Workshop Report
Beyond Birth Weight

Measuring Early Life Health Conditions Past, Present and Future

24-25 October 2014, University of Sussex

Executive summary

Recent research has found that children exposed to poor conditions *in utero* are at higher risk of non-communicable disease (especially heart disease, stroke and diabetes) in later life and have lower educational attainment, earnings and greater disability than those experiencing good conditions. These findings indicate that health conditions *in utero* need to be incorporated into a broader understanding of public health today. Unfortunately, measuring early life health conditions is difficult and the current favoured proxy, birth weight, is problematic. This workshop brought together researchers with varied expertise related to early life health to discuss the strengths, weaknesses and complexities of various proxies for early life health conditions, taking in part a historical perspective to gain insights into contemporary issues. We focused on two crucial questions: (1) Which early life health proxies could scholars collect and analyse in the nineteenth and twentieth centuries to understand changes in health? and (2) Which early life health proxies could be adopted around the world today in order to assess and monitor the profile of early life health?

For historical periods, the surviving evidence limits the degree to which researchers can move beyond traditional early life health proxies such as birth weight and perinatal deaths. However, we discussed a number of ways to analyse existing indicators in a more nuanced fashion and have plans for collaborative projects to do so in the future. In modern developed countries, we agreed that stratification of later risk would be enhanced if a wider range of newborn health indicators, such as birth length, anthropometry and possibly epigenetic markers were systematically collected along with current measures such as birthweight and Apgar score. With regard to developing countries, underdeveloped health infrastructure and widespread unassisted births prevent the kind of record keeping that we would recommend for developed countries. However, health surveys could be improved by providing a wider range of subjective measures of early life health and information about the pregnancy history rather than just birth history. While the evidence presented at the workshop suggests that it is time to move 'beyond birth weight', more research is needed for this to become a reality. Thus, we have developed a number of collaborative projects to extend the frontier of knowledge in modern day and historical research.

Organiser details

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Workshop resources: **www.sussex.ac.uk/globalhealthpolicy/events/workshops/beyondbirthweight**

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Background

Empirical studies have shown that exposure to poor conditions in early life influences children's development and can have negative, long-lasting health consequences. Children exposed to poor conditions *in utero* are at higher risk for heart disease, stroke and diabetes in later life, and they are more likely to have lower educational attainment, lifetime earnings and greater disability than children who experienced good conditions during prenatal development (Almond and Currie, 2011; Barker, 1997; Gluckman et al 2008). Biologists have also been developing evolutionary and life cycle theories to explain the relationships between poor conditions *in utero* and in early life and reduced fitness and poorer health and socioeconomic outcomes in later life (Gluckman and Hanson, 2006; Wells, 2012; Bogin *et al.*, 2007). In turn, the health of one generation contributes to the conditions in which the next develops, adding an intergenerational dimension to early life health. Socioeconomic and cultural factors such as gender inequality can also influence early life health conditions by excluding subgroups of society from the benefits of improving health and welfare (Bhalotra and Rawlings, 2011).

These important empirical and theoretical findings indicate that health conditions *in utero* need to be incorporated into a broader understanding of public health. Because measures of specific factors influencing conditions *in utero* are often unavailable, it is necessary to use proxies of the early life environment to compare the prevalence and consequences of deficiencies *in utero* across populations. Unfortunately, there are relatively few proxy measures for the early life environment to make this possible. The most commonly used indicator is birth weight, but it is problematic for several reasons. First, developmental plasticity manifests itself in many aspects of human development, not just growth. In addition, weight at birth does not capture information about growth trajectory *in utero*. Birth weight has also remained fairly constant across generations even when it seems likely that early-life conditions were improving. There are however a number of other proxies for historical and contemporary periods that have not been exploited fully and can provide a starting point for this discussion.

Aims and Objectives

This workshop brought together a group of researchers with disparate expertise related to early life health to discuss the strengths, weaknesses and complexities of various proxies for early life conditions: birth weight, neonatal mortality rate, stillbirth rate, childhood growth and final adult height to name a few. We focused on two crucial questions:

1) Which early life health proxies could historians, economists and demographers collect and analyse in the nineteenth and twentieth centuries to better understand improvements in health during those centuries?

2) Which early life health proxies would be most optimal to adopt in both developing and developed countries today in order to assess and monitor the profile of early life health?

The workshop opened on Friday with lectures and discussion on the problems with birth weight and historical developments in early life health. On Saturday we developed avenues of research to move beyond birth weight.

Discussion

We began by discussing the substantial evidence that birth weights may not be as simple an indicator of conditions *in utero* as was previously thought. For instance, although low birth weight is generally seen as problematic for health, both high and low birth weight are associated with higher risk of diabetes and cardiovascular disease. Children who experience rapid fetal weight gain and high fetal weight during the second half of pregnancy have a higher risk of being obese at age 3. In addition, the optimal birth weight in relation to perinatal mortality is not near the mean birth weight for several large cohorts from high income countries but is close to the 90th percentile. Finally, historical evidence suggests that the means and distributions of birth weights in North America have not changed substantially between the mid-nineteenth century and today despite substantial changes in social conditions. Thus, birth weight may not be a sensitive indicator of the intrauterine environment.

Perhaps the most problematic aspect of birth weight is that it is an outcome variable representing a small moment in an individual's life. There are many paths to any particular birth weight, some of which might be healthy and others not. It seems likely that many of the paths that lead to a low birth weight would be unhealthy, but this balance of healthy and unhealthy paths would change non-linearly across the birth weight distribution. This is because fetal weight gain is both a part of and a consequence of the adaptive responses to the uterine environment available to the fetus, responses that might not reduce fitness in the long run. Likewise, developmental plasticity in response to the uterine environment manifests in other physiological processes other than growth, which would not be captured by birth weight. Thus, when considering early life health, we are more concerned with the path, i.e. the physiological responses, that a child took rather than a simple birth weight outcome. Because birth weight is only partially correlated with these paths, we are potentially measuring early life health with a substantial amount of error by using birth weight as the sole proxy[1]. Thus, there is much to be gained in considering other proxies for early life health.

These questions about birth weight set the agenda for the rest of the workshop: to examine other indicators that might be useful to measure early life health in the past and around the world today.

In historical periods, researchers are limited by the sources that are available, and unfortunately, this means that birth weights and stillbirth and neonatal mortality rates are often the best proxies for early life conditions. However, we discussed a number of ways of analysing such proxies in a more sophisticated way that would provide a better understanding of early life health in the past. This included linking birth records to death records in order to test whether the relationship between birth weight and mortality existed before and during the mortality decline, and collecting additional birth weight records to be able to track changes in the birth weight distribution over time.

When exploring early life health proxies that would be constructive to measure today, there was general concern that clinicians in the UK and other developed countries are recording less and less information about infants. Indicators such as birth length, placental weight, the ponderal index and the Apgar score may be more effective at predicting later life morbidity and mortality than birth weight. Detailed records of the mother's health would provide additional context. We also considered the potential of measuring epigenetic markers as a proxy for early life health conditions. The science here is still quite new, but epigenetic markers may provide a clearer signal of the processes leading to good or poor intrauterine health than birth weight and other indicators.

We also addressed the recent INTERGROWTH-21st paper in the *Lancet* (Villar *et al*., 2014). The paper presents growth references for newborn weight, length and head circumference, strongly suggesting that these indicators can be used to derive a universal standard of optimal fetal growth. There was general agreement that there seemed to be substantial differences in these anthropometric measures between populations, and many participants were concerned that a defined optimal growth trajectory might encourage clinicians to carry out health interventions that might do more harm than good.

When discussing how to measure early life health in the developing world, it did not seem feasible to recommend the collection of new indicators since the existing health infrastructure is limited and should be the target of any increased investment. Expanding data collection might be more feasible for middle-income countries though, because they have more developed health systems and are now facing a greater mortality burden from non-communicable diseases. We also agreed that better record keeping for stillbirths and neonatal mortality would be advantageous for making comparisons across countries and informing health policy. In addition, we discussed a number of ways of incorporating more subjective measures of early life health such as comparing a child to a doll or using foot size as a proxy. Surveys could also be improved by including questions about pregnancy histories rather than solely birth histories.

Clearly, the workshop produced some very fruitful ideas that inspired participants and will lead to collaborative and inter-disciplinary research projects in the future.

[1] This measurement error could lead to omitted variable bias and/or attenuation bias in the regression analysis of birth weights on later life outcomes.

Outputs

The workshop participants are currently working on two outputs to be completed in the next six months. First, a team is writing a critical response to the INTERGROWTH-21st papers, arguing that imposing such a fixed standard of optimal fetal growth is highly problematic. It oversimplifies the plasticity in the developmental process whereby each fetus optimises its development based on the conditions in the womb, and it assumes that all populations share a universal fetal growth pattern, which seems dubious given the data presented in the INTERGROWTH-21st's papers. If clinicians use these standards to justify treatment decisions, they may interfere with natural development processes, harming the fetus.

Second, we are writing an article-length consensus statement for an interdisciplinary journal based on the discussion held at the workshop. The article will present a wide range of evidence about the limitations of birth weight as an early life health indicator and will then discuss ways that researchers and clinicians can move forward. We believe that an article written by such a wide range of scholars will clarify what the most important issues are in measuring early life health and how researchers in each discipline can be best deployed to address them.

In addition, we have started to work on a number of longer term, collaborative research projects. These include collecting more historical information on early life health; linking historical records to reconstruct life histories; using cohort studies to examine links in early life health across three generations; using Guthrie card blood spots to analyse epigenetic markers in populations going back to the 1950s; and thinking creatively about novel, inexpensive methods for collecting information on early life health in surveys in developing countries. These projects will provide a basis for future grant applications and workshops.

Further information

Please get in contact with Eric or Mark if you would like more information about the Beyond Birth Weight Network or its research projects. We plan to hold periodic workshops in the future to present the results of the project and explore the topic further.

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