Serhiy Dekhtyar, Centre for Economic Demography, Lund University.
serhiy.dekhtyar@ekh.lu.se

Early life environments and first-time parenthood: The experience of Swedish women, 1990-2009

It has been shown that individual measures of fetal growth restriction, such as birth weight or term status can exert long-lasting effects over female reproductive health. Also, birth contexts characterized by extreme nutritional shortages, for example famines, have been linked with female fertility. Such events, however, are rare and idiosyncratic and thus offer limited utility for health policy design in Western societies. The role of non-acute contextual characteristics of birth environments which encompass more than just the effects of fetal under nutrition for entry into motherhood is still unknown. Moreover, the few Swedish studies that did link early exposures and first-time fertility did not address the issue of postponement with long-enough follow-up periods. We address these gaps by relating entry into motherhood with non-extreme exogenously-determined contextual characteristics of female birth environments which reflect not only nutritional conditions, but also pollution, economic development, and disease burden. We do so by using high-quality Swedish register-based data. To strengthen the causal interpretations of our results we employ family-based comparisons and control for unobserved family-level confounding via sibling fixed effects models. Our results indicate that even mildly severe birth environments are associated with a reduced hazard of transitioning into motherhood.

1. Introduction

After established evidence has demonstrated that adult metabolic conditions may be related to early developmental processes (Gennser *et al.*,1988; Barker, 1998), extensive literature has followed linking a wide range of long-run health-, but also socioeconomic outcomes with developmental origins (Gale & Martin, 2004; Jeffries *et al.*, 2002). Among others, foundations of female reproductive success were hypothesized to originate early in life (Nohr *et al.*, 2009; Ekholm *et al.*, 2005). Epidemiologic literature exploring this relationship focused on *individual* proxies of fetal growth such as birth weight or term status. Central to this literature is the fact that the development of reproductive organs is completed around birth, making them susceptible to early programming processes which can alter their structure and

functioning (Gluckman & Hanson, 2006). It was indeed shown that fetal growth restriction is associated with reduced ovulation rate and smaller internal genitalia (Ibanez & de Zegher, 2006), while preeclampsia has been shown to develop more often among women who themselves were born small for gestational age (Zetterström *et al.*, 2007). Very low birth weight women also exhibited lower probabilities of entry into motherhood (Ekholm *et al.*, 2005) while premature mothers faced extended waiting time to pregnancy (Nohr *et al*., 2009).

A critique often levied against epidemiological studies examining the relationship between *individual* birth characteristics and long-term outcomes has been their over-reliance on low birth weight (<2,500g) as a proxy of fetal growth restriction, which according to some does not belong on a causal pathway to long-run health outcomes (Gluckman, Hanson, Bukjilas, 2010 ; Wilcox, 2001). It has been suggested that numerical properties of birth weight distributions, which have been thoroughly overlooked in epidemiological studies, could lead researchers to confuse statistical artifacts for true biological effects (see Wilcox, 2001 for an excellent discussion of the low birth weight paradox and related issues). Moreover, evidence of geographical variation in birth weight is abundant (Leary *et al.*, 2006), casting doubt over the popular adoption of universal thresholds. Finally, the proportion of babies delivered at <2,500g is already rather low (4% in Sweden in 2008 according to OECD, 2011), which highlights further problems with statistical power and/or selection in studies on the long-run effects of *very* low birth weight, defined as <1,500g or in some cases as <1,000g.

As these and other shortcomings of low birth weight as a proxy of fetal under nutrition have been exposed, a number of researchers shifted their attention to *contextual* characteristics of birth environments and their effects over long-run female reproductive outcomes. Hypothesized underlying mechanisms remained limited to fetal growth restriction, programming, and metabolic adaptations in these studies, yet the designs did change. Now, cohorts born into episodes characterized by severe nutritional shortages were contrasted in their reproductive outcomes with cohorts born just before or just after these well-defined shocks. Several such studies used Dutch Famine of 1944-1945 (Elias *et al.*, 2005; Lumey, 1997; Lumey, 1998; Lumey *et al.*, 1995*).* Although age at first pregnancy and completed family size for women prenatally exposed to the famine did not differ from the control group, the cases still experienced an increased risk of still birth and perinatal death of the offspring as opposed to the control cohorts (Lumey & Stein, 1998). Furthermore, surviving offspring of the prenatally exposed women reported suboptimal birth outcomes and early health (Lumey & Stein, 1997).

Although extremely informative, studies of disasters like the Dutch Famine have shortcomings too. It is not always straightforward to disentangle the *in utero* effects of the fetal origins hypothesis from the effects of shocks that occur in early childhood (Almond & Currie, 2011). The requirement that the exposed cohort and the two unexposed ones (the one to be conceived during the crisis and therefore too young to be affected prenatally, and the one already born during the shock and therefore too old to be effected) do not overlap is often hard to fulfill. As evidence, a study on children aged 3-12 at the time of the same Dutch Famine also finds a strong association between exposure to the famine and inhibited fertility (Elias *et al.*, 2005). Furthermore, when shocks as extreme as the Dutch Hunger or the Influenza Pandemic of 1918 in the U.S. descend, a number of unique compositional changes in the structure of the exposed cohort take place as well (Brown, 2011), making the crucial assumption of interchangeability a difficult one to enforce. Finally, disasters like these are thankfully rare, and the shocks they provide are hardly comparable with fairly mild modern exposure regimes, therefore offering little utility for health policy design in contemporary Western societies.

Based on the discussion above, it is clear that considering *non-extreme* characteristics of birth environments in the study of long-term reproductive outcomes is a way forward from a scientific as well as a public policy perspective. It is, however, unclear if nutritional mechanisms should be prioritized over other properties of birth settings in studies on *contextual effects*, where the aim is to uncover the existence of wider cohort morbidity phenotypes (Finch & Crimmins, 2004). Contextual influences are formed as a result of complex interactive processes among diverse features of the environments and if the aim is to assess a *total* environmental imprint over subsequent outcomes, more encompassing measures of these environments should be adopted. Barker's work has been instrumental in the amount of interest it generated in developmental origins of adult disease, however, together with the idea that foundations for adult health can reside in early life, a lot of scientists also borrowed Barker's strong emphasis on nutritional effects and stuck to it throughout. Such important features of birth environments as pollution, standard of living, neonatal care quality, or general disease burden received much less coverage as a result.

In this study we depart from the practice of focusing solely on the effects of nutritional-based attributes of birth environments for entry into motherhood and instead gauge early contexts with a more overarching indicator – regional-level infant mortality rate at the time of a woman's birth. This indicator has been shown to be sensitive to a number of environmental

forces, including pollution, discrepancies in economic development, epidemiologic burden, and nutritional conditions. As a result, it is an appropriate tool for measuring the totality of birth environment, rather than just one of its attributes. It has been suggested that identification of the effects may suffer when a mild predictor is considered (Almond & Currie, 2011), however this concern is hardly applicable here, since regional variation in infant mortality even in contemporary Sweden is rather dramatic (see Figure 1 as well as Serenius *et al.,* 2001). We believe that research into developmental origins of adult conditions could benefit from a slight change in perspective away from exclusively nutritional-based explanations and our study, although in a rather rudimentary way, provides just that.

To our knowledge, the relationship between birth environments and fertility outcomes in Sweden has been investigated to date in only one study (Ekholm *et al.*, 2005). Utilizing large population-based registers (N~150,000), researchers have demonstrated that very low-birth-weight women experienced a reduced probability of giving birth. A weaker association was also found for being preterm, while the results for size for gestational age were less clear-cut. Although extremely successful with respect to explicit biological pathways tested, this study had one major shortcoming – a relatively young age of women at the end of the follow-up period. The oldest subjects were only 28 years. This is especially unfortunate in light of recent developments in Swedish fertility, with childbearing rates increasing the most among childless women aged 30 and above.

Based on previous theoretical and empirical works, we expect to find a negative association between elevated severity of early environments and entry into motherhood among contemporary Swedish-born women. We hypothesize that the effect is direct and unaffected by familial confounding.

2. Data, Setting, and Methods

In this paper we use a sample of all native women born in Sweden between 1970 and 1976 obtained from population registers maintained by Statistics Sweden. These are roughly 300,000 individuals whom we observe annually starting from age 15 and until first birth, immigration, death, or the end of 2009. At the end of the follow-up our subjects are in the 33-39 age range, which is a significant advantage over the previous studies. We also adjust for annual labor market status of the woman, distinguishing between various levels of attachment, income (modeled categorically), and education.

We instrument the severity of birth environments by using infant mortality rate in the year and country of a woman's birth. This measure has been repeatedly used in studies on both modern and historical populations as an indicator of disease load environment around the time of birth (Bengtsson & Lindström, 2003; Delaney *et al.*, 2009). It is also an effective indicator of the neonatal care quality experienced by the newborn. Having access to regional IMR data for all 25 Swedish counties is important, since significant variation in exposure is observable at the regional level in Sweden (see Figure 1), which could otherwise be concealed if aggregated IMR statistics were to be used.

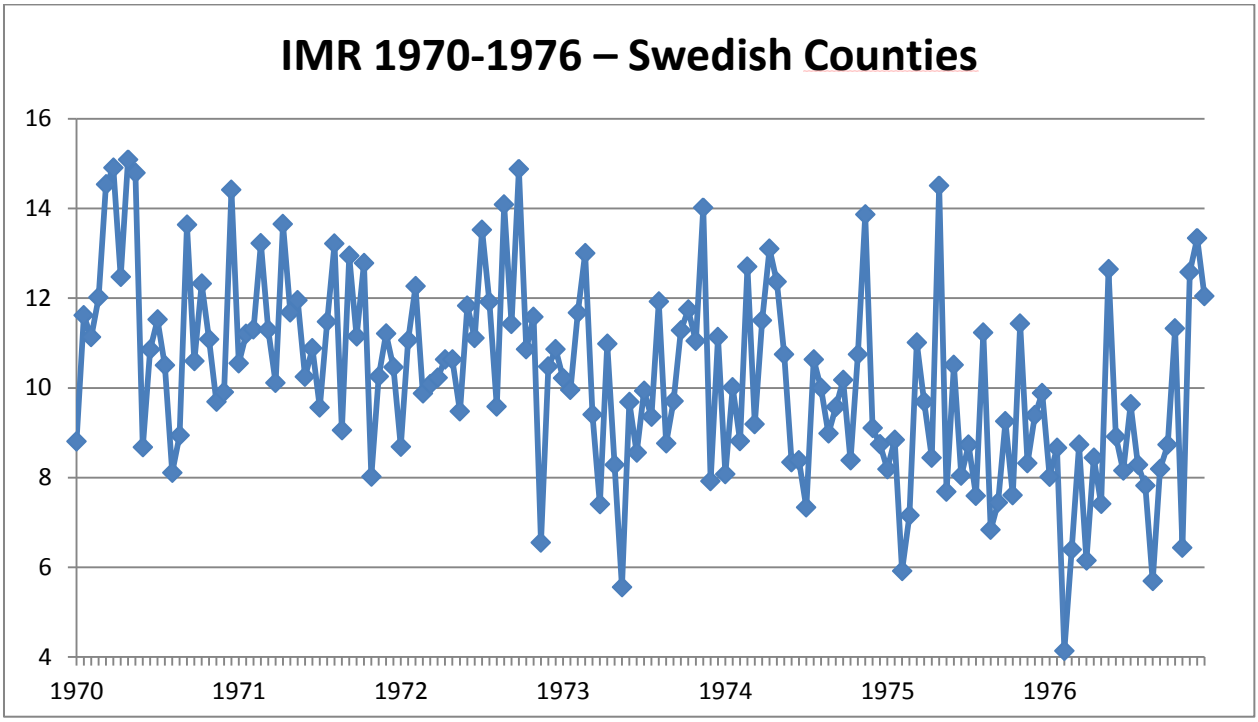

Figure 1.Regional IMR at birth for women born in Sweden 1970-1976

Previous studies using IMR at birth as a measure of early environments' severity considered extended periods of exposure and therefore faced a problem of a secularly declining trend in IMR series which complicated the comparison of individuals born in periods located at opposite ends of the series. The strong disparity in IMR values at different ends of long series is likely to be a product of a number of health-, but also non-health-related macro-constructs, for instance economic development, upsurge in literacy, or an evolution of beliefs and attitudes. Although undoubtedly interesting, these variables are beyond the scope of this and other studies concerned with direct effects of early health-related exposures, and can therefore pollute the specific results in question.

To deal with the problem of the trend, two solutions were suggested in literature. In one, short-term deviations are separated from the long-term development of the IMR through filtering procedures. In the empirical analysis one then focuses on the deviations from the trend, as they supposedly denote immediate health-related hazards, or acute shocks like harvest failures, economic shocks, epidemics, or natural disasters, - all of which have clear health implications. The rationale behind this technique is far from straightforward and the debate is on-going about its merits. Another solution attempts to ensure that the exposure's effect on the outcome is evaluated among individuals located as close as possible to each other along the IMR trend. This is achieved by comparing siblings as they are born within relatively short time periods of each other. The latter technique has a preferred by-product, as in addition to dealing with the trend it also ensures that all characteristics shared by the two siblings and unobservable to the researcher will nevertheless be controlled for in the sibling comparison models, leaving less room for residual confounding to pollute the results.

The trend poses the largest problem when extended IMR series are considered. In this study, we willingly restrict our analysis cohort to be born within 7 years of each other, essentially imposing a sibling-type birth interval on all our subjects. Although graphical examination of our series reveals some downward trend, it is hardly comparable with extended IMR series. Moreover, we model our exposure both continuously and categorically, where particularly unfavorable IMR regimes are isolated with a dummy indicator. Finally, we implement a sibling comparison technique too, isolating roughly 60,000 biological sisters and stratifying our models by the family. We strongly believe that the problem of the trend in IMR series is resolved in our study by implementing these solutions.

The advantage of instrumenting the quality of early environments with IMR at birth is its exogeneity with respect to the individual. Index women in the study are unable to affect the timing of their conception and consequently the IMR regime they experience at birth. This implies that residual confounding is likely to be less of a problem in this study. There is, however, a price for this preferred property of IMR as an exogenous indicator of early environments. Previous studies that managed to differentiate between gestational age, birth weight, or term status could better than us elaborate on the exact pathways and mediations involved. On the other hand, they had to face a more acute problem of residual confounding and unreasonably low age at last follow-up. We are aware that there may be drawbacks behind the design we implement here; yet having balanced advantages and disadvantages, we are confident that our study contributes to the literature by both addressing shortcomings of

earlier studies (low age at last follow-up), and strengthening the causal interpretation of the results (exogenous exposure, within-family comparison technique).

We follow indirect standardization methodology initially suggested in Hoem (1993) and further developed in Andersson & Scott (2005). Essentially, we estimate proportional hazards models, which are now standard tools for the analysis of time-dependent event sequences. We then present relative risks of first birth by the level of IMR into which the woman was born, standardized for a number of variables in our data, including demographic and socioeconomic characteristics, period, and region of birth indicators. We then repeat this analysis on a subsample of 60,000 sisters in our sample, taking into consideration the family structure of the dataset, essentially employing a version of family (sibling) fixed effects. This is achieved by adding the option *strata* to the proportional hazard estimation command in STATA.

3. Results

Preliminary results of econometric modeling are presented in Table 1. All models control for age, calendar period and region of birth fixed effects, birth order of the index woman, family size (index woman), as well as degrees of labor market attachment, income and education of the woman (all categorical). Model 1 is estimated on a full sample of women, while models 2 and 3 only use a sister subsample. The difference between the latter two specifications is that in #2 a family dimension is not explicitly explored, while #3 estimates a within-family parameter for each sibling pair. Only selected parameter estimates are presented below.

Table 1. Empirical results. Selected parameter estimates

	Model 1 (full sample;unrelated individuals) Outcome: birth of a first child	Model 2 (sibling sample; unrelated individuals) Outcome: birth of a first child	Model 3 (sibling sample; family stratification) Outcome: birth of a first child
	Hazard Ratio (CI-95)	Hazard Ratio (CI-95)	Hazard Ratio (CI-95)
IMR above county trend	0.953*** (0.944-0.961)	0.978** (0.957-0.998)	0.975* (0.940-0.998)
Low income	0.652*** (0.643-0.662)	0.648*** (0.627-0.669)	0.669*** (0.659-0.742)
High income	1.38*** (1.367-1.403)	1.390*** (1.349-1.432)	1.28*** (1.204-1.362)
Student	0.309*** (0.300-0.319)	0.306*** (0.285-0.328)	0.381*** (0.339-0.423)
Non-participant	0.500*** (0.490-0.510)	0.450*** (0.427-0.475)	0.561*** (0.515-0.612)
1 child - mothers' family	0.926*** (0.911-0.942)	N/A	N/A
3 kids - mothers' family	1.087*** (1.076-1.098)	N/A	N/A
4 kids/more - mother's family	1.366*** (1.308-1.425)	N/A	N/A
N	293,856	57,026	57,026

*** p<0.01, ** p<0.05, * p<0.1

Source: Own calculations

IMR in the analysis above is modeled categorically to denote if a given year of index woman's birth represents an unfavorable deviation from its regional infant mortality trend. Continuous specification of the exposure was attempted, but this non-linear specification seems to perform better and can be interpreted in a more straightforward way. According to Model 1, a woman born in a year when IMR was elevated above that region's trend experienced a 5% lower hazard of transitioning into parenthood. Additional parameter estimates of well-established predictors of first-parity transitions are presented to put the magnitude of early environments' effects into perspective. Thus, belonging to a high income group (reporting income exceeding 5 base amounts) is associated with a nearly 40% increased hazard of transitioning into motherhood. Roughly the same effect, but with a negative sign is associated with earning a low income (1-3 base amounts). Strong reductions in hazard of first-

birth for variables denoting weak labor market participation (student and non-participant) once again confirm that adequate labor-market attachment is almost a prerequisite for first-time parenthood in Sweden. The magnitude of the early environments' effect rather is weak as opposed to SES indicators; it is comparable with maternal family size effects.

Little change in estimated hazards is evident as the sister subsample is analyzed. Being born in a year with infant mortality at birth elevating above the county's trend is associated with a roughly 2.5% reduced hazard of transitioning into parenthood for the sisters in the analysis. Statistical significance of the effect is reduced in the within-family comparison, yet it is still significant at the 10% level. Only minor attenuation of the effect has occurred as a result of adopting extra efforts to correct for the trend in IMR series, once again confirming that it poses little modeling challenge in this study. Only slight attenuation in early environments' effects in the sibling fixed effects models also indicates that residual confounding in the study is negligible otherwise the difference between the unrelated analysis and the family-based comparison would be more striking.

4. Conclusion

In this paper we tested if entry into motherhood among contemporary Swedish women is affected by their exposure to exogenously-determined early life environments. Severity of these environments was modeled through regional infant mortality rates at the time and place of woman's birth. We followed a number of methodological strategies aimed to ensure our empirical models are not affected by trend from IMR series or residual confounding. Consistent with initial expectations, we uncovered a negative association between elevated severity of birth environments (IMR at birth above the trend for a given Swedish county) and a hazard of transitioning into parenthood. The association was robust to the inclusion of a number of demographic and socioeconomic controls, as well as family-based comparison. Although statistically significant, the magnitude of early environments' effects on motherhood is hardly comparable with established indicators of labor-market attachment. Further modeling is needed to uncover possible interactions between health and socioeconomic characteristics. Factors leading into parenthood are complex and are both social and biological and developmental effects should be considered as well.

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