkins, 1993; Cole, 1993; Moore et al., 1999; Marin et al., 1996; Hauspie & Pagezy, 1989) and these patterns interact with early growth and development and later health (Moore et al., 1999). Nevertheless, observed associations between season of birth and adult health may not always reflect *in utero* (endogenous) conditions (Buckles & Hungerman, 2008) and some studies in low and medium income countries have produced inconclusive evidence on seasonal effects on health (Simondon et al., 2004; Moore et al., 2004). Therefore, further examination of its meaning as a reflection of endogenous or exogenous conditions in these settings is warranted.

Annual IMR at the time of one's birth may also be a useful indicator of early life conditions. It has been shown to predict older adult mortality (Bengtsson & Lindstrom, 2003; Doblhammer, 2004; Van den Berg, Doblhammer, & Christensen, 2009; Barker & Osmond, 1986; Leon & Davey Smith, 2000). The components of IMR may be able to provide insight into the effects of endogenous or exogenous conditions on adult health. Neonatal mortality (deaths during the first month of life) is thought to be more strongly associated with non-environmental or endogenous (*in utero*) causes whereas post-neonatal mortality (deaths during 1–11 months of life) is believed to be more strongly associated with environmental or exogenous causes. At least within a certain range of lower IMR (44–114), studies have found strong positive linear associations between IMR or its components with cause-specific mortality at older ages (Barker & Osmond, 1986; Leon & Davey Smith, 2000). At higher IMR, neonatal mortality rates may become more constant and if so, post neonatal mortality rates will exhibit a strong linear association with IMR (Bourgeois-Pichat, 1951). This would imply strong associations between post neonatal mortality rates and IMR and adult health (if exogenous mortality is important to adult health such as in Bengtsson & Lindstrom, 2000) and weaker linear associations between neonatal mortality rates and IMR and adult health (if neonatal mortality is important). If significant seasonal effects on older adult health are observed in a regression model and if season of birth reflects endogenous causes, then when neonatal mortality rates are properly specified and introduced, the effects of season of birth should attenuate or disappear. On the other hand, if what matters are environmental (exogenous) causes, then when post neonatal mortality rates are properly controlled for, the effects of season of birth should weaken or disappear.

Neonatal mortality rates are the desired measure to make inferences about season of birth and adult health. However, while specific historical data on IMR during the early 20th century may be available, this is often not the case for neonatal or post neonatal mortality rates. Nevertheless, it may be possible to roughly infer the meaning of season of birth even in the absence of specific neonatal mortality rates by using the two general cases previously described that depict relationships between neonatal and post neonatal mortality rates and adult health at lower and higher IMR. Assuming that it is possible to identify a reasonable cutoff point, one test to examine the meaning of season of birth is to divide survey respondents according to whether they were born when IMR was lower or higher and compare the observed pattern of seasonal effects on adult health with the expected pattern of effects from the two general cases. Based on these cases, if season of birth reflects more *in utero*, endogenous causes, strong effects should appear for respondents born at lower IMR but weak or no effects should appear at higher IMR. If season of birth reflects more exogenous causes, there should be strong effects at higher IMR.

A reasonable cutoff point is to use the proportion of infant deaths less than one month to divide respondents according to when endogenous mortality is more predominant. The relationship between this proportion and IMR is well known, and at lower IMR the proportion is higher whereas at higher IMR the proportion is smaller and at some point becomes more constant ((Bourgeois-Pichat, 1951; Galley & Woods, 1999). When strong positive associations between neonatal mortality rates and adult health were observed (Barker & Osmond, 1996), the proportion was higher. At higher IMR when the proportion is smaller and becomes more constant, linear endogenous effects on adult health may weaken or disappear.

Puerto Rico is a compelling and relevant case study for at least two reasons. First, there was significant mortality decline during the early 20th century primarily due to declines in infant and child mortality. Because the mortality decline was not consistent across the island and because there were municipalities with very high levels of IMR but also municipalities with much lower IMR, there is an opportunity to test hypotheses regarding season of birth, levels of early mortality and older adult health. Second, the particular nature of the mortality decline in the late 1920s in Puerto Rico produced a cohort of individuals that is most at risk of having been affected by harsh early childhood experiences and, simultaneously, having had larger probabilities of surviving due to their exposure to the massive deployment of medical technologies and public health measures during the period after 1930 (Palloni et al., 2005). Older adults from this cohort are now experiencing increasing prevalence of heart disease and diabetes. This cohort may be able to provide us with some insights into whether early life experiences are important in later life since it was less affected by mortality-driven selection than the group of cohorts who preceded them.

In early 20th century Puerto Rico, diarrhea, gastro-enteritis, congenital disability and acute bronchitis along with other infectious diseases such as malaria, tetanus and tuberculosis were the predominant illnesses associated with IMR (Fernós Isern, 1925; Fernós Isern, 1928). Poor economic and environmental conditions which affected the mother, the unborn child and the infant together with a largely illiterate and therefore uneducated population with little knowledge of preventive health measures most probably compounded the problem of high IMR. Infant mortality began to significantly decline during the 1920s–1940s as environmental conditions began to improve (Figure 1) but IMR varied tremendously within and among municipalities (*municipios*) during the late 1920s and early 1940s as mortality declined (Figure 2) thereby creating different pockets of communities which experienced better or much worse environmental conditions. Higher IMR tended to be found in coastal areas where sugar cane was planted but especially in western Puerto Rico where both sugar cane and coffee were planted. In these areas, temperatures were consistently high throughout the year and malaria was a significant health problem. Higher IMR also existed in some urban centers because their population density was higher and they were located in coastal areas.

Times were difficult during the late 1920s through early 1940s for many Puerto Ricans, especially those who lived in the rural countryside. Most families living in rural areas were poor, landless, scattered, isolated, did not own their own homes, and had no strong social organization. Because most rural families did not have a garden plot nor did they own livestock, wages were the most important means to purchase food and have a proper diet. Agricultural employment was highly cyclical and thoroughly dominated by the sugar cane industry (Clark, 1930). Those born in the sugar cane harvest season (January-June) were potentially exposed to better nutritional and environmental conditions during late gestation than those born during the lean season (July-December) (Figure 3). The lean season also brought with it the hurricane season which augmented exposure to infectious diseases such

as dysentery, diarrhea and malaria (Rigau Pérez, 2000), further increasing risk of exposure to adverse conditions.

Our research suggests that seasonal patterns of birth reflecting early growth and development are associated with the health of older adult Puerto Ricans who lived most of their childhood in the countryside (McEniry et al., 2008; McEniry & Palloni, 2010). The odds of reporting heart disease and diabetes were higher for those adults born at the end of the lean season (fourth quarter) or during the lean season (third-fourth quarters). The magnitude of the effects was strong, especially for heart disease. To further test these results, we examined the effects of season of birth based on whether these respondents had been born when IMR was lower or higher. If hypotheses regarding the importance of early life exposures to adult health have merit and if we are able to identify a reasonable cutoff point to define lower IMR or higher IMR, then we expect to observe the following regularities if season of birth reflects endogenous causes: (1) the odds of adult heart disease and diabetes for those older adults born during the lean season should be strong in the group of respondents who were born when IMR was lower but, on the other hand; (2) this observed pattern should weaken or disappear in the group born at higher IMR; and (3) these patterns will be consistent even after controlling for other childhood and adult conditions. If season of birth reflects exogenous causes then we expect to observe strong seasonal effects at higher IMR. While it is not possible to directly test specific mechanisms operating *in utero* or infancy, it is possible to discuss plausible mechanisms that might explain the results.

Methods DONE—see blue below

Data

The data for this paper come from two major sources: (1) yearly data from 1927–1943 on IMR by *municipio* found in annual reports of the Puerto Rican Health Commissioner during the 1920s–1940s; and (2) comprehensive data from the Puerto Rican Elderly: Health Conditions (PREHCO, 2007), a project designed to gather quality baseline data on issues related to the health of the non-institutionalized population aged 60 and over and their surviving spouses. The Department of Health reported that almost all deaths and over 90% of births were reported during this period (Pérez, 1926). Classification of births and deaths by groups and the reporting of the cause of death and morbidity were less reliable. The PREHCO sample is a multistage, stratified sample of older adults residing in Puerto Rico with oversamples of regions heavily populated by people of African descent and of individuals aged over 80. The data were gathered through face-to-face interviews with targets and with their surviving spouses, regardless of age. The data collected offer a substantial amount of information within the limits permitted by face-to-face interviews in a cross-section. The questionnaire included extensive modules on a variety of topics including demographic characteristics, health status and conditions, cognitive and functional performance, anthropometric measurements and evaluation of physical performance. A total of 4,291 interviews with primary respondents were conducted between May 2002 and May 2003 and second wave data were collected during 2006–2007 both with very high response rates. Appropriate institutional ethics committee clearance and participants' informed consent were obtained for this study.

Measures

Infant Mortality—Data for infant mortality during 1927–1943 for each *municipio* were obtained from compilations by the Department of Health in Puerto Rico. For the years 1927–1931, data were reported by monthly births and deaths for each *municipio*. Yearly IMR data by *municipio* were then calculated using these numbers. For 1932–1943, IMR data were obtained using the Puerto Rican Commissioner of Health Annual Report to the

Governor of Puerto Rico which contained already calculated yearly IMR. Municipality-level annual IMR data were linked with the *municipio* and year of birth of PREHCO respondents who were born between 1927 and 1943 (excluding those respondents not born in Puerto Rico). Most respondents were born in years with relatively high levels of IMR (Figure 4).

Municipio-specific data on neonatal or post neonatal mortality rates during the late 1920s-early 1940s were not available but countrywide data were (Table 1). We assumed that *municipio*-wide patterns of neonatal mortality were similar to the overall country wide pattern of neonatal mortality over time. We then created a dichotomous variable to group PREHCO respondents according to the annual IMR in the *municipio* at the time of their births and according to whether they had been born when the proportion of infant deaths due to neonatal (endogenous) causes was higher or lower than an identified cutoff point. Predominance of neonatal (endogenous) mortality (defined by the proportion of infant deaths less than one month) appears at very low IMR in Table 1 (column 5) and there were an insufficient number of respondents from the PREHCO study who were born at these very low levels of IMR.

However, based on both historical data from Puerto Rico and results from research on the distribution of deaths during the first year of life (Bourgeois-Pichat, 1952; Galley & Woods, 1999) and on season of birth (Doblhammer, 2004), we used a reasonable but slightly lower proportion of infant death less than one month to divide respondents into groups. The resulting dichotomous variable with value 1 indicated the lowest tercile of IMR (less than or equal to 112.5 IMR) and implied that respondents had been born when the percent of infant deaths less than one month was at least 32% of IMR. The value 0 indicated the remaining terciles of IMR when neonatal mortality was assumed to be less than 32% of IMR.

We also created another dichotomous variable to reflect good or bad times. We fit a trend to the natural logarithm of IMR data in each *municipio* using the Hodrick-Prescott method (1997) with a filter value of 100. For each *municipio* we identified the years when the observed natural log IMR values exceeded those predicted by the mean trend by more than one standard deviation and called these “bad times” and all other years “good times.” We then created a dummy variable where a value of 1 was assigned to years to reflect bad times and 0 otherwise. The dummy variable was then linked with each PREHCO respondent according to birth year and place. The resulting variable used a value of 1 to indicate good times and 0 bad times. Respondents born in bad times were born mostly when IMR was higher (greater than 113) whereas respondents born in good times were born at lower or higher IMR.

Prenatal exposure to poor nutrition—We defined seasonal exposure to poor nutrition and infectious diseases based on the months of the slack or lean season (July–December) in the Puerto Rican sugar cane industry (Clark, 1930; Gayer, Homan, & James, 1938). We called this broad definition of exposure to poor nutrition and infectious diseases in model estimation *exposure period*, which identified whether the respondent had been born during the lean season or after the sugar cane harvest (July–December).

Adult Health—Elderly adult health was defined by dichotomous variables using self-reported heart disease and self-reported diabetes from the PREHCO study. Survey questions ask a respondent if a doctor has ever diagnosed them with heart disease or diabetes.

Childhood conditions—Respondents were asked to rate their childhood health using a five-point scale (“Would you say that your health as a child was excellent, very good, good, fair or poor?”) and to rate their childhood SES based on a three-point scale (“In general, would you say that the economic conditions in the home in which you were raised were

good, fair or poor?”). We used these responses to create dichotomous variables for (1) poor childhood health where 1 indicated that the respondent rated his or her health during childhood as poor or fair and 0 indicated better, (2) poor SES during childhood where 1 indicated if a respondent defined his or her childhood SES as poor and 0 indicated good or fair. Knee height was measured in the home of the respondents. We used gender-specific quartiles of knee height as a proxy for early stunting (Eveleth & Tanner, 1976). We also used questions which asked respondents to identify infectious diseases (e.g. malaria or dengue fever) experienced during childhood or adolescence. We created a dichotomous variable indicating whether the respondent had experienced the diseases during childhood or adolescence.

Adult conditions—Adult conditions included the number of years of education, obesity (a dichotomous variable with value 1 indicating if body mass index (BMI) was greater or equal to 30 and 0 otherwise) and adult behavior (smoking and exercising). The smoking variable was defined according to non-smokers (never smoked), former smokers and current smokers. In terms of exercising, respondents were asked if during the last year they had played sports, jogged, walked, danced or did heavy work three or more times per week. Responses to this question were dichotomized with 1 reflecting an affirmative response to the question and 0 reflecting a negative response.

A much more detailed explanation of the measures is provided in McEniry et al. (2008).

Analysis

Imputation—We used multiple imputation procedures (Rubin, 1987; Van Buren, Boshuizen, & Knook, 1999) using IVEware (Raghunathan, Solenberger, & Van Hoewyk, 2007) to ensure that all cases were included. For most study variables, the number of missing responses among the subsample of those born in Puerto Rico who lived in the countryside as a child was small (less than one percent); knee height and obesity had about 3% missing. However, we were primarily interested in imputing items about living in the countryside as a child, for which about 14% of the cases were missing primarily because proxies were not asked this question.

Subsample for estimation—We selected a subsample of older adults born in Puerto Rico who responded affirmatively to a survey question that asked them if they had lived for a prolonged period of time in the countryside prior to the age of 18. The imputation created five imputed data sets each of which varied slightly in sample size (from 1447–1464). We only considered respondents aged 60 to 74 to generate estimates for the subpopulation that was most at risk of having been affected by harsh early childhood experiences and, simultaneously, had larger probabilities of surviving due to their exposure to the massive deployment of medical technologies and public health measures after 1930 (Palloni et al., 2005).

Estimation—Before model estimation, we calculated average responses across relevant variables and examined associations between predictors and health outcomes both overall and within subgroups using chi-square and analysis of variance. Using a series of nested multivariate models, we then estimated the effects of season of birth on adult heart disease and diabetes, beginning with age, gender, and season of birth, followed by other childhood conditions and finally adding adult conditions using imputed and non-imputed data. Models testing for interactions between season of birth and infectious diseases (e.g. malaria or dengue fever) were also estimated. Because we were primarily interested in comparing the effects of season of birth between groups of **Lower/Higher IMR**, separate models were estimated for each group using the **Low/High IMR** dichotomous variable. The **Good/Bad**

Times indicator was less informative for this type of test because it is possible to have a mix of low/high IMR within each category. However, because the **Bad Times** indicator reflected, for the most part, higher levels of IMR, we also estimated separate models using the **Good/Bad Times** indicator, expecting to observe smaller seasonal effects as compared with seasonal effects in the **Low IMR** group. We then estimated models including all respondents to test for threshold effects using the indicators of **Low/High IMR** and **Good/Bad Times** and to test for interaction effects with season of birth.

Autocorrelation is an important problem when dealing with continuous time series data in multivariate model estimation. However, in this study we use time series data only to define dichotomous variables for **Lower/Higher IMR** or **Good/Bad Times** and then to link this information to survey responses from older adults born in different years. The time series data are thus not used as continuous variables in models as in other studies using IMR (e.g. Bengtsson & Lindstrom, 2003) and autocorrelation is not an issue. To address the potential non-independence of observations (respondents) from the same *municipio* in multivariate models, we re-ran all models using the “cluster” option in the logistic command in *Stata*. Using the *municipio* level, this command estimates the models assuming non-independence of the respondents from the same *municipio*. The results remained essentially the same.

The final heart disease models controlled for age, gender, education, obesity, poor childhood health, poor childhood SES, low knee height, and exposure (lean/harvest) period. Final models for diabetes also included a variable indicating whether the respondent had a family member with diabetes. Imputed results are presented here because they produced more conservative results. To assess the actual magnitude of effects of season of birth, we calculated predicted probabilities of experiencing heart disease or diabetes for an individual with average attributes and healthy behavior and then added poor childhood and adult conditions. The typical healthy respondent was 66 years old, had 7 years of education, had never smoked and consistently exercised.

Results

Grouping variables and differences between groups

The overall weighted average (standard deviation) for annual IMR among the PREHCO respondents was 119 (35.9). The average IMR for the **Lower IMR** group was 90 (15) and for the **Higher IMR** group 146 (27.5) and the means between groups were significantly different at $p=0.000$. Approximately 40% of respondents were classified into the **Lower IMR** group. The average IMR and its standard deviation were higher in the **Bad Times** group (143 (38.6)) as compared with the **Good Times** group (110 (30.2)) and the means between groups were significantly different at $p=0.000$. About 30% of respondents were classified into the **Bad Times** group. Only about 13% of those classified in the **Lower IMR** group were also born in bad times as compared with about 41% in **Higher IMR** group.

Table 2 describes the variables used in the study. Overall, there were significant associations between annual IMR and older ages ($p=0.001$)—a result to be expected since infant mortality improved between 1927 and 1943; lower adult education ($p=0.029$); low knee height ($p=0.000$); and no rigorous exercise as an adult ($p=0.003$). However, there were no associations between IMR and adult heart disease and diabetes. When groups of respondents were compared, similar differences appeared in the same variables. Respondents born in higher IMR environments had lower knee height, were older and did not practice sustained rigorous exercise. Comparisons between the **Good/Bad Times** IMR groups produced similar results except for education and heart disease where significant associations were found.

Multivariate analyses

There were strong effects of season of birth on adult heart disease for all respondents and these effects did not dramatically change in a series of nested models (results not shown). There were no interaction effects between season of birth and reported infectious diseases during childhood (results also not shown). In the full model for heart disease (Table 3, Model 1), the odds of reporting heart disease for all respondents were about 40% higher for those born during the lean season than for those born during the harvest season. Obesity, smoking and exercise were associated with heart disease. Overall models to test for interactions between season of birth and IMR group showed no significant effects for season of birth (OR = 1.12, 95% CI = 0.79–1.59), marginal effects for **Low/High IMR** groups (OR = 0.64, 95% CI = 0.42–0.99) and significant effects for the interaction between the two (OR = 1.87, 95% CI = 1.05–3.33). Separate estimation by the two IMR groups showed that the (1) effects of exposure (lean) period are significant and stronger for the **Lower IMR** group (Models 2a) and become insignificant for the **Higher IMR** group (Models 2b). The odds of reporting heart disease are over two and a half times higher for those born in the lean season in comparison with those born during the harvest season; (2) the effects of obesity are stronger in the **Lower IMR** group and are very similar to the effects of season of birth; (3) being a previous smoker doubles the odds of heart disease in the **Lower IMR** group; (4) exercise reduces the odds of reporting heart disease by about 40% in the **Higher IMR** group. Overall models to test for interactions between season of birth and **Good/Bad Times** groups showed no significant interaction and group effects and significant effects for season of birth (OR = 1.47, 95% CI = 1.05–2.05). Separate estimation according to **Good/Bad Times** produced similar results to the **Lower/Higher IMR** group analysis in that there were significant seasonal effects but only for those respondents born during good times (on average lower IMR). As expected, seasonal effects were much smaller in the **Good Times** group than they were in the **Low IMR** group.

The model for heart disease using the low IMR indicator (Model 2a) suggested that the probability of heart disease for the average healthy male respondent (i.e., 65–69 years of age with 7 years of education, never smoked and exercises) in Puerto Rico was of the order of 0.06 for those born during the harvest and 0.13 for men born during the lean period (Figure 5). For women the figures were 0.09 and 0.18, respectively. Thus, for the average healthy respondent, a shift from the best to the worst exposure category increased the probability of self-reported heart disease by slightly over 100% for men and 100% for women. The predicted probability of heart disease increased when we added poor childhood conditions (health, knee height and SES) and adult conditions (obese, previous smoker and no exercise). For the full model, the probability of heart disease for men (women) was of the order 0.42 (0.51) for those born during the harvest and 0.62 (0.71) for those born during the lean period. While both childhood and adult conditions contributed to increased probability of adult heart disease, adult conditions increased the probability more.

There were also significant seasonal effects on adult diabetes and these effects did not change across different nested models (results not shown). There were no interaction effects between season of birth and reported infectious diseases during childhood (results also not shown). In the full model for diabetes (Table 4, Model 1), there were very significant and strong effects for having a family member with diabetes. The odds of reporting diabetes were about four times higher for respondents with a family member with diabetes in comparison with respondents without a family member with diabetes. In addition, being born in the exposure (lean) period, having a family member with diabetes and being obese were associated with adult diabetes whereas exercise reduced the odds of reporting diabetes. The odds of diabetes for those born in the lean season were about 1.86 times higher than for those born in the harvest season but being born in the lean season and having a family member with diabetes reduced the odds of diabetes by about 50%. There were no IMR

group or interaction effects between season of birth and IMR although significant effects existed for season of birth (OR = 1.88, 95% CI = 1.14–3.09). When models are estimated separately, the effects of: (1) exposure (lean) period on diabetes are stronger in the **Lower IMR** group (Model 2a) than in the overall model and insignificant in the **Higher IMR** group (Model 2b). The odds of diabetes for those born in the lean season were about two times higher than for those born during the harvest season in the **Lower IMR** group; (2) having a family member with diabetes are strong in both the **Lower IMR/Higher IMR** group; (3) interaction effects between family member with diabetes and exposure period are significant only in the **Lower IMR** group; (4) obesity is significant only in the **Higher IMR** group; (5) exercise shows a protective effect on lowering the odds of diabetes by about 30–42% across models and smoking has a protective effect on the **Higher IMR** group. There were no group or interaction effects between season of birth and **Good/Bad Times** (results not shown) although significant effects existed for season of birth (OR = 1.81, 95% CI = 1.11–2.96). Separate estimation according to **Good/Bad Times** produced similar results to that of the **Lower/Higher IMR** groups. There were significant seasonal effects but only for those respondents born during good times.

We found that predicted probabilities for diabetes for the typical healthy male respondent in Puerto Rico (using Model 2a) were 0.10 for those born during the harvest season and 0.18 for those born during the lean season (Figure 6). For women the figures were 0.11 and 0.19, respectively. Thus, for the average healthy respondent a shift from the best to the worst exposure category increased the probability of self-reported diabetes by about 80% for men and 73% for women. When we added childhood conditions (health, knee height and SES) and adult conditions (obese, never smoked and does not exercise), the predicted probability of diabetes increased. For the full model, the probability of diabetes for men (women) was of the order 0.32 (0.34) for those born during the harvest and 0.48 (0.50) for those born during the lean period. Childhood conditions had a slightly larger impact on increasing the probability of heart disease than did adult conditions.

Discussion

We used season of birth and historical data on annual infant mortality by *municipio* linked with survey data of older adults in Puerto Rico to examine the degree to which early life exposures *in utero* or early infancy are associated with adult heart disease and diabetes. We used what is known about the relationship between early life mortality rates and adult health, and the relationship between IMR and the proportion of infant deaths less than one month to devise a test to verify if season of birth is a good indicator for early life conditions *in utero* that precipitate adult onset of disease. When we estimated the effects of season of birth on the health of older adults born in Puerto Rico for all respondents and for respondents born when IMR was either lower or higher, we found a pattern of effects that suggest that season of birth reflects endogenous causes. The effects of being born during the lean season on adult health (1) were strong and significant for respondents born when IMR was lower, even after controlling for other childhood and adult conditions but (2) were not significant for respondents born when IMR was higher. The results were particularly strong for adult heart disease.

The results support the idea of the importance of the timing of adverse prenatal factors such as poor nutrition and infectious diseases on adult heart disease and diabetes. As such, the results build on previous studies using season of birth (Doblhammer, 2004; Costa, 2005; Gavrilov & Gavrilova, 2005; Muñoz-Tuduri & García-Moro, 2008; McEniry et al., 2008; McEniry & Palloni, 2010). It is difficult to discern the specific mechanisms by which prenatal factors actually do affect later adult health. However, certain inferences can be made. For one, the seasonality effects for those born during the lean season suggest a

disproportionate growth pattern where a more favorable nutritional environment in early gestation sets the fetus on a path of rapid growth with higher expected nutrient demands which makes the fetus more vulnerable to undernutrition in late gestation (Barker et al., 2001). This is not to negate the possibility of the importance of infection and inflammatory processes over the life course (Finch & Crimmins, 2004). The synergy between nutrition and infectious disease makes it difficult to disentangle their effects (Scrimshaw, 1968; Scrimshaw, 1997). Certainly the chronically undernourished state of the rural population during the late 1920s-early 1940s had serious effects on the ability to fight infectious diseases such as diarrhea and dysentery which were still important causes of death in infants and young children during the 1930s and early 1940s (Vázquez Calzada, 1988). Although we found no significant interactions between season of birth and some severe infectious diseases during childhood such as malaria, there may be important effects due to infectious diseases and their interaction with nutrition that we were not able to adequately capture. The unborn child may have been exposed to maternal infections, possibly aggravated from poor maternal nutrition. Indeed, in the late 1920s and early 1940s, mothers in the countryside were at risk of chronic infections due to malaria and hookworm and public health officials noted an association between congenital mortality and malaria (Fernós Isern & Rodríguez Pastor, 1930). Both malaria and hookworm are known to adversely affect the unborn child (Guyatt & Snow, 2004; WHO, 2009). Alternatively, it may be that a culling effect *in utero* (Catalano & Bruckner, 2006) and especially in very early gestation provide an explanation. Those born in the second quarter (no exposure) were exposed in very early gestation to the effects of the lean period which may have culled the cohort leading to more robust individuals. The culling effect during the third trimester is less likely to explain the results obtained since if this were the case we would expect those born at the end of the lean season to exhibit better health which they do not. Finally, although there are differences between viewing poor maternal nutrition as either a factor which sets the trajectory of growth *in utero* (Barker, 1998), which leads to infection and inflammation over the life course (Finch & Crimmins, 2004) or which acts as a stressor which invokes a culling effect (Catalano & Bruckner, 2006), it may be that each of these mechanisms contributes to explaining the results, depending on the timing of the insult *in utero*.

The non-significance of seasonality effects in the **Higher IMR** group should not be interpreted to mean that *in utero* effects are not important to adult health in this group. Rather, the results reflect the restricted conditions under which season of birth illuminates the effects of nutritional deficiencies *in utero*. Having other indicators of *in utero* exposure to poor nutrition (Doblhammer, 2003) in addition to having more specific data on the early life environments in which people were exposed are needed to more fully understand the effects of early life on older adult health.

The results have implications for understanding the health of older adults in low to middle income countries because many older adults in these settings were undernourished and exposed to similar infectious diseases in early life as were the Puerto Ricans. Countries such as Costa Rica and Chile experienced a similar mortality decline in the late 1920s and early 1940s due to public health interventions and medical technology as did Puerto Rico. The adult survivors of these cohorts are now experiencing increasing prevalence of heart disease and diabetes (Palloni et al., 2005). We should therefore expect to observe similar findings using season of birth assuming that there was also marked seasonality of nutrition and infectious diseases at the time of birth. Finally, there may be other factors that confound the effects of season of birth, making it less meaningful as an indicator of early life (Simondon et al., 2004; Moore et al., 2004). Replication of the study will help test the external validity of the results and further clarify the meaning of season of birth for older adults born under different environmental conditions in the developing world.

More precise historical data on neonatal mortality at the *municipio* level are not available and thus we made assumptions about the cutoff point to divide respondents based on historical reports on country-wide neonatal and IMR and based on studies of the distribution of deaths during the first year of life (Bourgeois-Pichat, 1952; Galley & Woods, 1999) and season of birth studies in the developed world (Doblhammer, 2004). These cutoff points, although reasonable, need further testing and refining. Further examination is required to better understand how the level of early mortality and season of birth are associated with older adult health.

As with some historical data on IMR during the early 20th century, there is unknown error caused by the reporting of deaths and births. The reporting of numbers of births and deaths was viewed as being fairly accurate in Puerto Rico (see for example, Ortiz, 1929/30), although births may have been underreported in some instances by as much as 10%, especially during the late 1920s. The use of dichotomous variables and not continuous variables for IMR partially addresses concerns of errors in reporting. The underreporting of births would have resulted in reporting higher IMR in some *municipios* and thus some respondents may have been classified in the **Higher IMR** group when they belonged in the **Lower IMR** group. However, as there was little clustering around the cutoff points for low/high IMR, this is less likely to have made a large difference in the results.

Other results merit attention. The results for heart disease are stronger than those of diabetes, possibly reflecting differences between diseases and timing of insults. The very strong effects of having a family member with diabetes may reflect either genetic background or family lifestyle and this variable requires further examination. Differing effects of obesity, smoking and exercise between groups for heart disease also require more examination. There is no apparent reason for the noted differences between IMR groups in these variables.

The study has limitations in terms of the measurement of early life conditions. Admittedly, season of birth is a broad indicator of very early life exposures and it cannot provide insight into the exact timing of nutritional or infectious disease insults. Nor can it adequately address the complexity of possible causes for poor nutrition *in utero* due to either the inadequate supply of nutrition to mother or the unborn child or due to the demand for better nutrition because of infections. Seasonality of nutrition based on harvest times which affect the supply of nutrition may or may not coincide with seasonality of weather patterns (very dry versus very rainy) which affect the demand for nutrition because of higher exposure to infectious diseases. In the case of Puerto Rico, the rainy season coincided with the lean season but in other settings this may not be the case. Thus, the meaning of season of birth becomes less clear without historical data to discern the environmental setting in early life. A much more thorough examination is needed to better understand the meaning of season of birth and its effect on adult health, especially in low and middle income countries where results using season of birth have been mixed (Moore et al., 1999; Moore et al., 2004; Simondon et al., 2004).

There are other limitations to the study. First, morbidity is underestimated in self-reported health measures; however, other studies have shown that the underestimation provides more conservative estimates but not extremely so (Banks et al., 2006; Goldman et al., 2003). Second, selectivity bias could also explain the results due to the cross sectional nature of the study, although this is less of an issue with the age group examined (60–74 years old). Third, the use of IMR at the *municipio* level to account for those born in rural areas also permit the introduction of unknown error into model estimation. However, Puerto Rico during the 1920s–1940s was primarily rural and thus a high percentage of Puerto Ricans lived in rural areas in most *municipios* (US Census, 1932).

In spite of these limitations, there is sufficient evidence from this study to merit further examination of season of birth in similar settings in low and middle income countries where older adults were exposed to poor nutrition and infectious diseases in early life. If proven to be a reasonably good indicator of early life exposures under certain restricted conditions, season of birth could provide insight in population studies of older adults in the developing world which have limited indicators of early life exposures. Given the increase in aging populations, heart disease and diabetes along with the continued presence of undernourished communities and infectious diseases in the developing world, further illumination of the effects of early life based on season of birth is thus important.

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Figure 1.

Infant mortality per 1000 live births

Puerto Rico 1927–1943

Source: Annual reports of Commissioner of Health; Note: slope is -2.27 , $p=0.000$

Figure 2.

Infant mortality rates by municipio

Puerto Rico 1927–1943

Source: Annual reports of Porto Rico commissioner of health; 1929 & 1943 bolded.

Shown is IMR for each *municipio* for each year during the period 1927–1943 but sorted from lowest to highest IMR based on the year 1929 (bolded line). The bold dashed line indicates 1943.

Fig 3.
Seasonal Variation in Plantation Employment
And Hypothesized Exposure During Late Gestation
Source: Clark, V.S. 1930; Data are for Sugar, Tobacco & Coffee Plantations, 1924–1926

Figure 4.
Annual IMR at time of respondents' birth
PREHCO respondents born in countryside, 60–74 yrs old
Note: PREHCO, n=1447, using first imputed data set, avg 125, sd 36.5

Fig 5.

Predicted prevalence of heart disease

By season of birth, 60–74 years old

Source: PREHCO, imputed data

Note: The predicted probabilities for heart disease corresponding to the (a) typical healthy respondent (66 years old, with 7 years of education and who had never smoked but exercises), (b) plus poor childhood conditions (poor child health, poor child socioeconomic status, low knee height), (c) plus adult obesity, previous smoker and does not exercise, follow. Women: harvest (0.09, 0.16, 0.51), lean period (0.18, 0.30, 0.71). Men: harvest (0.06, 0.11, 0.42), lean period (0.13, 0.23, 0.62).

Fig 6.

Predicted prevalence of diabetes

By season of birth, 60–74 years old

Source: PREHCO, imputed data

Note: The predicted probabilities for diabetes corresponding to the (a) typical healthy respondent (66 years old, with 7 years of education and who had never smoked but exercises), (b) plus poor childhood conditions (poor child health, poor child socioeconomic status, low knee height, (c) plus adult obesity, previous smoker and does not exercise, follow. Women: harvest (0.11, 0.23, 0.34), lean period (0.19, 0.37, 0.50). Men: harvest (0.10, 0.21, 0.32), lean period (0.18, 0.35, 0.48).

Table 1

Infant mortality in Puerto Rico

Year	IMR	Neonatal	Post-neonatal	% Neonatal
1935-39	122.7	36.1	86.6	29.5
1940-44	105.3	32.9	72.4	31.2
1945-49	78.8	28.8	50.0	36.5
1950-54	64.7	26.6	38.1	41.2
1955-59	52.6	25.9	26.7	49.2
1960-64	44.7	25.1	19.6	56.3
1965-69	34.8	23.0	11.8	66.1
1970-74	26.1	20.2	5.9	77.3
1975-79	19.9	15.7	4.2	78.7
1980-84	17.5	14.0	3.5	80.0
1985	14.9	12.1	2.8	81.1

Source: Vázquez Calzada (1988) based on five-year averages.

Notes: Mortality expressed in terms of deaths per 1,000 live births.

The “% neonatal” in column five refers to the percent of infant deaths less than one month.

Table 2

Annual IMR and comparison between IMR groups

Variable	IMR	Lower IMR	Higher IMR	Significance	Good Times	Bad Times	Significance
	Mean (sd)	%	%	p-value	%	%	p-value
Gender							
Female	119 (36.6)	54	50	0.239	52	51	0.989
Male	120 (35.1)						
Age group							
60–64	107 (26.2)	51	31	0.000	49	18	0.000
65–69	121 (32.5)	33	38		37	33	
70–74	138 (45.3)	15	32		14	49	
Education							
None	125 (38.1)	6	7	0.271	5	11	0.005
Primary	120 (35.8)	46	45		47	43	
Secondary	119 (36.7)	35	35		35	35	
Higher	116 (32.1)	12	12		13	11	
Obesity							
Obese	120 (37.1)	28	26	0.338	28	25	0.385
Not obese	119 (35.4)						
Poor childhood health							
Yes	121 (33.9)	23	26	0.298	26	22	0.563
No	119 (36.5)						
Poor childhood SES							
Yes	120 (36.6)	38	38	0.995	37	40	0.408
No	119 (35.4)						
Low knee height							
Yes	128 (41.7)	19	28	0.000	25	22	0.773
No	117 (33.4)						
Family w/diabetes							
Yes	120 (35.9)	60	60	0.423	61	57	0.450
No	118 (35.9)						

Variable	IMR	Lower IMR	Higher IMR	Significance	Good Times	Bad Times	Significance
	Mean (sd)	%	%	p-value	%	%	p-value
Broad exposure							
Harvest	119 (33.7)	48	50	0.755	50	47	0.183
Lean	120 (37.8)						
Smokes?							
Never	118 (35.3)	69	62	0.145	66	64	0.891
Previous	121 (37.0)	23	27		24	26	
Current	124 (36.3)	9	11		10	9	
Exercises?							
Yes	117 (34.6)	47	41	0.017	45	41	0.034
No	121 (36.7)						
Heart Disease							
Yes	122 (38.5)	16	19	0.366	16	23	0.016
No	119 (35.3)						
Diabetes							
Yes	120 (36.9)	33	29	0.892	31	32	0.104
No	119 (35.4)						

Source: PREHCO, first wave, imputed data set, weighted; only those living in countryside as children and between 60–74 years of age (n=1447) using first imputed data set and weighted results. Group indicator: **Lower IMR** is the group of respondents in the lowest tercile of annual IMR at the time of respondent's birth and **Higher IMR** is the group of respondents from the remaining terciles of IMR at the time of respondent's birth. **Good/Bad Times** defined according to if the observed IMR was greater than 1 standard deviation from the mean trend in a particular *municipio*. Shown are p-values from chi-square analyses examining differences between IMR groups across selected variables.

Table 3

Effects of early life conditions on heart disease overall and by groups

	Overall		IMR ¹		Times ²	
	Model 1		Model 2a	Model 2b	Model 3a	Model 3b
	OR (95% CI)		Lower OR (95% CI)	Higher OR (95% CI)	Good OR (95% CI)	Bad OR (95% CI)
Female	1.12 (.83–1.53)		1.41 (.84–2.38)	0.99 (.67–1.44)	1.44 (.98–2.12)	0.71 (.42–1.20)
Age 60–64 (ref)						
Age 65–69	1.40 (1.01–1.95)		1.55 (.92–2.62)	1.33 (.86–2.06)	1.30 (.89–1.92)	1.50 (.75–3.02)
Age 70–74	1.62 (1.14–2.29)		1.76 (.95–3.27)	1.56 (.99–2.46)	1.53 (.98–2.40)	1.40 (.72–2.73)
Education (yrs)	0.99 (.96–1.03)		0.98 (.93–1.03)	1.00 (.97–1.05)	1.00 (.96–1.04)	0.96 (.91–1.02)
Obesity	1.86 (1.39–2.47)		2.29 (1.43–3.67)	1.69 (1.17–2.44)	1.89 (1.32–2.71)	1.80 (1.08–2.99)
Poor child health	1.49 (1.09–2.04)		1.52 (.90–2.56)	1.45 (.98–2.14)	1.53 (1.05–2.25)	1.45 (.85–2.47)
Low knee height	1.03 (.74–1.44)		1.13 (.62–2.09)	0.97 (.66–1.43)	1.19 (.79–1.78)	0.79 (.45–1.39)
Poor child SES	1.10 (.83–1.45)		1.10 (.68–1.77)	1.07 (.75–1.54)	1.21 (0.84–1.72)	0.89 (.52–1.52)
Lean period	1.42 (1.08–1.86)		2.20 (1.38–3.50)	1.12 (.80–1.59)	1.47 (1.05–2.05)	1.32 (.82–2.12)
Never smoked (ref)						
Previous smoker	1.44 (1.02–2.03)		2.27 (1.31–3.92)	1.11 (.73–1.71)	1.86 (1.22–2.82)	0.94 (.53–1.65)
Current smoker	0.77 (.44–1.35)		0.40 (.12–1.41)	0.91 (.48–1.73)	0.84 (.42–1.69)	0.63 (.24–1.63)
Exercises	0.71 (.53–.94)		0.96 (.60–1.54)	0.59 (.40–.85)	0.68 (.48–.97)	0.76 (.46–1.26)
Range of n ²	1428–1443		570–577	851–860	998–1007	421–434
Range of LL ²	–688, –672		–251, –242	–428, –419	–452, –439	–229, –224

Source: Puerto Rican Elderly: Health Conditions project (PREHCO 2007), imputed; all 60- to 74-year olds who lived in the countryside as children. Results shown are based on combining multiple imputation results.

¹ **Lower IMR** is defined as the lowest tercile of annual IMR at the time of respondent's birth and **Higher IMR** is defined as the second and third tercile of annual IMR at the time of respondent's birth. **Good/Bad Times** defined according to if the observed IMR was greater than 1 standard deviation from the mean trend in a particular *municipio*.

² The multiple imputation procedure required us to work with five alternative completed data sets. In this case it was not clear how to calculate conventional statistics, such as chi-square, all of which are functions of data-specific log-likelihood functions. As a partial resolution to the conundrum, we present in this table the range of values for the chosen statistics obtained after estimating models for each of the imputed data sets. Sample sizes for groups vary slightly because differences between **Low/High IMR** and **Good/Bad Times** groups resulted in slightly different division into groups.

Table 4

Effects of early life conditions on diabetes overall and by groups

	Model 1		IMR ¹		Times ¹	
	Model 2a Lower	OR (95% CI)	Model 2b Higher	OR (95% CI)	Model 3a Good	Model 3b Bad
Female		0.94 (.72–1.23)	1.11 (.73–1.68)	0.83 (.58–1.17)	1.02 (.74–1.41)	.80 (.49–1.30)
Age 60–64 (ref)						
Age 65–69		1.18 (.89–1.56)	1.39 (.91–2.13)	1.05 (.72–1.53)	1.24 (.90–1.70)	0.98 (.52–1.84)
Age 70–74		1.27 (.94–1.71)	1.82 (1.11–2.99)	1.02 (.68–1.52)	1.18 (.80–1.76)	1.07 (.59–1.94)
Education (yrs)		0.99 (.96–1.02)	1.01 (.97–1.06)	0.98 (.94–1.02)	0.99 (.96–1.02)	0.99 (.94–1.05)
Obesity		1.42 (1.06–1.90)	1.11 (.74–1.67)	1.67 (1.15–2.42)	1.48 (1.05–2.07)	1.29 (.76–2.17)
Poor child health		1.22 (.93–1.61)	1.33 (.85–2.08)	1.22 (.85–1.74)	1.28 (.92–1.79)	1.11 (.66–1.86)
Low knee height		1.28 (.97–1.69)	1.25 (.77–2.02)	1.33 (.94–1.87)	1.40 (1.00–1.96)	1.09 (.66–1.81)
Poor child SES		1.03 (.79–1.35)	1.47 (.99–2.19)	0.79 (.54–1.17)	1.19 (.87–1.61)	0.75 (.47–1.21)
Family member w/diabetes		4.08 (2.74–6.07)	4.17 (2.23–7.78)	3.91 (2.35–6.50)	4.12 (2.50–6.77)	3.88 (1.96–7.69)
Exposure period		1.86 (1.19–2.90)	2.09 (1.08–4.07)	1.62 (.86–3.05)	1.91 (1.08–3.37)	1.78 (.85–3.73)
Family member X exposure period interaction		0.54 (.32–.93)	0.44 (.20–.99)	0.71 (.33–1.51)	0.51 (.26–.99)	0.63 (.25–1.60)
Never smoked (ref)						
Previous smoker		0.78 (.57–1.06)	1.01 (.63–1.62)	0.63 (.42–.94)	0.85 (.59–1.22)	0.64 (.37–1.09)
Current smoker		0.79 (.52–1.22)	0.44 (.19–1.02)	0.94 (.55–1.60)	0.72 (.42–1.23)	0.86 (.39–1.90)
Exercises		0.67 (.52–.86)	0.63 (.42–.93)	0.66 (.47–.92)	0.70 (.52–.94)	0.58 (.37–.92)
Range of n ²		1429–1444	570–577	851–860	998–1007	421–434
Range of LL ²		–832, –859	–341, –332	–503, –484	–586, –571	–264, –251

Source: Puerto Rican Elderly: Health Conditions project (PREHCO 2007), imputed; all 60- to 74-year olds who lived in the countryside as children. Results shown are based on combining multiple imputation results.

¹ **Lower IMR** is defined as the lowest tercile of annual IMR at respondent's year of birth and **Higher IMR** is defined as the second and third tercile of annual IMR at respondent's year of birth. **Good/Bad Times** defined according to if the observed IMR was greater than 1 standard deviation from the mean trend in a particular *municipio*.

² The multiple imputation procedure required us to work with five alternative completed data sets. In this case it was not clear how to calculate conventional statistics, such as chi-square, all of which are functions of data-specific log-likelihood functions. As a partial resolution to the conundrum, we present in this table the range of values for the chosen statistics obtained after estimating models for each of the imputed data sets. Sample sizes for groups vary slightly because differences between **Low/High IMR** and **Good/Bad Times** groups resulted in slightly different division into groups.