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Abstract

Season of birth may help disentangle the effects on health of early life exposure to poor nutrition and infectious diseases from effects associated with other childhood conditions. Using data from 60 to 74 year old Puerto Ricans who lived in rural areas during childhood (n=1459), we estimated effects of exposure to poor nutrition and infectious diseases during late gestation on the probability of (a) chronic conditions (diabetes, heart disease, obesity), (b) decreased functionality (limitation in at least one ADL and IADL), and (c) poor self-reported health controlling for childhood health and SES and knee height. Findings: (1) strong associations between exposure and heart disease; (2) virtually no attenuation of effects of self-reported childhood health with controls for exposure; (3) no association between exposure and diabetes, obesity, functionality, poor health. Conclusions: timing of birth may reveal conditions experienced perinatally which affect adult heart disease, but there is little evidence of similar effects on adult diabetes and obesity.

INTRODUCTION

Research accumulated in developed countries suggests that early childhood conditions have important consequences for adult mortality and morbidity. Exposure to poor nutrition during pregnancy can lead to adult chronic conditions such as diabetes and heart disease (Barker, 1998; Eriksson, Forsen, Tuomilehto, Osmond and Barker, 2001). Infection during pregnancy and early infancy can also negatively impact child health (Moore, Cole, Collinson, Poskitt, McGregor and Prentice, 1999; Gamble, 1980; Guerrant, Lima and Davidson, 2000). Both poor childhood socioeconomic conditions (SES) and childhood health can have substantial impacts on adult health (Lundberg, 1991; Hertzman, 1994; Wadsworth and Kuh, 1997; Gunnell, Davey Smith, Holly and Frankel, 1998; Davey Smith and Lynch, 2004; Elo and Preston, 1992). The relationship between early life conditions and adult health is complex and includes multiple pathways.

Disentangling the effects of substandard nutrition in utero or shortly after birth from the effects of other childhood conditions that could influence adult health status requires good measures of early growth and development. In the developing world there is now some cross-sectional data on the health of older adults, but longitudinal data on cohorts of individuals from childhood to adult is lacking. The measurement of early childhood conditions in cross-sectional surveys relies on retrospective questions regarding childhood health or socioeconomic status (SES) and on anthropometric measures (birth weight, height, knee height, leg length). Birth weight has been used in studies as an indicator of early growth (Barker, 1998) although it has been criticized as being contaminated by the influence of other life course factors (Joseph and Kramer, 1996; Huxley, Neil and Collins, 2002), and is only rarely available in population surveys of elderly populations. Height is a marker of cumulated nutritional status throughout childhood and adolescence while leg length and knee height are thought to be sensitive markers of nutritional status during early childhood (Wadsworth, Hardy, Paul, Marshall and Cole, 2002; Leitch, 1951; Gunnell et al., 1998; Davey Smith et al., 2001; Palloni, McEniry, Wong and Pelaez, 2006). However, these anthropometric indicators (leg length and knee height) are seldom included in population-based surveys. Self-rating of childhood health by adult respondents has been associated with indicators of early growth (Haas, 2007) but it is not yet clear which dimensions of health are being captured nor the extent to which adult health status self-perception influences self-rating of childhood health. Thus, measures of early childhood conditions used in population surveys of adults are, for the most part, either weak sensitive markers of exposure to poor nutrition in utero and/or early infancy or their effects are confounded with those of other life course factors and individual socioeconomic background.

Even if one had suitable measures of early growth and development, the validity of inferences would be threatened to the extent that background conditions that influence early growth and development could also have independent effects on later health and mortality. Thus, failing to control properly for such background conditions will inflate the association between a valid indicator of early growth and adult health and mortality.

Season of Birth and Its Association with Nutrition and Infectious Disease

A way out of this quandary is to utilize an indicator of early growth and development unrelated to background conditions. In theory, season of birth is such an indicator. To start with there is agreement that it is largely independent of social class of origin and of other health-related life course factors (Doblhammer, 2004). The key issue that remains to be settled is whether or not it adequately reflects conditions experienced in utero or immediately after birth.

In decades past there were important seasonal differences in the supply of food and the disease environment. Food supply (quantity, variety, freshness) varied sharply according to season. Differences in access to high quality food supply could potentially influence intrauterine growth depending on the month of gestation. The last trimester of pregnancy is especially sensitive to variation in the supply of nutrients. Being born during or right after a harvest, when nutritional supplies are more plentiful, is associated with longer life (Prentice and Cole, 1994, Doblhammer, 2004, Gavrilov and Gavrilova, 2005; Costa, 2005; Bengtsson and Lindstrom 2003). To summarize, a marked seasonality in the supply of the principal source of nutritious food can lead to a similar seasonal pattern in maternal nutrition. Under these circumstances, season of birth may be a good indicator of maternal nutritional abundance and ultimately of the extent to which the unborn child is exposed to higher risk of poor nutrition in utero.

In addition to nutritional risks, season of birth may also capture increased risks of infectious and parasitic diseases affecting mother and fetus alike and these risks may work together with the effects of nutritional deficiencies.[1] Climate conditions may become favorable to the reproduction of vectors thus augmenting exposure to infectious and parasitic diseases. To the extent that maternal nutritional status is hampered by contraction of infectious or parasitic diseases, normal intrauterine growth will be impaired. By the same token, as increased exposure translates into increased incidence of infectious and parasitic diseases, we expect deterioration in the quantity and amount of nutrition received by babies from breastfeeding, the main source of nutrition in early life (John et al., 1987). Thus, being born at the beginning of seasons with more moderate temperatures has been shown to be beneficial at least with regard to risk of infectious diseases in early infancy (Kevan, 1979; Doblhammer, 2004).

As health and nutritional conditions improved throughout the twentieth century, the influence of seasonal differences weakened in the developed world (Kevan, 1979; Gavrilov and Gavrilova, 2005; Costa, 2005). However, there is ample evidence that nutritional status and infectious diseases still follow strong seasonal patterns in developing countries, especially around the rainy and dry seasons in tropical regions (Eveleth and Tanner, 1976; Trowbridge and Newton, 1979; Tomkins, 1993; Cole, 1993; Moore et al., 1999; Marin, Segura, Bern, Freedman, Lescano, Benavente et al., 1996; Hauspie and Pagezy, 1989; Cowgill, 1966) and that these patterns interact with early growth and development and later health (Moore et al., 1999). Rural areas in developing countries are particularly prone to the effects of poor nutrition (Ferro-Luzzi and Branca, 1993; Tomkins, 1993) since food supplies may be less vulnerable in larger cities. The effects of season of birth may thus be stronger among individuals who lived prolonged periods of time in the countryside during childhood.

Biological Plausibility for the Timing of Nutrition In Utero and Early Infancy and Its Effects on Adult Health

Given the right conditions, exposure to poor nutrition in utero during mid to late gestation is believed to predispose individuals for later coronary heart disease and diabetes (Barker, 1995). This is the period of rapid fetal growth and organ development. Malnutrition during the weeks leading to birth causes slower growth which can permanently affect organ development and lead to disproportionate fetal growth. Postnatal conditions such as slow infant growth or rapid weight gain in childhood have also been shown to be associated with heart disease, diabetes and obesity (Osmond, Barker, Winter, Fall and Simmonds, 1993; Barker, Eriksson, Forsen and Osmond, 2002; Eriksson et al., 2001). It is believed that these postnatal conditions increase the effects of exposure to poor nutrition in utero (Barker et al., 2002). The combination of both prenatal and postnatal conditions thus potentially can lead to higher risk of heart disease, diabetes or obesity later in life.

The effects of the timing of events occurring in mid to late gestation or early infancy on later adult health have yet to be fully examined. There is little empirical evidence thus far that would indicate that the timing of poor nutrition in the third trimester would produce any different outcome than the timing of poor nutrition during early infancy beyond strengthening the effects if a combination of both events occur. It is also plausible that events occurring in late gestation may originate earlier in the gestation process (Godfrey and Barker, 2000). Studies of famine conditions show that the effects of poor maternal nutrition on later heart disease in fact are greater among those exposed to famine during early rather than late gestation (Painter de Rooij, Bossuyt, Simmer, Osmond and Barker, 2006; Roseboom, van der Meulen, Osmond, Barker, Ravelli, Schroeder-Tanka, et al., 2000). Timing in non-famine conditions may also be different than timing during conditions of famine (Godfrey and Barker, 2000).

However, there have been repeated suggestions that the period of late gestation (third trimester of pregnancy) is particularly important in terms of later adult heart disease (Gardiner, 2007) and diabetes (Ravelli, van der Meulen, Michels, Osmond, Barker, Hales, et al., 1998). Fetal demand for nutrients is thought to be small until late in pregnancy (Godfrey and Barker, 2000) and thus the third trimester is particularly sensitive to variation in the supply of nutrients; the most critical period of development for the heart is the third trimester (Gardiner, 2007) and the third trimester is thought to be the peak period of fetal growth (Doblhammer, 2004). Empirical evidence of the importance of the third trimester in adult health have come from studies of exposure to famine which have shown that exposure during the third trimester can lead to later higher risk of disease such as impaired glucouse tolerance (Ravelli et al., 1998).

Demographic and sociological studies have also been based on the implicit assumption of the importance of the third trimester (Doblhammer, 2004).

Birth seasonality in countries of Latin America and the Caribbean

The Latin American and Caribbean (LAC) region is an interesting case to study because the speed of aging is contributing to large increases in the elderly population (Kinsella, 2001). Further, although the precise determinants of health status among the new cohorts of elderly people have been only vaguely identified, conjectures suggest a pessimistic outlook, particularly among those who will attain age 60 between the years 2000 and 2020. These conjectures hinge entirely on there being a strong connection between early health status and adult health and mortality (Palloni et al., 2006).

Recent comprehensive health surveys of elderly populations in the region provide an opportunity to examine the effects of early health and growth on adult health. Some LAC surveys of elderly populations asked respondents whether they lived a prolonged period of time in the countryside during childhood (before the age of 18). This information combined with historical accounts describing periods of abundant harvest (Gayer, Homan and James, 1938) could shed light on the importance of early childhood nutrition on growth and development. The weakness of the test we propose is that we do not have historical data *at the community level* to attach local patterns of seasonal harvest during the past to individuals. Yet, as in other research, we can rely on information about timing and place of birth, places lived during childhood as well as on seasonality indicators at the *national level* to construct a weak test of the hypothesis. The test should be more robust in smaller and more homogenous countries such as Puerto Rico where national and regional seasonality are quite similar.

Prenatal and Early Infant Exposures: the Case of Puerto Rico

A large proportion of older adults born and raised in Puerto Rico in rural areas and who reached the age of 60 in the year 2000 experienced poor nutrition during pregnancy and early infancy due to social and economic circumstances in the first decades of the twentieth century. This is because during this period a large proportion of Puerto Ricans were unemployed or underemployed during extended periods of the year and many of them lived in rural areas where conditions were precarious (Clark, 1930). Most families living in rural areas were poor, landless, did not own their own home, and were scattered and isolated with no strong social organization. There were limited opportunities for alternative sources of employment which could have supplemented income. Most families depended on a single crop and single employer for their livelihood (Clark, 1930).

Because of the scarcity of cultivable land and the increased dominance of sugar production in Puerto Rico beginning in the early twentieth century, minor crops and the development of subsistence plots were neither encouraged nor supported especially in the sugar cane areas (Gayer, Homan and James, 1938). Since most rural families did not have a garden plot and did not own livestock (Clark 1930), wages were the single most important means to purchase food and have a proper diet. By the 1920s-1930s-early 1940s Puerto Rico had became almost completely dependent on the US mainland to satisfy the demand for food and because wages in Puerto Rico were lower than in the US, food was expensive especially for rural families. In general, those living in rural areas had “insufficient income for proper nourishment” and the diet of a rural family was “monotonous and debilitating” (Clark, 1930, pages 34, 39).

Wages followed a marked seasonal pattern for agricultural workers and this was particularly true of those working in the sugar cane industry which dominated the agricultural sector. By the late 1920s-1930s and early 1940s, about 20-25 percent of the total labor force and perhaps as high as 80 percent of the agricultural labor force worked in the sugar cane industry (Clark, 1930; Gayer, Homan and James, 1938). The cutting season or harvest for sugar cane was intense and occurred in the first half of the year (January-June). This period was followed by a slack season lasting most of the second half of the year. Although sugar cane workers were better paid on average than other agricultural workers and although during the sugar cane harvest they could afford higher expenditures in food than other agricultural workers, during the slack season many of them became unemployed (Gayer, Homan and James 1938; Clark, 1930). Coffee and tobacco were crops that could have supplemented income during the sugar cane slack season but because of their reduced importance, they could not accommodate the large number of individuals who joined the unemployed during the slack season of the sugar cane industry. A composite employment index weighting the number of days worked in the three most important agricultural areas (sugar cane, coffee and tobacco) by the number of laborers reported in these industries in the 1920 census illustrates that agricultural employment followed a highly cyclical pattern similar to that of the sugar cane industry where employment was highest during the first 6 months of the year and lowest during the later part of the year (Figure 1) (Clark, 1930).

[Insert Figure 1 about here.]

In addition, during the economically leaner part of the year, the hurricane season peaks in Puerto Rico between August and October, bringing with it a long period of hot and humid weather. This augments exposure to infectious diseases such as dysentery, diarrhea, malaria and dengue fever (Rigau Pérez, 2000). Thus, poor nutrition due to reduced purchasing power was complicated by exposure to infectious diseases thus producing more negative environments for mothers, unborn children and infants alike.

In summary, the seasonality of agricultural employment in the late 1920s-1930s and early 1940s in Puerto Rico generated conditions for highly variable nutritional status for many rural families. During the earlier part of the year, when employment was more plentiful in the agricultural sector rural families had more purchasing power and hence a greater ability to maintain adequate nutritional standards. But during the second half of the year rural people faced a period of decreased employment and low purchasing power which combined with weather cycles to engender conditions that heightened exposure to malnutrition, to infections and to the synergistic deleterious effects of both.

Conjectures

The aim of this paper is to examine the degree to which seasonality of birth is predictive of adult chronic conditions. More concretely, we seek to identify three regularities. Suppose that, as suggested by some research (Barker, 1998), nutrition in utero (especially during late gestation) and during early infancy are indeed important determinants of adult chronic diseases, particularly diabetes and heart disease. The exact mechanism through which the relation operates is unimportant. We only require that a deterioration of the nutritional environment in utero or right after birth generate conditions that lead to increased susceptibility to adult chronic illness. Suppose also that season of birth is a good proxy for supply of nutrients and for other exogenous conditions that worsen prospects for 'normal' intrauterine and infant growth patterns. Finally, assume that the empirical evidence discussed above regarding weather and employment seasonality reflect well the past history of Puerto Rico. It would follow then that the probability of key adult chronic conditions (such as diabetes, heart disease and obesity) would be higher among those who lived in the country as a child and who were born during lean seasons [prior to the beginning of the harvest] and lower for those born during seasons of abundance [close to the end of the harvest season]. This is the **first** regularity we seek to identify.

The **second** regularity has to do with the potential association between season of birth and other health outcomes such as adult functionality and self-reported health because these traits are influenced by chronic conditions. However, the strength of the relations should be weaker as functionality and self-reported health status are also responsive to a host of conditions occurring during adulthood (Melchior, Lert, Martin and Ville, 2006). To the extent that functional limitations are largely the result of chronic conditions, we would also expect that any relation between it and season of birth should vanish when controlling for chronic conditions (Kuh and Ben-Shlomo, 2004).

The **third** and final regularity is as follows: consider the case that secondary measures of early childhood health status (such as self-reported child health status, self-reported child SES) do in fact confound effects of early nutrition and growth with those associated more generally with social class of origin. Then, if season of birth is a good proxy for early nutritional status and if the latter is indeed an influential factor for adult conditions, we expect that the effects of secondary measures should be attenuated when controlling for season of birth.

Figure 2 illustrates the hypothesized relations between exposure to poor nutrition and infection (July-December) and season of birth.

[Insert Figure 2 about here.]

METHOD

Data

The Puerto Rican Elderly: Health Conditions (PREHCO) project was designed to gather quality baseline data on issues related to the health of elderly Puerto Ricans. The data collected offers a substantial amount of information within the limits permitted by face to face interviews in a cross-section. PREHCO is a cross-sectional survey of the non-institutionalized population age 60 and over and their surviving spouses. The sample is a multistage, stratified sample of the elderly population 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 elderly adults, including those with cognitive limitations who required the presence of a proxy to provide information, and with their surviving spouses, regardless of age. The fieldwork consisted of interviews conducted with a laptop and specialized anthropometric measurement and physical performance tests. More than 20,600 households were visited in 233 sample sections. A total of 4,293 in-home face-to-face target interviews were conducted between May 2002 and May 2003 and second wave data were collected during 2006-2007.   In addition 1,444 spouses were interviewed during the first wave, 1,043 of them 60 or older. The fraction of interviews requiring a proxy was 12.4 percent. Only 4.7 percent refused to participate and the overall response rate was 93.9 percent. The questionnaire includes modules on demographic characteristics, health status and conditions, cognitive and functional performance, labor and economic status, income and assets, health insurance and use of health services, family structure, intergenerational transfers, housing, anthropometric measurements and physical performance. Despite the very high response rate, we conducted an analysis of nonrespondents but found no significant differences between those who responded and those who did not respond.

Measures

Prenatal Exposure to Poor Nutrition

We defined the exposure period to poor nutrition to be between July-December, the months of the slack season in the Puerto Rican sugar cane industry, a time when opportunities for employment were reduced and unemployment in the agricultural sector was highest (Gayer, Homan and James, 1938; Clark, 1930). Mid to late gestation and early infancy may all be periods sensitive to poor nutrition. However, we began with the supposition that late gestation is most relevant and based on this assumption we identified different levels of exposure according to the degree of overlap between the third trimester of gestation calculated from the report of month of birth and the months of the slack season defined above. 'Full exposure' (fourth quarter of birth) means that the third trimester fell completely within the slack period. 'Partial exposure' means that the third trimester of gestation fell partially within the window defined by the slack months either early (third quarter) or late (first quarter). 'No exposure' during the third trimester was reserved for those whose third trimester of gestation fell completely out of the window of slack months. Dummy variables were created to represent these levels of exposure, with the reference group being the "no exposure" group.

Childhood conditions

To assess childhood conditions, we used retrospective questions on childhood health and childhood SES and anthropometric measurement of knee height. Respondents were asked to rate their childhood health using a 5-point scale: "Would you say that your health as a child was excellent, very good, good, fair or poor?" We know that this type of self-reported childhood health has good reliability in the developed world and that it has been associated with indicators of poor intrauterine development (Haas, 2007). We also know that in the PREHCO study these self-reports are quite consistent across waves and that their changes are not associated with changes in self-reported conditions or health.[2] If the effects of early exposure in utero are confounded with childhood health and if season of birth is an adequate measure of in utero nutritional experiences then we should be able disentangle the effects of childhood health.

Early childhood SES has been shown to be an important factor affecting later adult health (Lundberg, 1991; Hertzman, 1994; Wadsworth and Kuh, 1997). The PREHCO study used a retrospective question on childhood SES to measure the degree to which living conditions were poor during childhood. Respondents were asked to rate their childhood SES based on a 3-point scale ("In general, would you say that the economic conditions in the home in which you were raised were good, fair or poor?"). This type of question has been used in previous surveys in the Latin American and Caribbean region (Palloni and Pelaez 2002). It has face validity and appears to be consistent across waves and reliable.[3]

There is no consensus in the literature regarding the definition and use of these variables. However, in our study we were most interested in the effects of poor child health and child SES and thus we created a dichotomous variable for poor childhood health where 1 indicated that the respondent rated their health during childhood as poor and a 0 indicating all other responses. Similarly, a dichotomous variable for poor socioeconomic status during childhood is defined as 1 if a respondent defined their childhood SES as poor and 0 if a respondent described childhood SES to be good or fair.

Knee height was measured in the home of the respondents. We use gender-specific quartiles of knee height as a proxy for early stunting (Eveleth and Tanner, 1976). Knee height is thought to be particularly sensitive to nutritional status during childhood (Leitch, 1951) although there is no consensus regarding its definition for adults and it has not been frequently measured in population surveys. In the anthropometric literature height is often measured using quantiles (Gunnell et al., 1998) and thus we used quartiles of knee height and defined gender-specific dichotomous variables where 1 indicated the lowest quartile of knee height and 0 indicated all other quartiles.

Adult health outcomes

We use self-reported chronic conditions (diabetes, heart disease), obesity, functionality and self-reported health status as health outcomes. Respondents were asked if a doctor had ever diagnosed them with any of several chronic conditions. We create dichotomous variables for diabetes and heart disease (1=have condition, 0=do not have condition). Self-reported health is widely used in population surveys and has been shown to identify quite well underlying conditions (Banks, Marmot, Oldfield and Smith, 2006). However, it is known that self-reported chronic conditions are underreported because their identification depends on the degree of access to appropriate health services (Goldman, Lin, Weinstein and Lin, 2003; Baker, Stabile and Deri, 2004). However, at least for diabetes it has been shown that differences in prevalence measured with self-reports and with biomarkers produce only slightly different values (Banks et al., 2006; Palloni, Wong and Rios-Mena, 2007).

Self-rated health is a 5-item scale (excellent-poor). We define poor self-reported health to be a dichotomous variable with 1 representing poor health and 0 better than poor health. Self-reported health is an indicator of general health with good construct validity (Smith, 1994; Manton, Stallard and Corder, 1997; Wallace and Herzog, 1995; Soldo and Hill, 1995), and is a good predictor of mortality risks (Idler and Benyamini, 1997), disability (Idler and Kasl, 1995) and morbidity (Schechter, Beatty and Willis, 1998; Beckett, Weinstein, Goldman and Yu-Hsuan, 2000), though these properties vary somewhat with national or cultural contexts (Idler and Benyamini, 1997). Although we are beginning to learn about its main pitfalls (Kaptein, Scharloo and Weinman, 2001), we know little about the degree to which self-reported health status is contaminated by cultural idiosyncrasies and about the impact that the associated distortions may have on the validity of direct cross-cultural comparisons of self-reports (Sen, 2002).

We define functionality using activities of daily living (ADLs) (Katz, Hedrick and Henderson, 1979) and instrumental activities of daily living (IADLs) (Lawton and Brody, 1969). The ADL questions ask the respondent if they have difficulty with basic daily activities such as eating, dressing, using the toilet, walking across the room, getting out of bed. The IADL questions ask the respondents if they have difficulty with activities that require more cognitive and community activity such as using a telephone, using transportation, shopping, preparing meals, doing housework, taking medication and managing money. We create dichotomous variables for both ADLs and IADLs where 1 indicates at least one reported condition and 0 indicates no reported condition.[4]

Obesity is an important risk factor for chronic conditions such as heart disease and diabetes and in terms of its association with functionality and overall (Kuh and Ben-Shlomo, 2004). We calculate body mass index (BMI) as weight in kilos divided by height in meters squared and then created a dichotomous variable to indicate obesity (greater than or equal to a BMI of 30).

Main controls

Gender is a dichotomous variable (female=1/male=0); age groups are represented by two dummy variables for age groups 65-69 and 70-74 with the reference group being 60-64. Education is assessed with a dummy variable (1=primary and below, 0=secondary and higher).

Respondents were asked the occupation of their father using an open ended question and then following fieldwork we coded responses into occupational categories according to the International Standard Classification of Occupations based on the International Labor Organization (http://www.ilo.org/public/english/bureau/stat/isco/index.htm). We also introduced a dichotomous variable to indicate if the respondent's father worked in agriculture because agriculture played such a dominant role in the life of the rural community.

Models and estimation

Imputation

We used multiple imputation procedures (Rubin, 1987; Schafer 1997; Raghunathan, Reiter and Rubin, 2003) to ensure that all cases were included. We created multiple data sets following the procedure suggested by Van Buren and colleagues (Van Buren, Boshuizen and Knook, 1999) and implemented in IVEware (http://www.isr.umich.edu/src/smp/ive/). The results we obtain with multiple imputation are statistically efficient and avoid systematic biases likely to arise when one deletes cases with missing observations. The validity of our results relies on a weak assumption about missingness (Rubin, 1987).

Subsample for estimation

We selected a sub-sample of elderly who stated that they were born in Puerto Rico and who responded affirmatively to a survey question which asked them if they had lived for a prolonged period of time in the countryside prior to the age of 18. A high percentage of respondents were born in Puerto Rico (97 percent). We hypothesize that those who lived in the country as a child had the highest risk of exposure to deficient prenatal nutrition. Ignoring rural/urban differences and estimating effects on the entire samples will underplay the role of weather seasonality. In addition, we selected respondents aged 60-74 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 during the period after 1930 (Palloni et al., 2006). Thus, this cohort may be able to provide us some insights into whether indeed early childhood experiences are important in later life since it is less affected by mortality-driven selection than the group of cohorts who preceded them (those 75 and above).

Estimation

To examine the *pattern of season of birth effects*, we first estimate nested logistic regression models for each health outcome identified above, including obesity. The baseline models include only the controls for age and gender. These were then expanded to include education, season of birth, poor childhood health, poor childhood SES, knee height and obesity (the latter included as a control in the models for diabetes, heart disease and functionality). We estimated obesity models excluding those with a BMI of less than or equal to 18 because it is well-known that a high proportion of these are individuals who have experienced other health problems. We used imputed results but also compared imputed and non-imputed results. To examine the *magnitude of effects* for countries showing significant season of birth effects, we calculated predicted probabilities of experiencing a health outcome or condition for an individual with average attributes and then added poor childhood conditions and obesity. The typical respondent was 66 years old, had only attended up to primary school, was not obese, reported that he (she) was not poor and did not have poor health as a child and had a father who worked in agriculture.

RESULTS

General Characteristics of the Sample

Those who experienced full exposure to economically harder times (July-December) during late gestation [third trimester] had a larger prevalence of heart disease than did those with partial exposure during late gestation and those with no exposure during late gestation (Table 1). These differences were significant at p=0.0049 using one way analysis of variance. A Bonferroni test further showed that the differences lie between the full exposure during late gestation (fourth quarter) and no exposure (second quarter) (p=0.002, average difference is 0.10). There were no statistical differences between the remaining selected study variables and exposure to harder economic times.

[Insert Table 1 about here.]

Patterns for chronic conditions, functionality and self-reported health

The effects of exposure level were statistically significant and in the expected direction for heart disease (Table 2). The odds of self-reporting heart disease in Puerto Rico for those born at the time with the worst expected conditions [fourth quarter] are about 1.86 times (95% CI 1.28-2.70) that of those born in the hypothesized better time [second quarter]. Self-reported childhood health status and the marker of early malnutrition (low knee height) had moderate to strong effects for heart disease as the odds of reporting heart disease among Puerto Ricans experiencing poor childhood health status were 1.52 times (95% CI 1.11-2.06) as large as the odds for their counterparts who did not. Obesity also contributed to heart disease as being obese nearly doubled the odds of reporting heart disease (OR 1.82, 95% CI 1.38-2.41). As for diabetes, being in the lowest quartile of knee height increased the odds of reporting diabetes by about 1.42 (95% CI 1.08-1.86) and being obese increased the odds by 1.53 (95% CI 1.20-1.96). In contrast to heart disease and diabetes, there were no discernible childhood or exposure effects on adult obesity. Non-imputed data produced similar results although the effects of season of birth were stronger for heart disease (results not shown).

[Insert Table 2 about here.]

There were no discernible associations between extent of exposure in utero and functionality and poor adult health (Table 3). However, there were strong associations between markers of early childhood conditions, on the one hand, and functionality and poor adult health, on the other. Poor childhood health increased the odds of functional limitations and poor health by about 1.44 (95% CI 1.09-1.90) to about 2.00 times (95% CI 1.42-2.78) and poverty during childhood increased the odds of functional limitations and poor adult health by about 1.38 (95% CI 1.01-1.90) to 1.84 (95% CI 1.33-2.54). Low knee height had a protective effect on IADLs (OR 0.72, 95% CI 0.53-0.95).

[Insert Table 3 about here.]

Are the effects relevant?

The full model for heart disease suggests that the probability of heart disease for the average respondent in Puerto Rico increases from 0.12 to 0.20 for males and from 0.12 to 0.21 for females from unexposed individuals (second birth quarter) to individuals fully exposed during late gestation (fourth birth) (Figure 3). Thus, for the **average respondent** a shift from the better to worse extent of exposure increases the probability of self-reported heart disease by about two thirds for men and three quarters for women. When poor childhood conditions and adult obesity are added, the probability of heart disease continues to increase. This is arguably a very large impact. **At the population level**, however, its impact must be rather tenuous since the distribution of births by seasons is unlikely to change much from year to year, except after or before social and economic upheavals or population crisis of one sort or another.

[Insert Figure 3 about here.]

Potential bias when season of birth is omitted

Table 4 shows nested models for heart disease which was the only instance where the extent of exposure showed significant results.   We note that the effects of extent of exposure are only modestly altered when the baseline model including age, gender and extent of exposure (Model 1) is compared to a model adding early childhood health (Model 3) and then childhood SES and low knee height (Model 4). Likewise, the effects of self-reported childhood health change only slightly when other childhood conditions are added including extent of exposure (Models 2-4) and the effects of knee height and self-reported childhood SES are virtually the same in a model excluding extent of exposure (Model 3) and in a model that includes them (Model 4).   A BIC test enabled us to approximately[5] compare these different models. The best fitting model was model 4 based on a comparison of BIC for each model: 1474 (Model 1), 1461 (Model 2), 1475 (Model 3) and 1489 (Model 4).

This suggests that season of birth and the other indicators of child health status/nutrition are tapping different and unrelated dimensions. More importantly, the results indicate that it is not the case that the effects of self-reported childhood health status or self-reported childhood SES are inflated due to correlations across individuals' life cycle of conditions that determine the adult onset of chronic disease. Alternatively, it could well be that season of birth is a poor indicator of early nutritional status and that its apparent relevance for heart disease in Puerto Rico is due to other factors.

[Insert Table 4 about here]

DISCUSSION

This study uses season of birth as an indicator of poor nutrition and impaired intrauterine and infant growth on adult health among the Puerto Rican elderly population who had lived a prolonged period of time in the countryside prior to the age of 18. Our main findings are two:

First, the effects of season of birth on self-reported heart disease are strong and in the expected direction. Those born towards the end of the harvest period [second quarter] had lower probabilities of self-reporting heart disease and those born prior to the beginning of the harvest [fourth quarter] had higher probabilities of self-reporting heart disease. As confirmed by examination of predicted values of self-reported heart disease, the actual magnitude of the effects is far from trivial. The strong associations found in Puerto Rico provide some support for the idea that there is a relation between early nutrition during pregnancy and early infancy and later chronic conditions (Barker, 1998). Although maternal infections could be playing a role as well, it is less likely that infections during the first few months of infancy are of significance since the peak of the season for more serious infectious diseases during the early twentieth century in Puerto Rico occurred in the second and third quarter (Rigau Pérez, 2000).

Beyond the findings for heart disease there is no strong evidence about further effects for other chronic conditions. By and large, the estimated effects on other adult health outcomes are weak and insufficient to sustain claims about the importance of early growth on adult health in general or on functionality.

There are plausible reasons for these findings. In the case of diabetes, it may be that our results reflect differences the timing of critical periods for heart disease and diabetes and that we are not able to adequately model that process for diabetes. In the case of obesity, we know that the Barker hypothesis supposes that it is poor nutrition in utero in combination with later rapid growth in childhood that leads to obesity (Barker 1998). Given the unpredictable conditions of those living in the Puerto Rican countryside during the late 1920s-1930s-early 1940s, it may be that fewer children experienced the rapid growth during childhood that would have led them to become obese. It may be that obesity is not a problem among rural but among the urban population and indeed in the PREHCO survey we observed that there was a higher prevalence of obesity among those who did not live in the country as children and that these differences were statistically significant (results not shown). Catch-up growth could be a more important factor for those not living in country as children because there might have been more consistency of an abundant diet during childhood that would have permitted rapid growth.

It may also be true that the pathway to adult disease is confounded by infectious diseases during pregnancy or early infancy (malaria in particular). The hurricane season peaks during August-October and brings with it a long period of hot and humid weather that augments exposure to diseases such as dysentery, diarrhea, malaria and dengue fever (Rigau Pérez, 2000). Thus, we cannot discard the possibility of the importance of infectious disease interacting with poor nutrition.

Another potential confounding factor could be that of breastfeeding and weaning patterns in Puerto Rico. While we do not have data to examine the specific variations in breastfeeding in the rural countryside in Puerto Rico during the 1930s-1940s, we do know that the use bottled formula became prevalent only beginning in the late 1940s in Puerto Rico (Becerra and Smith, 1990) and that thus breastfeeding probably followed traditional norms (always and of long duration) in the rural countryside. If this was the case and nutritional status of mother does influence the production as well as quality of mother's milk (John et al., 1987), then children whose mothers experience infection/malnutrition right before birth and sometime thereafter could be affected. Therefore, breastfeeding could be a mechanism (not a confounder) through which season of birth affects early nutritional status and growth.

Our **second** finding is that the effects of other indicators of early childhood health change only slightly when season of birth is included in the models, particularly in the models for heart disease where season of birth behaves as expected. Similarly, the effects of season of birth remain invariant when one controls for the other, secondary measures of early childhood conditions. It could be that early life exposures (as proxied by season of birth) have direct effects on adult heart disease that are not mediated through childhood health (see Figure 1). However, this explanation is inconsistent with a body of literature documenting the influence of early childhood health on adult health (Elo and Preston, 1992; Davey Smith and Lynch, 2004; Lundberg, 1991; Hertzman, 1994; Wadsworth and Kuh, 1997; Kuh and Ben-Shlomo, 2004).

Alternative explanations are the following: (a) self-reported childhood health status and season of birth are, to put it bluntly, mediocre measures. In fact, although we know that self-reported childhood health has good reliability in the developed world (Haas, 2007) and in the PREHCO study (see footnotes 2 and 3) we know less about its reliability and validity in the developing world. Similarly, month of birth could be an excessively coarse measure of intrauterine environment except under the most extreme conditions (Doblhammer, 2004; Prentice and Cole, 1994, Gavrilov and Gavrilova, 2005; Costa, 2005; Bengtsson and Lindstrom 2003) which may not have applied to rural population of Puerto Rico during the early nineteenth century, despite strong seasonality in the food supply. Furthermore, measurement of season of birth is not exact and may not coincide with the critical time for everyone. Finally, focusing exclusively on the third trimester may miss the mark; (b) self-reported childhood health reflects dimensions of childhood health that are not strongly associated with early exposures in utero and early infancy; or, (c) self-reported childhood health is more closely associated with current adult health status than it is with early life exposures.

The rather tenuous importance of season of birth can also be explained by factors other than measurement inaccuracies. An important one is that there may be traits that vary across cohorts that operate to attenuate (exaggerate) the linkages between early exposures and adult health status. Thus, researchers suggest that differences in immune functions and exposures to other infections or environmental risks (none of which are measured in our study) as one factor that explains the heterogeneous importance of season of birth between populations (Moore et al., 1999; Simondon, Eleguero, Marra, Diallo, Aaby and Simondon, 2004). Other factors such as differences between cohorts' experiences (exposure to famine or turbulence caused by civil conflict or international migration) may reduce the effects of season of birth on adult health.

It is still too premature to fully assess the pessimistic conjectures regarding those who will attain age 60 between the years 2000 and 2020 because they hinge entirely on there being a strong connection between early health status and adult health and mortality (Palloni et al., 2006) and we found no relation between season of birth and diabetes or obesity. However, the strong associations with heart disease and the historical relevance of the case for the findings for heart disease in Puerto Rico give us reason to believe that further examination of the effects of season of birth on adult health in the LAC region have merit and that these pessimistic conjectures may not be so far off the mark.

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Footnotes

[1] It is well known that infectious diseases and nutritional status among children and adults alike have synergistic effects (Scrimshaw, 1968; Scrimshaw 1997). In particular, contraction of infections debilitates the immune system and may have a severe impact on the ability of an individual to absorb or efficiently utilize nutrients, especially when an individual's nutritional standard is low at the onset of an infection.

[2] Palloni and Garcia-Gurucharri (unpublished report).

[3] See footnote 2.

[4] To the extent that self-reported measures (conditions, status and ADL or IADL) contain errors that are systematically related to some of our predictors (month of birth and self-reported child health and child SES) our estimates will be biased. However, it is very unlikely to imagine a scenario relating errors in month of birth and self-reports. We have also shown that using the two waves of PREHCO data there are no discernible patterns to suspect the kind of systematic errors that would lead to biases. The worst case scenario is probably one where random errors lead to underestimates of the standard errors and/or to attenuation of the estimated effects.

[5] This is an approximation since the multiple imputation procedure requires us to work with alternative completed data sets (in our case we chose a recommended number of 5). In this case it is not clear how to calculate conventional statistics, such as a chi-square, BIC or AIC all of which are functions of data-specific log-likelihood functions. Instead, we chose an approximation and guide the results obtained from BIC tests performed with the non-imputed data and also one of the imputed data sets.

Table 1: Selected characteristics of sample

	Extent of Exposure During Late Gestation				
	Full	**Partial Late**	**Partial Early**	**None**	**All Cases**
Demographic					
Female (%)	55	51	47	50	50
Age (yrs)	66(4)	66(4)	66(4)	66(4)	66(4)
Primary (%)	62	68	57	65	63
Childhood					
Poor health (%)	29	19	29	22	25
Poor SES (%)	38	42	40	36	39
Knee height (cm)	46(5)	46(5)	47(5)	46(5)	46(5)
Father worked in Agriculture (%)	64	68	58	71	65
Adult Risk					
Obese (%)	27	30	28	28	28
Heart Disease (%)	26	20	16	13	18
Total Number	366	345	350	398	1459

Source: PREHCO imputed and weighted; all 60-74 years old born in Puerto Rico and who lived in countryside as a child. Standard deviations appear in parentheses. Exposure period of harder economic times is July-December. Extent of exposure is: ‘Full exposure’ (fourth quarter); ‘partial late exposure’ (first quarter); ‘partial early exposure’ (third quarter) and ‘no exposure’ (second quarter).

Table 2: Effects of extent of exposure during late gestation and other childhood conditions on adult chronic conditions

	Heart	Diabetes	Obesity
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**
Female	1.09 (0.81-1.45)	1.07 (0.84-1.36)	1.97 (1.52-2.55)
Age 60-64 (ref group)			
Age 65-69	1.42 (1.03-1.97)	1.10 (0.84-1.43)	0.81 (0.61-1.08)
Age 70-74	1.69 (1.19-2.39)	1.10 (0.83-1.47)	0.72 (0.53-0.98)
Primary	1.12 (0.83-1.51)	0.97 (0.76-1.24)	1.23 (0.96-1.59)
Obese	1.82 (1.38-2.41)	1.53 (1.20-1.96)	
Father works in agriculture	0.99 (0.74-1.32)	1.01 (0.79-1.29)	1.16 (0.89-1.51)
Poor child health	1.52 (1.11-2.06)	1.30 (0.98-1.72)	0.80 (0.60-1.07)
Poor child SES	1.09 (0.81-1.46)	1.05 (0.83-1.34)	1.15 (0.89-1.49)
Low knee height	1.05 (0.76-1.45)	1.42 (1.08-1.86)	0.82 (0.61-1.09)
No exposure (ref group)			
Partial late exposure	1.37 (0.92-2.03)	0.83 (0.60-1.16)	1.30 (0.93-1.82)
Partial early exposure	1.39 (0.94-2.05)	1.02 (0.73-1.43)	1.09 (0.77-1.53)
Full exposure	1.86 (1.28-2.70)	1.07 (0.79-1.46)	1.06 (0.73-1.54)
Constant	0.08 (0.05-0.13)	0.33 (0.23-0.47)	0.26 (0.18-0.38)

Source: PREHCO I. All those 60-74 years old born in Puerto Rico and who lived in countryside before the age of 18 (n=1459). Results of combining imputed results. For the obesity model we eliminated those cases where BMI was less than or equal to 18.

Table 3: Effects of extent of exposure during late gestation and other childhood conditions on adult functionality and poor self-reported health

	ADLs	**IADLs**	**Poor Health**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**
Female	1.78 (1.27-2.50)	2.10 (1.62-2.71)	1.20 (0.87-1.64)
Age 60-64 (ref group)			
Age 65-69	1.03 (0.72-1.46)	1.03 (.76-1.39)	0.94 (0.64-1.37)
Age 70-74	0.94 (0.63-1.40)	1.43 (1.05-1.95)	1.07 (0.72-1.58)
Primary	1.16 (0.83-1.62)	1.30 (0.99-1.71)	1.54 (1.08-2.20)
Obese	1.06 (0.75-1.51)	1.24 (0.93-1.67)	1.22 (0.86-1.72)
Father works in agriculture	1.20 (0.86-1.68)	1.18 (0.89-1.56)	0.96 (0.68-1.36)
Poor child health	1.99 (1.42-2.78)	1.44 (1.09-1.90)	1.49 (1.07-2.07)
Poor child SES	1.38 (1.01-1.90)	1.29 (0.99-1.68)	1.84 (1.33-2.54)
Low knee height	0.80 (0.53-1.22)	0.71 (0.53-0.95)	1.11 (0.78-1.59)
No exposure (ref group)			
Partial late exposure	0.90 (0.59-1.38)	1.06 (0.75-1.49)	0.70 (0.43-1.13)
Partial early exposure	0.95 (0.63-1.45)	0.95 (0.67-1.35)	0.81 (0.52-1.24)
Full exposure	1.10 (0.74-1.65)	1.16 (0.83-1.61)	1.02 (0.68-1.52)
Constant	0.08 (0.05-0.12)	0.13 (0.09-0.20)	0.13 (0.05-0.14)

Source: PREHCO I. All those 60-74 years old born in Puerto Rico and who lived in countryside before the age of 18 (n=1459). Results of combining imputed results. ADLs=at least one ADL; IADLs=at least one IADL; poor health=respondent reported poor health.

Table 4: Effects of extent of exposure during late gestation and other childhood conditions on adult heart disease

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)
Female	1.20 (0.90-1.59)	1.29 (0.90-1.58)	1.20 (0.91-1.59)	1.09 (0.81-1.45)
Age 60-64 (ref group)				
Age 65-69	1.39 (1.01-1.91)	1.40 (1.02-1.93)	1.40 (1.20-1.92)	1.42 (1.03-1.97)
Age 70-74	1.62 (1.16-2.27)	1.70 (1.21-2.37)	1.69 (1.20-2.36)	1.69 (1.19-2.39)
Primary				1.12 (0.83-1.51)
Obese				1.82 (1.38-2.41)
Father agriculture				0.99 (0.74-1.32)
Poor child health		1.51 (1.12-2.04)	1.48 (1.09-1.99)	1.52 (1.11-2.06)
Poor child SES			1.14 (0.86-1.51)	1.09 (0.81-1.46)
Low knee height			1.04 (0.76-1.42)	1.05 (0.76-1.45)

No exposure (ref group)				
Partial late exposure	1.38 (0.93-2.03)			1.37 (0.92-2.03)
Partial early exposure	1.38 (0.94-2.03)			1.39 (0.94-2.05)
Full exposure	1.84 (1.28-2.67)			1.86 (1.28-2.70)
Constant	0.12 (0.08-0.18)	0.15 (0.11-0.20)	0.14 (0.10-0.19)	0.08 (0.05-0.13)
BIC	1474	1461	1475	1489

Source: PREHCO I. All those 60-74 years old born in Puerto Rico and who lived in countryside before the age of 18 (n=1459).

Results of combining imputed results.

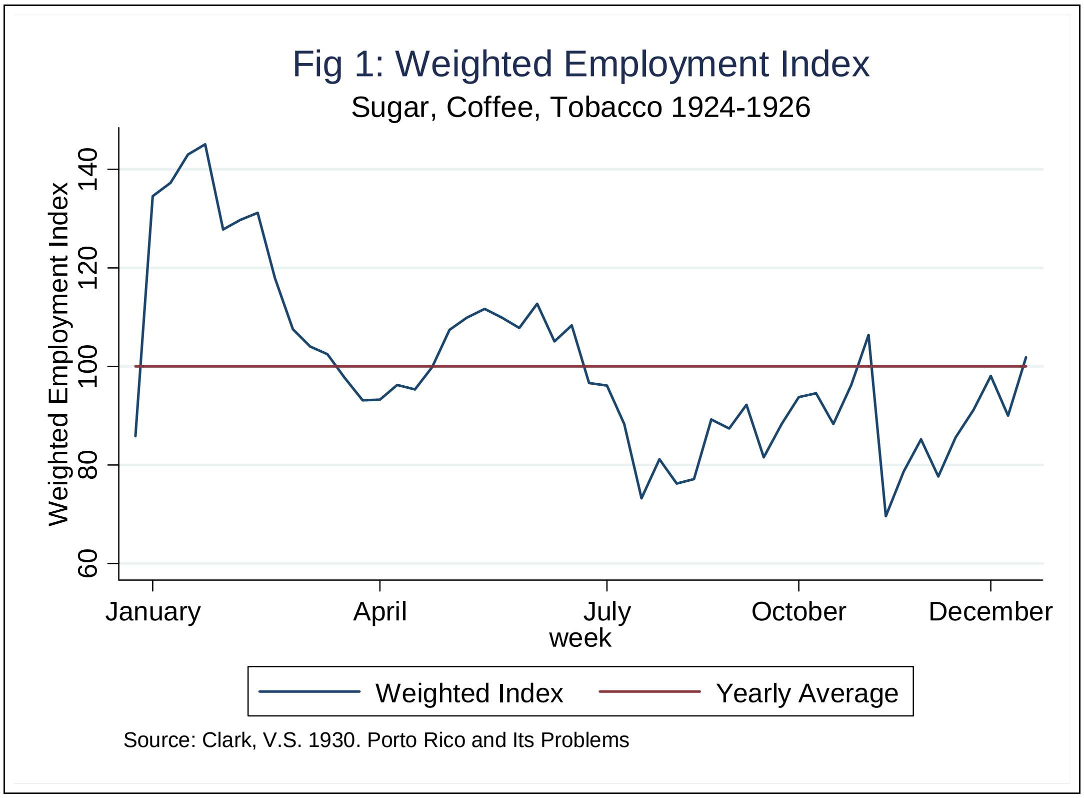
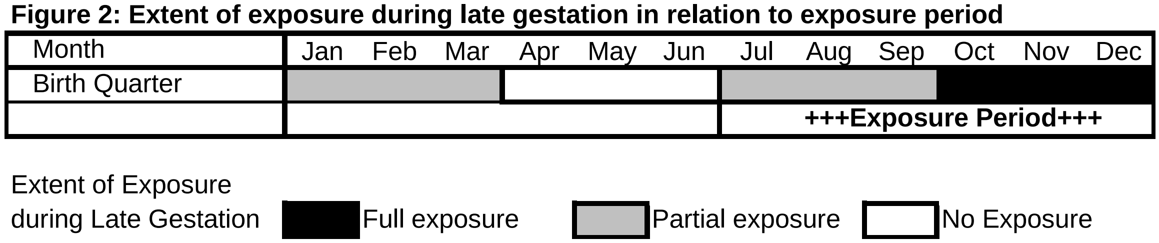


Fig 1: Weighted Employment Index

Sugar, Coffee, Tobacco 1924-1926

Source: Clark, V.S. 1930. Porto Rico and Its Problems

Figure 2: Extent of exposure during late gestation in relation to exposure period



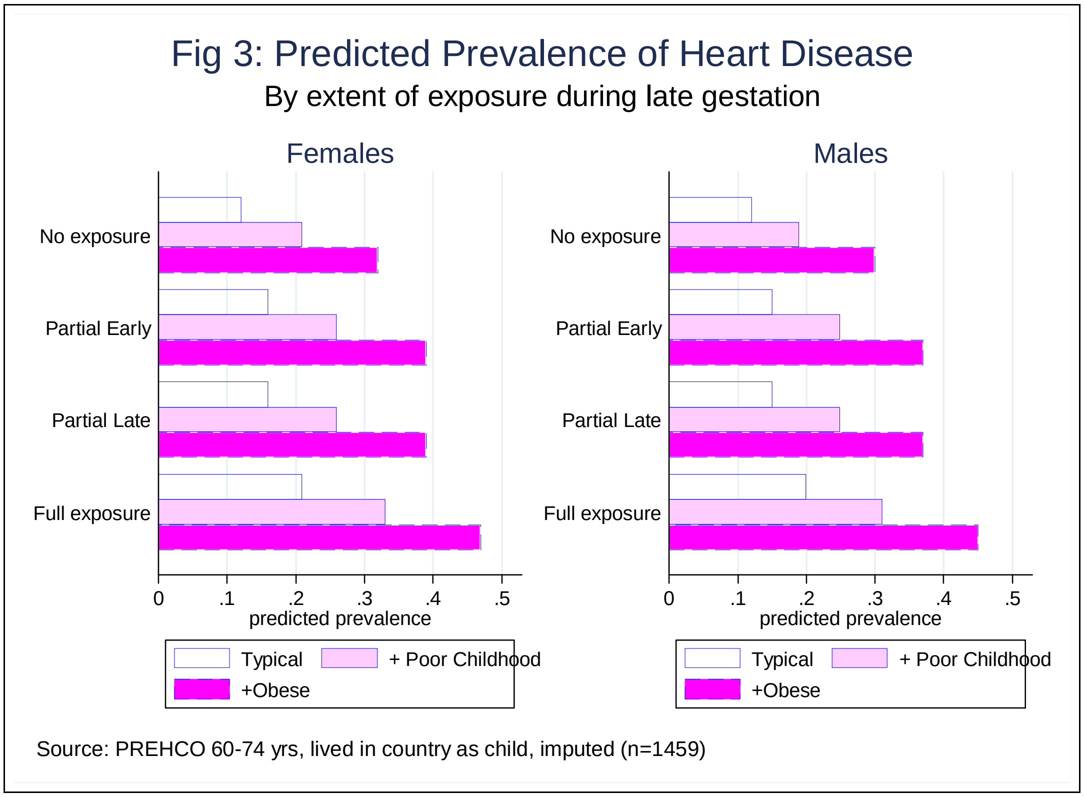


Fig 3: Predicted Prevalence of Heart Disease
By extent of exposure during late gestation
Females
Males
No exposure
Partial Early
Partial Late
Full exposure
0
.1
.2
.3
.4
.5
predicted prevalence
Typical
+ Poor Childhood
+Obese
Source: PREHCO 60-74 yrs, lived in country as child, imputed (n=1459)

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