Early life exposures, life in mainland US

and the health of older adult Puerto Ricans

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Abstract

Recent research shows a strong association between season of birth (an indicator of early life *in utero*/early infancy exposures to poor nutrition and infectious diseases) and heart disease among older adult Puerto Ricans. Yet, the relative importance of these early life conditions in terms of circumstances in adulthood such as living on the US mainland, work-related health problems or lifestyle is not clear. To better understand these relationships, survey data from the Puerto Rican Elderly: Health Conditions (PREHCO) study (n=4291) and aggregate historical data from reports and studies during the early 20th century are used. A series of multivariate models incorporating early life conditions (*in utero*, childhood health, childhood SES) and adult circumstances (having lived on the mainland US, smoking, exercise, obesity) were estimated for Puerto Ricans born during the late 1920s and early 1940s. Findings: (1) The effects of being born during the lean season of the sugar cane harvest on older adult health were much stronger for Puerto Rican men who migrated, lived and/or worked on the US mainland before returning to Puerto Rico at older ages. Having experienced a work-related health problem intensified these effects; (2) Albeit weak, there is evidence that the longer one lived on the US mainland, the weaker the effects of early life conditions became for men; (3) Among men who lived on the US mainland, *in utero* exposures are a main contributor to adult heart disease. We conclude that there is merit to the idea of gender differences in terms of how maternal undernutrition *in utero* affects later susceptibility to adult heart disease in a more enriched adult environment. There is also merit to the idea that this particular cohort of older adults may be more susceptible to the effects of poor early life conditions at older ages and that these effects may be modified under certain conditions at older ages.

Introduction

There is a large literature, from the fields of demography and biology at least, that suggests that poor early life conditions (poor nutrition, infectious diseases and poor early SES) are important to older adult health in the developed world (Almond & Currie, 2010; Barker, 1998; Bengtsson & Lindstrom, 2000; Bengtsson & Lindstrom, 2003; Case & Paxson, 2010; Davey Smith & Lynch, 2004; Doblhammer, 2004; Elo & Preston, 1992; Eriksson et al., 2001; Finch & Crimmins, 2004; Forsdahl , 1978; Gluckman & Hanson, 2006; Gunnell et al., 1998; Hertzman, 1994; Leon et al. 1995; Leon & Davey Smith, 2000; Lundberg, 1991; Newnham & Ross, 2009; van den Berg, Lindeboom, & Portrait, 2006; Wadsworth & Kuh, 1997). Evidence now accumulating from older adults born during the early 20th century in low and middle income countries such as China, Costa Rica, Mexico, Puerto Rico, Bolivia, and Latin American and Caribbean cities also suggests the importance of poor early life conditions on older adult health (Brenes, 2008; Campbell & Lee, 2009; Huang & Elo, 2009; Kohler & Soldo, 2005; McEniry et al., 2008; Monteverde, Norhonha & Palloni, 2009; Moore et al., 1999; Palloni et al., 2005; Victora et al., 2008; Xu et al., 2009; Zhang, Gu & Hayward, 2010).

The story of older adult chronic conditions such as heart disease or diabetes in some settings is in part a nutrition story intertwined with infectious diseases originating in early life (Barker, 1998; FAO, 2004; Popkin, Horton & Kim, 2001). The Barker hypothesis suggests that exposure to poor nutrition *in utero* is associated with adult heart disease because of metabolic changes made *in utero* which increase the risk of adult heart disease (Barker, 1998). Undernutrition *in utero* may have a more negative impact on males than females because of differences in growth patterns (Eriksson et al., 2010). Famine studies have shown that males are more affected by mother malnutrition than females (Ravelli et al., 1999). Males grow faster than females *in utero* and therefore may be more at risk for suffering the consequences of nutritional deprivation at particular times. Females may be more influenced by maternal protein metabolism as reflected in shorter height. Later life events compound the effects of nutritional insults *in utero* but do not confound them (Barker, 1998).

However, ambiguities remain in terms of the relative importance of early life conditions, the degree to which they are a main contributor to adult health, and the exact nature of the biological mechanisms involved. Not all variation in older adult health originates from poor environmental conditions in early life. Health may also be an accumulation of events across the life course (Kuh & Ben-Shlomo, 2004). Events such as migration during adulthood and adult lifestyle can negatively affect adult health. Even though on average migrants may be healthier (Williamson, 1988), the stress of migration during adulthood may have negative health consequences and the length of time in an enriched environment such as the US may over the long run have negative effects even for healthier migrants (Palloni & Arias, 2004). There may be particular characteristics of those who migrate and those who stay behind which explain older adult health. Timing of migration to urban areas may also play a role in the circumstances experienced. Poor early life conditions may also affect adults differently who migrate to urban areas (Alter, 2005). Immigrants who move from an environment of poor nutrition and infectious diseases to a more nutrition-rich environment in later life may be at a disadvantage because of their early life circumstances. Adult lifestyle (smoking, poor diet, and lack of physical activity) increases the risk of poor older adult health (Kuh & Ben-Shlomo, 2004) and may compound these effects. There may also be work-related health problems as an adult which influence health. Alternatively, it may be that healthy immigrants in combination with later adult lifestyle in the target country lead to poor adult health. In this scenario, early life circumstances may not play an important role in chronic conditions such as heart disease.

Although surveys of older adults have limited measures of early life exposures, season of birth has been found to be a helpful marker of exposure *in utero*. Season of birth is a potentially viable broad indicator of early life exposures and is easily obtained in most population studies of older adults. It has been shown to be a good indicator for early life conditions *in utero* and early infancy that precipitates poor adult health in the developed world (Costa, 2005; Doblhammer, 2004; Gavrilov & Gavrilova, 2005; Mazumder et al., 2009; McEniry, Palloni, Dávila, & García, 2008; Moore et al., 1999; Muñoz-Tuduri & García-Moro, 2008; Prentice & Cole, 1994). In the developing world there are several studies with children or younger adults (Gonzalez, Goncalves, & Victora, 2009; Hawkesworth et al., 2009; Richards, Fulford, & Prentice, 2009; Veena et al., 2009) but only a few studies which examine older adult health (McEniry, Palloni, Dávila, & García, 2008). Some results using season of birth have been attributed to the importance of the timing of nutritional insults during late gestation (Doblhammer, 2004) which provide support for interpretations such as the Barker hypothesis (Barker, 1998). Being born in the lean season is associated with low birth weight (Ceesay et al., 1997). Season of birth may capture 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 (Availability of food was closely related to the harvest season and to rainfall. For historical patterns of rainfall throughout the world see FAO 1984, 1985, 1987). Season of birth is not a perfect indicator because other factors, such as differences among populations in immune functions and exposure to other infections or environmental risks may be important. It has not always produced anticipated associations with adult health and thus it remains a broad measure useful in some restricted circumstances (Gamble, 1980; Guerrant, Lima, & Davidson, 2000; Moore et al., 1999; Moore et al., 2004; Richards, Fulford, & Prentice, 2009; Simondon et al., 2004). 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 thus needed to more fully understand the effects of early life on older adult health. Season of birth has been shown to be independent of other life course factors such as socioeconomic conditions (Doblhammer, 2004).

The Case of Puerto Rico

The case of Puerto Rico is an intriguing one. Poor environmental conditions in early life along with lower standards of living and stagnant economic growth describe the predominant conditions in Puerto Rico during the early 20th century prior to the mid-1940s. 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). These cohorts may now be at risk of poor health at older ages because of the scars left by their early life circumstances. 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 that preceded them.

In previous work, being born at the end of the lean season greatly increased the odds of older adult heart disease among older adult Puerto Ricans controlling for other childhood conditions and adult obesity (McEniry et al., 2008; McEniry & Palloni, 2010). Follow-up analyses showed that seasonal effects on heart disease were strongest for those respondents who had lived on the US mainland. The aim of the current paper is to extend this analysis and more thoroughly examine the impact that migration to the US mainland and adult lifestyle has had on adult heart disease among older adult Puerto Ricans born during the late 1920s and early 1940s. *In utero* exposures, selection and adult lifestyle could all be possible explanations for older adult health. If there are no significant differences between those who have lived on the mainland and those who have never lived on the mainland, if this cohort of older adults indeed is more susceptible to the effects of poor early life conditions and if a Barker-type hypothesis has merit we should expect to observe (1) a higher prevalence of heart disease among those who lived on the mainland and who were born during the lean season; (2) being born in the lean season (in particular at the end of the lean season) should have greater effect on males then on females because males are more influenced by maternal malnutrition than females; (3) these effects should be stronger for males who lived on the US mainland; and (4) adult lifestyle variables (smoking, drinking and obesity) may be important for adult heart disease but should be independent of seasonal effects of being born at the end of the lean season.

Methods

The comprehensive data are from the Puerto Rican Elderly: Health Conditions study (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 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 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.

Measures

Prenatal exposure to poor nutrition.—We defined seasonal exposure to poor nutrition and infectious diseases based on birth quarter and the months of the slack or lean season (July–December) in the Puerto Rican sugar cane industry (Clark, 1930; Gayer, Homan, & James, 1938). 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 (Barker, 1998; Gardiner, 2007). We thus used a more detailed definition of exposure and identified different levels of exposure according to the degree of overlap between the third trimester of gestation (calculated from month of birth) and the months of the slack season defined above. We defined this indicator of exposure to poor nutrition and infectious diseases, *level of exposure*, as follows: *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), and *no exposure* during the third trimester was reserved for those whose third trimester of gestation fell completely outside the window of slack months. We created binary variables to represent 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?"). Although it is true that cultural factors can affect self-reported child health, it is also true that this type of self-report has good reliability and is associated with indicators of poor intrauterine development (Haas, 2007). Respondents were also asked if they had experienced rheumatic fever as a child (yes/no), and we used these responses to create a dichotomous variable because rheumatic fever in childhood is an important risk factor for adult heart disease (Elo & Preston, 1992). Early childhood SES is an important factor affecting later adult health (Hertzman, 1994; Lundberg, 1991; Wadsworth & Kuh, 1997; Wickrama, Conger, & Abraham, 2005). PREHCO 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?"). Previous surveys in the Latin American and Caribbean region (Palloni, Pinto-Aguirre, & Pelaez, 2002) have used this type of question. It has face validity, and preliminary results from the second wave of PREHCO suggest that it is consistent across the PREHCO waves. There is no consensus in the literature regarding the definition and use of these variables. However, in our study we were most interested in testing hypotheses concerning the effects of poor childhood health and childhood SES, and, thus, after examining the distribution of responses, we created a dichotomous variable for poor childhood health where 1 indicated that the respondent rated his or her health during childhood as poor or fair and 0 indicated good. Similarly, a dichotomous variable for poor SES during childhood was defined as 1 if a respondent defined his or her childhood SES as poor and 0 if 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) and a reflection of leg length, which is thought to be particularly sensitive to nutritional status during childhood (Leitch, 1951). In the anthropometric literature, height is often measured using either quartiles or quintiles (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. IMR at birth was obtained from published reports of the commissioner of health of Puerto Rico during the late 1920s through the early 1940s (Fernós Isern, 1932; Garrido Morales, 1937; Ortiz, 1927). Municipal class (an indication of wealth) was defined as high, mid and low according to the classification used by the Puerto Rican government in the 1930s (Clark, 1930).

Adult lifestyle/environment.—Respondents were asked a series of questions regarding their adult lifestyle including smoking (Have you smoked one hundred cigarettes or more in your life? Do you currently smoke?) and exercise (In the last year, have you engaged in any of the following activities: sports, jogging, walking, dancing or heavy labor, three or more times a week?). We used these questions to define dichotomous variables (1=yes, 0=no) for each element of adult lifestyle. We calculated body mass index (BMI) as (measured) weight in kilograms divided by (measured) height in meters squared and then defined adult obesity as 1 if BMI was greater than or equal to 30 and 0 otherwise. There were general categories of adult occupation (e.g. public employee, private employee, self-employed, never worked) and we used this question to identify who had ever worked in their adult life along with a question which asked respondents if they had a health problem due to work related questions (yes/no).

Lived in US.—A series of questions in the PREHCO questionnaire attempted to ascertain the timing and length of stay on the mainland after the age of 18. We used these questions to define a dichotomous variable that indicated if the respondent had ever lived on the mainland and then another group of variables which indicated the number of years lived on the mainland.

Adult health outcomes.—Respondents were asked if a doctor had ever diagnosed them with heart disease (1 = have condition, 0 = do not have condition). Self-reported health is widely used in population surveys and identifies underlying conditions quite well (Banks, Marmot, Oldfield, & Smith, 2006). Self-reported chronic conditions are underreported because their identification depends on the degree of access to appropriate health services (Goldman, Lin, Weinstein, & Lin, 2003) although it has also been reported that differences in prevalence measured with self-reports and with biomarkers produce only slightly different values (Banks, Marmot, Oldfield, & Smith, 2006; Riosmena & Wong, 2008).

Main controls.—Gender was a dichotomous variable (female = 1, male = 0). We represented age groups by two binary variables for 65 to 69 and 70 to 74, with the reference group being 60 to 64. We assessed education as the number of years of education completed. We used two criteria to identify respondents who had lived in the countryside as a child: (a) respondent indicated that he or she was born in Puerto Rico and (b) respondent answered affirmatively to a survey question about whether he or she had lived in the countryside as a child before the age of 18.

Models and Estimation

Imputation.—We used multiple imputation procedures (Royston, 2006) using Stata's ICE 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 for most variables of interest (less than one percent); knee height and obesity had about 3% missing. However, we were primarily interested in imputation because there was a higher percentage of missing cases for variables used in the determination of whether the respondent had lived in the countryside as a child.

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 (n=1471). 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 during the period after 1930. Thus, this cohort may be able to provide some insights into whether early childhood experiences are indeed important in later life because it was less affected by mortality-driven selection than the group of cohorts who preceded it (those aged 75 and older).

Pre-estimation.—We reexamined differences between four groups of older adults according to their age (the 60-74 year olds and the 75 years and older adults) and childhood birthplace (urban, rural). We examined differences between those who had lived on the mainland and those who have never lived on the mainland across several demographic, early childhood, adult lifestyle/environment and adult health outcomes. We also examined differences between season of birth for those who had lived and never lived on the mainland along with the prevalence of heart disease by season of birth.

Estimation.—Finding statistical significance in season of birth for only those born in rural areas aged 60-74, we then estimated a series of logistic regression models for heart disease using non-imputed and imputed data first and then according to residence or not on the US mainland controlling for years of residence on the mainland. An additional series of models examined the effects of season of birth according to gender, residence on the mainland and length of residence on the mainland. Predicted probabilities were obtained for the best fitting models for males and for females. Non-imputed results showed similar results as imputed results for rural country living but imputed results were more conservative. We present imputed results in the paper.

Results

US lived versus never lived on the mainland

About 75% of PREHCO respondents born in rural areas during the late 1920s and early 1940s reported that they never lived on the US mainland. For those who said that they had lived on the mainland, the average length of residency was 17 years. Of particular note is that a much higher percentage of males had lived on the mainland. Only forty-one percent (36%) of respondents who lived on the mainland were females as compared with 57% who never lived on the mainland (Table 1). Those who lived on the mainland also tended to have slightly higher educational attainment and higher income as adults. A higher percentage of those who had lived on the mainland reported poor childhood health (33% versus 22%) but a lower percentage reported poor childhood SES conditions (79% versus 84%). A higher percentage who had lived on the mainland also indicated that they drink, smoke, and do exercise. There were differences in reporting work-related health problems especially among men. Men who had lived on the mainland reported a higher degree of work-related health problems. There were also differences in occupation between those who lived or never lived on the mainland. There was much higher percentage of women who had never worked and who had never lived on the mainland. Overall there was a tendency to be employed in private business versus the public sector for those who lived on the mainland. Yet, curiously enough, there were no overall differences in adult health outcomes such as heart disease, diabetes, and problems with functionality between those who had lived on the mainland and those who had not with the exception of women. Women who have lived on the mainland reported more difficulty with functionality than women who have never lived on the mainland.

[Insert Table 1 about here]

Examining this pattern according to residence on the mainland by gender generally showed similar results with the following exceptions. A higher percentage of males who had lived on the mainland reported poor childhood health (30% versus 21%) but no significant difference for females. A higher percentage of males who had lived on the mainland reported smoking as compared to females. There were no differences among males in terms of exercise whereas there were a higher percentage of females reporting that they exercised who had lived on the mainland (46% versus 36%). A higher percentage of females who had lived on the mainland reported difficulty with functionality (22% versus 16%).

Season of Birth and Prevalence of Heart Disease

There were no significant differences in the distribution of season of birth according to whether the respondent had lived on the mainland or not although there were a high percentage of females who had lived on the mainland who were born at the end of the lean season (Table 2). There were also no significant differences in distribution of season of birth according to the length of time lived on the mainland. This suggests that there is no selection of people who lived on the mainland according to a particular season of the year. Season of birth appears to be random in terms of the decision to live on the mainland.

[Insert Table 2, Panel A about here]

However, there were significant differences in the prevalence of heart disease according to season of birth similar to previous findings (McEniry et al, 2008). Those born at the end of the lean season (fourth quarter—full exposure) showed a higher prevalence of heart disease of 24% (Table 2, Panel B). The prevalence of heart disease becomes higher for those born at the end of the lean season and who lived on the mainland (28%) especially so for men (32%) and these differences are significant. Given that the distribution of season of birth was similar for men who had never lived or who had lived on the mainland, it must be the case that there are other factors related to the US mainland which contribute to a higher prevalence of heart disease for men who are born at the end of the lean season. There were also significant differences between season of birth and the prevalence of heart disease for those who lived on the mainland less than 10 years. Sample sizes are small by gender but it appears that this may be particularly true for men (results not shown), suggesting that the longer length of time on the US mainland may have a modifying effect on early life conditions.

[Insert Table 2, Panel B about here]

Multivariate Models: Overall and Residence on the mainland

Repeating previous analyses for those born in the countryside during the late 1920s and early 1940s (McEniry et al., 2008) showed strong seasonal effects of season of birth particularly for those born at the end of the lean season (Table 3, Model 1) (OR 1.69, 95% CI 1.17-2.45). When elements of adult lifestyle are added seasonal effects of birth do not change much (Model 2). There are strong protective effects of exercise as exercise reduces the odds of reporting heart disease by about 30% (OR 0.71, 95% CI

0.54-0.95) as has been reported elsewhere (Popkin, Horton & Kim, 2001). There were much stronger seasonal effects on adult heart disease for those who lived on the mainland (Model 3) as compared with those who never lived on the mainland (Model 5). The odds of reporting heart disease for those born at the end of the lean season and who had lived on the mainland were about two times higher than for those born at the end of the harvest season (OR 2.39, 95% CI 1.12-5.11). For those we never lived on the mainland there were no significant seasonal effects. Controlling for length of time lived on the mainland increased the effect of being born at the end of the lean season slightly for those who lived on the mainland (results not shown). Less robust results are obtained for models with just those who lived on the mainland less than 10 years versus those who lived 10 years or more due to small sample sizes although there was an indication that there are stronger seasonal effects for those who lived less than 10 years on the mainland (results not shown). Thus, it may be that seasonal effects due to *in utero* exposures disappear or are modified the longer one lives on the mainland as other factors becomes more important. Models adding lifestyle (Models 4 and 6) slightly increased the effects of season of birth. For those who never lived on the mainland, lifestyle factors such as smoking were not significant in explaining adult heart disease although exercise reduced the risk of heart disease but about 30% (Model 6). The odds of reporting heart disease as an adult were greatly increased for those who reported having had rheumatic fever as children and for those who had lived on the mainland (Model 4, OR 14.12, 95% CI 2.42-82.17). Being obese increased the odds of heart disease for those who had never lived on the mainland (OR 1.82, 95% CI 1.31-2.53; OR 1.80, 95% CI 1.29-2.51) but not for those who had lived on the mainland.

[Insert Table 3 about here]

Multivariate Models: Overall, Gender, Residence on the Mainland

Overall there were no significant seasonal effects (Table 4, Model 1) for females and for females who had lived on the mainland (Model 2). However, for those females who had never lived on the mainland being born at the beginning of the lean period (the peak of the infectious disease season) increased the risk of heart disease by almost 90% as compared with those born at the end of the harvest (OR 1.86, 95% CI 1.05-3.31). Lifestyle factors such as smoking were notably not significant in all models. For males (Model 4), there were stronger significant effects for the end of the lean period (OR 1.96, 95% CI 1.09-3.54), leading one to suspect that there may be differences in how females and males are affected by nutritional or infectious disease exposures. Exercise had protective effects although not significant. For males who had lived on the mainland (Model 5), seasonal effects intensified (OR 5.08, 95% CI 1.73-14.95) and became stronger when work-related health problems were added (Model 6) (OR 5.59, 95% CI 1.83-17.10). There were also strong effects of work-related health problems (OR 5.00, 95% CI 1.85-13.51) although no interaction effects between season of birth and work-related health problems (results not shown). For those who never lived on the mainland (Model 7) there were no significant seasonal effects and no significant effects of work-related health problems (Model 8). Controlling for years lived on the mainland produced similar results (results not shown).

Predicted Probabilities

Seasonal effects of birth were strongest for females who had never lived on the mainland and the lowest probabilities of heart disease were for women born at the end of the harvest (Figure 1, no exposure). The probability of heart disease for healthy women who were born at the end of the harvest was 0.11 compared with healthy women born in other quarters (0.18-0.20). Thus, being healthy but being born in other quarters increased the probability of heart disease by about 64-82%. For women born at the end of the harvest who had experienced poor early childhood conditions, the probability of heart disease was 0.27 compared with similar women born in other quarters (0.40-0.42). Having experienced poor early childhood conditions but being born in other quarters thus increased the probability of heart disease by about 48-56%. Adding poor adult lifestyles also increased the probability of heart disease to 0.46 for those born at the end of the harvest season and 0.60-0.63 for other quarters. Exercise slightly reduced the chances of reporting heart disease for those born at the end of the harvest (0.39) and for those born in other quarters (0.53-0.55). Thus, overall early life conditions play an important role in predicting adult heart disease for women as do adult lifestyle.

[Insert Figure 1 about here]

For males, seasonal effects were strongest for those who had lived on the mainland. Healthy men born at the end of the lean season (full exposure) had the highest probability of heart disease (0.24) as compared with healthy men born during the harvest (0.05-0.06) and at the beginning of the lean period (0.08). Thus, compared with being born at the end of the lean season being a healthy adult born during the harvest season reduced the chances of heart disease between 75-79% and for those born at the beginning of the lean season by about 67%. For men born at the end of the lean season who had also experienced poor childhood conditions, the probability of heart disease increased to 0.93 as compared with similar men born during the harvest season (0.69-0.73) and at the beginning of the lean season (0.78). Thus, compared with men born at the end of the lean season for similar men born in other quarters, heart disease was reduced by about 16% (beginning of the lean season) and 22-26% (during the harvest season). Adding risky adult lifestyle increased the probability of heart disease slightly (end of the lean season: 0.96; during the harvest: 0.79-0.83; beginning of the lean season: 0.86). Adding a work-related health problem increased the probability of heart disease slightly (end of lean season: 0.99; harvest season: 0.96-0.97; beginning of lean season: 0.97). Adult exercise decreased the probabilities very slightly (end of lean season: 0.99; harvest season: 0.95-0.96; beginning of lean season: 0.97). As compared with women, poor early life conditions had a stronger impact on men and adult lifestyle played a less important role in predicting adult heart disease.

[Insert Figure 2 about here]

Discussion

The purpose of this paper was to more thoroughly examine the effects of season of birth on older adult heart disease in Puerto Rico in the context of living on the US mainland and adult lifestyle. We selected a group of Puerto Rican older adults from the PREHCO study who were born in Puerto Rico during the late 1920s and early 1940s and who had lived in rural areas during childhood and found that a higher percentage of male respondents had lived on the mainland. Compared with their male counterparts who had never lived on the mainland there was a higher percentage of men who reported having had poor childhood health, ever smoked, and exercised. Yet, there were no differences between men who had lived and never lived on the mainland in terms of season of birth, the overall prevalence of heart disease or the reporting of adult health-related work problems. However, upon further examination, men who had lived on the mainland and were born at the end of the lean season reported a higher prevalence of heart disease and the effects of being born during this period were much stronger than for males who had never lived on the mainland. Furthermore, these effects became stronger when work-related health problems were added. Although sample sizes are small, there is some indication that males who lived on the mainland less than 10 years showed stronger seasonal effects than males who lived 10 years or greater on the mainland. Adult lifestyle (smoking and obesity) did not change the effects of season of birth although adult exercise greatly reduced the overall odds of heart disease. Being obese was only important for those who had never lived on the mainland. Curiously, there were very strong effects of rheumatic fever on heart disease for men who had lived on the mainland but not for men who had never lived on the mainland. The pattern of seasonal effects was slightly different for females. Being born at the end of the harvest greatly reduced the odds of heart disease and was strongest for those who never lived on the mainland. Similar to males, adult lifestyle factors (smoking and obesity) did not greatly influence seasonal effects although adult exercise reduced the probability of heart disease and being obese was more strongly associated with those who never lived on the mainland.

The results support the idea that there are gender differences for how poor early conditions *in utero* influence older adult health and that males may be more susceptible later on in life to undernutrition *in utero* than females. The explanation that maternal undernutrition may be more critical for males *in utero* than it is for females in relation to later adult heart disease (Eriksson et al., 2010) may be relevant in the case of Puerto Rican males born at the end of the lean season and who were then later exposed to a richer nutritional environment on the mainland. This may explain why Puerto Rican females who had lived on the mainland showed no seasonal effects even though a high percentage of them had been born at the end of the lean season.

The finding of no significant differences between groups in terms of work-related health problems and yet strong work-related health problems and increased seasonal effect of being born in the lean season for men leads one to postulate that those born during this period were at higher risk in later life not only for heart disease but also other health problems (however, no interaction effects between season of birth and work-related health problem). Given that there were no strong effects for women also leads to the conclusion of gender differences during *in utero* exposures.

Selection effects in regards to the idea that a larger number of poor people who had been born in the lean season migrated to the US mainland do not appear to account for differences between males who lived and did not live on the mainland. Those who lived in the mainland US were not significantly different from those who never lived there in terms of parental SES or season of birth. Furthermore, the idea that healthier Puerto Ricans migrated to and lived on the mainland does not hold true for males because there was a higher percentage of males who lived in the mainland and who also reported poorer childhood health. Yet, poor childhood health was not a significant factor in adult heart disease for this group of men. However, it is also true that we are able to observe only those who survived to older ages and who returned to Puerto Rico. There is no way to know what happened to Puerto Ricans who never returned to Puerto Rico at older ages or who died along the way although studies on the US mainland do suggest that older adult Puerto Ricans are generally in poorer health compared with other US mainland groups (Noel et al., 2009).

One possible explanation for the findings on adult lifestyle (at least as it was defined in this study) could be due to the particular characteristics of the cohort of Puerto Ricans born during the late 1920s and early 1940s. This cohort of individuals may be particularly susceptible to the effects of poor early life conditions due to the nature of the mortality decline during this period. They were more at risk of having been affected by harsh early childhood experiences and, simultaneously, having had larger probabilities of surviving in the context of stagnant economic conditions due to their exposure to the massive deployment of medical technologies and public health measures during the period after 1930 (Palloni et al., 2005). The results for season of birth suggest that poor early life conditions may very well be an important determinant of older health for this cohort. On the other hand, measurement of adult lifestyle using smoking and obesity is limited at best. Diet in particular has been shown to dramatically reduce heart disease among adults (Popkin, Horton & Kim, 2001) and studies of Puerto Ricans on the mainland have shown a strong association between diet and adult diabetes (Noel et al., 2009). However, there was only one general question that related to diet in the PREHCO questionnaire and thus these effects remain unknown. Thus, a more complete examination of adult diet is not possible with the PREHCO data. It is also puzzling why smoking was not an important determinant of heart disease as it is strongly associated with the disease in other settings (Kuh & Ben-Shlomo, 2004).

Questions also remain that cannot be fully addressed due to limitations in sample sizes for those who lived on the mainland. For example, it not possible to discern if maternal protein metabolism is more important for females *in utero* as suggested by some as a reason for differences between gender *in utero* (Eriksson et al., 2010). It is also not clear the degree to which length of residence on the mainland has an effect on the conclusions. There is tentative evidence that seasonal effects of birth for men who lived less than 10 years in mainland US were much stronger than for men who lived 10 years and more. This might indicate that seasonal effects are modified over time by living in the mainland US. It may be that adult lifestyle becomes a more important determinant of heart disease for men as they live longer on the mainland. While there are differences in occupation between those who lived and never lived on the mainland more granular level of data is not available on adult occupation that would help better understand the nature of work-related health problems. There are limitations in early life measurement that have been pointed out elsewhere (McEniry et al., 2008). Season of birth can be a useful measure of *in utero* exposures in certain restricted conditions but it is a very broad and crude measure of *in utero* exposures that cannot indicate the exact timing or nature of exposure. Other childhood measures asked in surveys are retrospective and in the case of childhood health have not been thoroughly tested for validity. Finally, there is the limitation of sample sizes for those who lived in the US. These smaller sample sizes prohibit a more rigorous testing of the questions raised in the paper.

Nevertheless, the analysis presented here in this paper has raised the intriguing possibility of how being born at the end of the lean season—a peak period for poor nutritional environment—may have impacted males more than females leading to the question posed by Barker and colleagues regarding the idea that maternal nutrition for males *in utero* may be more critical in later adult health than for females. It also continues to raise the possibility that this particular cohort of older adult Puerto Ricans—born during the late 1920s and early 1940s—may be more susceptible to the effects of poor early life conditions than those who proceeded them. Although these particular data from Puerto Rico may not be the best to more thoroughly test hypotheses such as those proposed by Barker and colleagues they may lead others who do have suitable data to test them.

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Table 1: Sample characteristics of for born in Puerto Rico during the late 1920s and early 1940s and who lived in rural areas during childhood

Variable being compared	Overall	Lived on the mainland			Lived mainland—males			Lived mainland—females		
		Yes	No	p-value	Yes	No	p-value	Yes	No	p-value
Demographic										
Age (sd)	66 (4)	66 (4)	66 (4)	0.9825	67 (4)	66 (4)	0.3880	66 (4)	66 (4)	0.6571
Female (%)	51	36	57	0.0000						
Years of Education (sd)	7 (5)	8 (4)	7 (5)	0.0366	8 (4)	8 (5)	0.8099	8 (4)	7 (5)	0.0925
Household income (sd)	5761 (8861)	6613 (9216)	5425 (8700)	0.0000	7589 (10,785)	6445 (12,289)	0.0152	4635 (3993)	4668 (4309)	0.0057
Early Life										
Poor childhood health (%)	25	33	22	0.0082	35	21	0.0148	28	22	0.1245
Poor childhood SES (%)	82	79	84	0.0201	81	87	0.0139	75	81	0.3715
Knee height (%)	23	20	24	0.6990	17	21	0.6143	24	26	0.8236
No school-mother (%)	48	48	47	0.5594	44	47	0.3024	54	48	0.4802
No school-father (%)	41	39	42	0.3970	37	43	0.5145	43	41	0.9633
IMR in birth year	120 (36)	123 (32)	119 (37)	0.7531	125 (32)	116 (36)	0.2093	118 (32)	120 (38)	0.4115
Municipality class (%)										
Wealthiest	16	18	15		18	14		17	16	
Middle	31	32	31		33	32		30	30	
Poorest	53	50	54	0.791	49	54	0.426	53	54	0.886
Adult Lifestyle/environment										
Drink (%)	25	33	22	0.0000	40	34	0.0366	22	14	0.0006
Smoke (%)	36	51	30	0.0000	62	46	0.0011	30	18	0.0000
Exercise (%)	45	54	42	0.0002	62	51	0.2096	39	36	0.0138
Obesity (%)	28	23	29	0.1205	18	23	0.2834	32	34	0.7120
Work-related health	12	17	9	0.0077	16	8	0.0240	18	10	0.1191

problem (%)										
Adult occupation (%)										
Never employed	15	3	20		0	1		10	34	
Private business	62	76	57		78	68		72	49	
Public employee	17	15	18		14	22		15	15	
Self-employed/other	6	6	5	0.000	8	9	0.086	3	4	0.000
Adult Health										
Corazon (%)	18	18	19	0.9679	15	17	0.5870	24	20	0.3726
Diabetes (%)	31	30	31	0.7162	30	30	0.6202	35	32	0.6046
Difficulty with at least one ADL (%)	13	14	12	0.5635	8	11	0.7567	23	14	0.0411

Source: PREHCO first wave for respondents born in Puerto Rico during the late 1920s and early 1940s who lived in rural areas during childhood, n=1471, weighted and imputed. Other sample sizes: Lived in US mainland (n=405) and never lived (n=1066). Lived in US mainland males (n=240) and females (n=165). Never lived males (n=399) and females (n=667).

Notes: Household income is yearly per capita household income. Standard deviations are in parentheses. Statistical differences computed on non-weighted data.

Table 2: Season of birth, life on the US mainland and prevalence of heart disease

Panel A: Distribution of season of birth (%)	Overall	Lived in US Yes	No	Lived in US—Males Yes	No	Lived in US—Females Yes	No	Years lived in US LT 10	GE 10
Partial late	23	20	24	21	24	19	24	15	23
No exposure	27	27	28	28	28	25	28	26	26
Partial early	24	25	23	28	23	21	23	24	23
Full exposure	26	28	25	24	25	35	24	34	28
p-value			0.248		0.589		0.060		0.392
Panel B: Prevalence of Heart Disease (%)									
Partial late	21	20	21	12	18	31	23	32	17
No exposure	15	15	15	10	17	22	14	6	18
Partial early	20	16	22	15	19	17	24	10	21
Full exposure	24	28	22	32	21	25	23	31	22
p-value	0.017	0.055	0.104	0.009	0.881	0.586	0.062	0.014	0.902

Source: PREHCO first wave for respondents born in Puerto Rico during the late 1920s and early 1940s who lived in rural areas during childhood, n=1270; imputed data but not weighted. Other sample sizes: Lived in US mainland (n=405) and never lived (n=1066). Lived in US mainland males (n=240) and females (n=165). Never lived males (n=399) and females (n=667).

Notes: Season of birth defined as: partial late exposure (first quarter), no exposure (second quarter), partial early (third quarter), full exposure (fourth quarter). For Panel A the column percentages add to 100% because the numbers reflect the distribution of season of birth in the selected sample. In Panel B the column percentages do not sum to 100 because they reflect the percent born in a particular season that report adult heart disease. In Panel A p-values reflect the results of testing for statistical significance between season of birth and living on the US mainland. In Panel B p-values reflect the results of testing for statistical differences between the prevalence of heart disease and season of birth in various settings.

Table 3: Effects of season of birth on the odds of adult heart disease

	Original	Original plus lifestyle	US lived		Never lived US	
Variables	**Model 1**	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Female	1.12	1.12	1.26	1.33	1.00	1.00
Age	1.05**	1.05*	1.03	1.03	1.06**	1.05**
Years education	0.98	0.99	0.98	0.99	0.98	0.99
Rheumatic fever	3.29***	3.01**	15.37***	14.11**	1.91	1.80
Poor childhood health	1.50*	1.52**	1.44	1.43	1.56*	1.58*
Poor childhood SES	0.86	0.85	0.97	1.00	0.83	0.80
Low knee height	0.99	0.98	0.91	0.88	1.03	1.02
Obese	1.79***	1.74***	1.72	1.58	1.82***	1.80***
Partial late exposure	1.38	1.39	1.38	1.51	1.39	1.38
Partial early exposure	1.37	1.40	0.96	0.99	1.52	1.55
Full exposure	1.69**	1.73**	2.39*	2.54*	1.48	1.49
No exposure (ref)	1.00	1.00	1.00	1.00	1.00	1.00
Smoke now		0.70		0.57		0.79
Smoked in past		1.35		1.73		1.26
Exercise		0.71*		0.77		0.71*
χ^2 (df)	54-64 (11)	68-77 (14)	30-38 (11)	38-47 (14)	35-44 (11)	42-51 (14)
p-value	0.000	0.000	0.000-0.002	0.000-0.001	0.000	0.000
Log likelihood	-708, -687	-702, -681	-184, -168	-180, -163	-524, -508	-520, -505

Source: PREHCO first wave for respondents born during the late 1920s and who lived in rural areas during childhood, using imputed data with n=1471. Other sample sizes: Lived in US mainland (n=405) and never lived (n=1066). Lived in US mainland males (n=240) and females (n=165). Never lived males (n=399) and females (n=667)

Notes: Original model is from McEniry et al., 2008. Models controlling for length of time lived on the mainland produced similar results. Season of birth defined as: partial late exposure (first quarter), no exposure (second quarter), partial early (third quarter), full exposure (fourth quarter). Also note that 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, presented in this table is the range of values for the chosen statistics obtained after estimating models for each of the imputed data sets. Chi-square shows degrees of freedom in parentheses.

Table 4: Effects of season of birth on adult heart disease by gender and residence on the mainland

	Females			Males				
Variables	Model 1 Overall	Model 2 Lived mainland	Model 3 Never lived mainland	Model 4 Overall	Model 5 Lived mainland	Model 6 Lived mainland	Model 7 Never lived mainland	Model 8 Never lived mainland
Age	1.05*	1.07	1.05	1.04	0.99	1.03	1.06	1.07*
Years education	0.97	0.96	0.96	1.02	1.01	1.02	1.03	1.02
Rheumatic fever	2.26	14.15	1.74	4.50**	20.59*	18.95*	2.16	2.28
Poor childhood health	1.63*	1.23	1.70	1.31	1.70	1.86	1.24	1.11
Poor childhood SES	0.85	0.81	0.85	0.86	0.98	0.79	0.77	0.86
Low knee height	0.98	0.77	1.01	0.97	0.89	0.97	1.04	1.14
Obese	1.73**	1.38	0.80**	1.79*	1.60	1.73	1.83	1.91*
Smoke now	0.35	0.29	0.38	0.98	0.61	0.59	1.28	1.22
Smoked in past	1.39	2.08	1.22	1.38	1.58	1.32	1.34	1.39
Exercise	0.73	0.62	0.75	0.69	0.85	0.80	0.65	0.72
Work-related health problem						5.00**		1.81
Partial late exposure	1.63	2.08	1.64	1.05	1.19	1.27	0.97	0.99
Partial early exposure	1.55	0.41	1.86*	1.18	1.54	1.71	1.04	0.91
Full exposure	1.54	1.17	1.65	1.96*	5.08**	5.59**	1.25	1.24
No exposure	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
χ^2 (df)	48-51 (13)	15- 31 (13)	37-40 (13)	28-36 (13)	30-33 (13)	38-44 (14)	12-18 (13)	13-23 (14)
p-value	0.0000	0.0030, 0.3138	0.0001, 0.0004	0.0007, 0.0072	0.0017, 0.0057	0.0001, 0.0005	0.1237, 0.5139	0.0646, 0.4914
Log likelihood	-408, -396	-79, -68	-330, -319	-289, -279	-94, -89	-87, -85	-189, -181	-183, -175

Source: PREHCO first wave for respondents born during the late 1920s and early 1940s and who lived in rural areas during childhood, using imputed data with n=1471. Other sample sizes: Lived in US mainland (n=405) and never lived (n=1066). Lived in US mainland males (n=240) and females (n=165). Never lived males (n=399) and females (n=667)

Notes: In Model 2 there were an insufficient number of cases reporting rheumatic fever in childhood. Models controlling for length of time lived on the mainland produced similar results. Model for health problems for males only because a high percentage of females never worked. Season of birth defined as: partial late exposure (first quarter), no exposure (second quarter), partial early (third quarter), full exposure (fourth quarter). Also note that 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, presented in this table is the range of values for the chosen statistics obtained after estimating models for each of the imputed data sets. Chi-square shows degrees of freedom in parentheses.

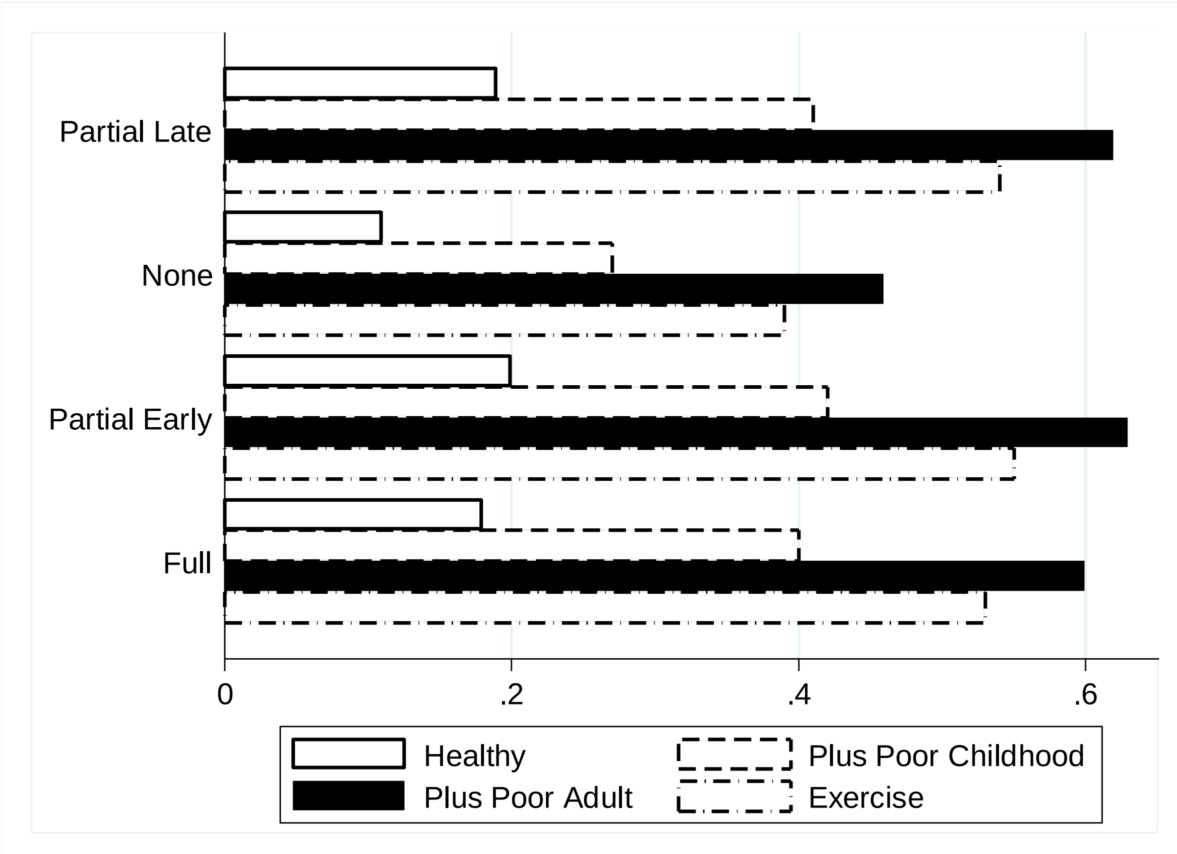

Figure 1: Predicted probabilities of adult female heart disease according to level of exposure and for women who never lived on the US mainland (n=667). The predicted probabilities correspond to the typical individual who was 65 years old with 7 years of education and included (a) healthy individuals, (b) plus poor childhood conditions, (c) plus poor adult lifestyle, (d) plus exercise. Partial late (first quarter) predicted probabilities respectively are (0.19, 0.41, 0.62, 0.54). No exposure (second quarter) predicted probabilities (0.11, 0.27, 0.46, 0.39). Partial early exposure (third quarter) predicted probabilities (0.20, 0.42, 0.63, 0.55). Full exposure (fourth quarter) predicted probabilities (0.18, 0.40, 0.60, 0.53). Legend (from top to bottom bar): White bar is healthy individual, dotted bar adds poor childhood conditions, black bar adds poor adult lifestyle; dashed-dotted bar adds exercise. *Source:* PREHCO data for those born in Puerto Rico during the late 1920s and early 1940s and who lived in rural areas as children; imputed data.

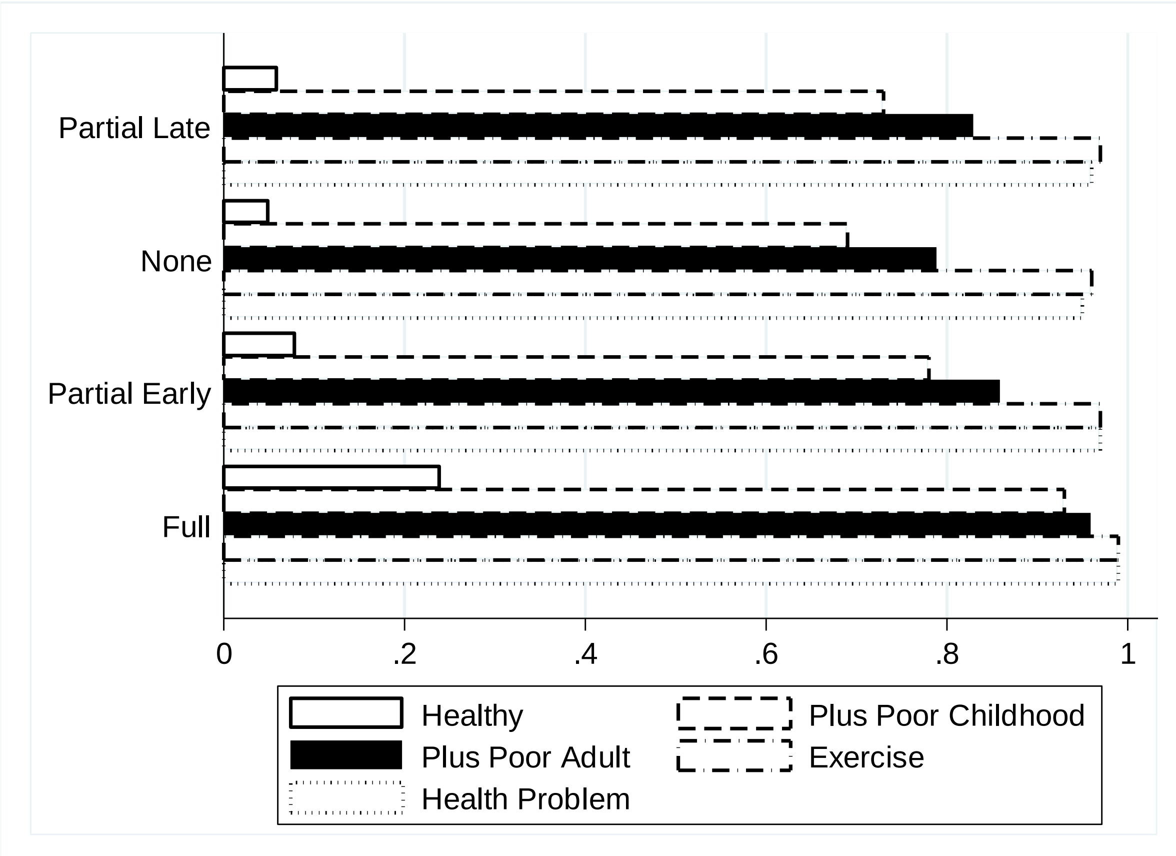

Figure 2: Predicted probabilities of adult male heart disease according to level of exposure and for men who lived on the US mainland (n=240). The predicted probabilities correspond to the typical individual who was 66 years old with 8 years of education and included (a) healthy individuals, (b) plus poor childhood conditions, (c) plus poor adult lifestyle, (d) plus work-related health problem; (e) plus exercise. Partial late (first quarter) predicted probabilities respectively are (0.06, 0 .73, 0.83, 0.97, 0.96). No exposure (second quarter) predicted probabilities (0.05, 0.69, 0.79, 0.96, 0.95). Partial early (third quarter) predicted probabilities (0.08, 0.78, 0.86, 0.97, 0.97). Full exposure (fourth quarter) predicted probabilities (0.24, 0.93, 0.96, 0.99, 0.99). Legend (from top to bottom bar): White bar is healthy individual, dotted bar adds poor childhood conditions, black bar adds poor adult lifestyle; dashed-dotted bar adds health-related work problem. *Source:* PREHCO data for those born in Puerto Rico during the late 1920s and early 1940s and who lived in rural areas during childhood; imputed data.