

Insights into determinants of health

Life-course approaches to health emphasize how effects of experiences across the life span influence health or disease. Crucial to this are social determinants of health, defined by the WHO as “The conditions in which people are born, grow, live, work and age.” In other words, they constitute the broad range of personal, social, economic and environmental factors that determine individual and population health. They include income level, educational opportunities, employment, (in)equality based on gender or race, food security, housing, early childhood experiences and development, the state of neighbourhoods and social support...the many proposed factors go on. The fact that addressing such determinants may have a greater impact on overall health than pure healthcare spending is very clear, and not new: The Strategic Review of Health Inequalities in England by Prof Sir Michael Marmot (2010) *Fair society, healthier lives* is 10 years old now, and made recommendations in six domains: (i) give every child the best start in life, (ii) improve education and life-long learning, (iii) create fair employment and jobs, (iv) ensure a minimum income for a healthy standard of living, (v) build healthy and sustainable communities, and (vi) apply a social determinants’ approach to prevention.

There are several relevant examples in this issue of BJOG. Alison Richardson and colleagues highlight that “socio-economic status, whether measured by education, income, or other indices of social class, has a significant impact on health. With few exceptions health outcomes are worse in more deprived communities”. They studied the effect of socio-economic status on IVF outcome in a cohort of over 3000 women undergoing their first NHS-funded, single, fresh embryo transfer. Clinical pregnancy and livebirth rates were significantly lower in the most deprived group compared with the least deprived group. The accompanying mini-commentary is important reading: it cautions against adjusting for all confounding variables as many can - in turn – be linked to social deprivation, for example smoking. The conclusion: women that are more socio-economically deprived are significantly less likely to achieve clinical pregnancy or livebirth through IVF than less deprived patients.

Early childhood events are also an important determinant of future health. Childhood abuse has previously been shown to have many adverse effects, including on reproductive health. For example, studies have suggested that women who suffered abuse in childhood have an increased risk of having an unintended pregnancy in later life. As the reader can imagine, this is a difficult area to research, with a high risk of selection bias (for example by recruiting in antenatal clinics, meaning women who do not attend or those that opted for pregnancy termination are not included); and also a high risk of recall bias. The large study by Jennifer Drevin et al has overcome some of these issues by using data from a very large, prospective, national cohort – the Norwegian Mother and Child Cohort Study. Their analysis shows very clearly that exposure to childhood abuse increases the chance of having an unplanned pregnancy in later life, and this is true for emotional, physical and sexual abuse in childhood. As Miland Joshi discusses in our series on research methods on **pxxx**, type 1 errors can occur when we falsely reject a null hypothesis; studies as this one, that have a

very large sample size, can sometimes reach statistical significance despite a lack of clinical importance. Nevertheless, I think we can be very sure that emotional, physical and sexual abuse all separately increase the risk of having an unplanned pregnancy: the carefully collected and analysed data mean that the effects could not be explained by bias, and that different combinations of categories of abuse did not show strong interactions. In the accompanying Mini-Commentary, Shawn Walker highlights some of the important steps we can take as caregivers to develop services in ways which address the needs of those who have experienced childhood abuse.

In the field of obstetrics we are particularly aware that the intrauterine environment can affect future health of offspring. The study by Maren Ellingsen and colleagues offers important insights in this regard: it reports long term infant follow up data from a randomised controlled trial (RCT). The initial RCT – again from Norway - randomised 855 women to follow a 12-week structured exercise protocol or standard antenatal care during pregnancy. In this issue they present data from objective follow-up at the age of seven years, assessing multiple dimensions of child development, including motor, language, and social skills, executive function and emotional/behavioural problems. The results suggest that moderate intensity exercise during pregnancy did not have any adverse effects on neurodevelopment of offspring at the age of seven. Such long-term studies are not easy to perform and the accompanying mini-commentary by Michelle Fernandes highlights the importance of such follow up in answering important clinical questions. Journal Club questions also accompany this paper, and I would encourage those with an interest in research to have a go at thinking through the methods using this framework.

Many of the links between the intrauterine environment and subsequent health outcomes are based on epidemiological observations; the classic example, from Barker, is the link between birthweight and subsequent cardiovascular health. It is therefore of great interest when measurable manifestations are prospectively linked, and two important areas are highlighted in this issue. Syahrizan Samsuddin and colleagues studied 507 mothers in Malaysia, (of whom 145 had gestational diabetes mellitus); maternal insulin, C-peptide, triglycerides and non-esterified fatty acid were examined at the time of the glucose tolerance test and at 36 weeks. The authors found that high levels of maternal fasting triglycerides were independently associated with birth of a large for gestational age baby even after adjusting for maternal glucose, body mass index and insulin sensitivity. Maternal gestational weight gain (of greater than 10kg) also had an impact on neonatal adiposity. These findings are of interest from the biological perspective, but whether they can lead to treatments that can modify pregnancy outcome remains to be seen. The StAmP trial (Statins to Ameliorate Pre-Eclampsia), a RCT by Asif Ahmed and colleagues is of relevance here: in this study the biological finding that high circulating levels of soluble fms-like tyrosine kinase-1 (sFlt-1), and low circulating levels of placental derived growth factor (PlGF) precede the onset of preeclampsia, was the starting point. This opened up the interesting concept of treatment of preeclampsia by removing excess sFlt-1; initial studies in vitro and in animals suggest such removal can eliminate signs of preeclampsia, and that pravastatin could be a suitable agent. StAmP was a relatively small trial, and failed to demonstrate significant reductions in sFlt-1 (the primary outcome). Nevertheless, this is an important paper as it is the first RCT of pravastatin for the amelioration of early onset preeclampsia. Read the trial

and the accompanying Mini-Commentary by Maged Constantine to learn about the findings, and the contribution regarding the safety of Pravastatin use.

An important aspect of social and economic influences on health includes, of course, access to health services. Trying to standardise the provision of healthcare, and ensuring that evidence-based practice is provided, is supported by guidelines. In the study by Anne Rousseau et al, a large number of practitioners in France were asked what they would do in a hypothetical scenario, based on a vignette (for example, a 26-year-old woman with a first twin pregnancy, in which the sonographer reports an isolated short cervix (8 mm) at 22 weeks of gestation). The study elegantly demonstrates that adherence to existing guidelines was low; equally worrying was that the adherence remained low after repeating the survey following active dissemination of guidelines. In the Mini-Commentary accompanying the paper Phil Steer discusses how these findings are certainly not confined to France, and how improvements in implementation are needed.

Of course, there are many other determinants of health and disease – genetic, environmental, and infective to name a few. In the case of cervical and vaginal cancer, the role of Human Papilloma Virus (HPV) is well documented, and in the paper by the effects of total hysterectomy, in which the cervix is removed, on the risk of HPV-related cancer in the vagina was assessed in a large population based study by Emilia Alfonzo and colleagues. The authors used national Registry data from the Swedish National Board of Health and Welfare and linked this to the Swedish National Cancer Registry, resulting in a cohort of five million women.

Women with prevalent CIN at the time of surgery, or with a history of CIN3, were found to have a substantially increased risk of subsequent vaginal cancer compared with women who had hysterectomy in the absence of these risk factors. Based on these and existing data, the authors and the accompanying Mini-Commentary by John Tidy make recommendations for who to screen, how and when following hysterectomy.

Few areas are as closely linked to life course approaches to health as those in fetal and perinatal medicine with the first 1000 days of life having important effects on subsequent health and development. With this in mind, please remember the special issue of BJOG on Fetal Medicine: Screening, Diagnosis and Therapy. The deadline is April 2020, so there is still time to submit! Having the paper in the special issue does not delay online publication; paper that are accepted will be published online as soon as they are ready, with the printed version (for those who still like paper!) scheduled for January 2021. Further information is available at https://obgyn.onlinelibrary.wiley.com/hub/journal/14710528/cfp_2021.

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