Editor’s Choice

Intergenerational influences on health: how far back do we have to go?

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They fuck you up, your mum and dad.
They may not mean to, but they do.
They fill you with the faults they had.
And add some extra, just for you.1

The publication of Philip Larkin’s “This be the verse” in his collection “High Windows” in 1974 generated considerable disapproval from some quarters of the British press. It was unthinkable that a Sunday newspaper would actually print the words, and of course the coy descriptions led me to read through the whole book in a local shop and buy a recording of Larkin reading from it. It is a sign of considerable generational change that even so staid a journal as the IJE can now quote this without a second thought. It came instantly to mind when reading the set of papers on intergenerational influences on health in the current issue. If Philip Larkin were to read these papers he would be led to consider whether grandparents, as well as mums and dads, are responsible for the woes of the next generation. An innovative cross-generational linkage of the Uppsala birth cohort tested the effects of social circumstances of grandparents, as well as parents, on cognitive ability and body mass index of the third generation.1 The bottom line of a complex analysis is that there is indeed evidence that the shadow of at least two generations is passed downwards to the next. As Larkin said, “Man hands on misery to man. It deepens like a coastal shelf.”

With just one generation under scrutiny, several papers in this issue report associations between maternal smoking during pregnancy and a variety of behavioural and cognitive measures in the offspring.2–5 Interpretation of these associations is problematic, however.6,7 Is smoking by mothers during pregnancy actually having a biological effect on the offspring through an intrauterine mechanism, or are the many confounding factors that relate to smoking generating the associations? Barbara Maughan in her excellent editorial discusses these issues at length.8 Various strategies are utilised in the studies we publish. For example Sabine Roza and colleagues show that adjustment for confounding factors considerably attenuates associations between maternal smoking during pregnancy and child outcomes. Furthermore smoking by the fathers – which cannot have the same intrauterine effect as smoking by the mothers, but will reflect confounding to a similar degree – is associated with child outcomes in the same way as is maternal smoking. Carsten Obel and colleagues demonstrate associations between maternal smoking during pregnancy and Attention Deficit Hyperactivity Disorder (ADHD) in offspring in three Nordic cohorts. They demonstrate relationships in all the cohorts, which are attenuated by adjustment for confounding factors, but remain elevated. They suggest that because similar associations are seen between cohorts with different prevalence of maternal smoking this suggests confounding is not generating the associations, since the expectation is that the level of confounding is differentially patterned across such populations. However an elegant recent study9 relates maternal smoking to outcomes in offspring biologically related and biologically unrelated to the mother, the latter produced through in vitro fertilisation. For an outcome that we know is influenced by smoking during pregnancy – lower birth weight – the association is seen whether or not the offspring is biologically related to the mother who smokes (Figure 1), but for ADHD the association is only seen if the offspring is biologically related to the mother. If the mother smokes and the fetus she is carrying is biologically unrelated to her no adverse influence of smoking is seen (Figure 2). This suggests that confounding by genetic factors related both to smoking and to ADHD may generate the association, although effect estimates have wide confidence intervals and larger studies are required for findings to be definitive. Eva Morales and colleagues apply a Mendelian randomisation10 approach, by utilising genetic polymorphisms that are related to detoxification of components of cigarette smoke, with intriguing findings4 Again, however, a major conclusion from the study is that larger sample sizes are required for these genetically informed approaches.

Other studies reported in this issue demonstrate that cardiovascular risk factors among mothers may influence both pre-term birth of their offspring and the mothers’ own risk of cardiovascular disease11, that acetaminophen use during pregnancy demonstrates little robust effect on adverse pregnancy outcomes12 and that weight gain during the childhood of mothers is related to higher birth weight for the next generation.13 All three of our cohort profiles relate to studies that have already, or can in the future, investigate
intergenerational influences on health in subsequent generations.\textsuperscript{14–16} Perhaps it would be good if future studies investigate positive, as well as negative, aspects of intergenerational transfers. As the late, great, Adrian Mitchell wrote, parodying Philip Larkin,

\textit{They tuck you up, your mum and dad}\\
\textit{They read you Peter Rabbit, too.}\\
\textit{They give you all the treats they had}\\
\textit{And add some extra, just for you}\\
\textit{They were tucked up when they were small,}\\
\textit{(Pink perfume, blue tobacco-smoke),}\\
\textit{By those whose kiss healed any fall,}\\
\textit{Whose laughter doubled any joke.}\\
\textit{Man hands on happiness to man.}\\
\textit{It deepens like a coastal shelf.}\\
\textit{So love your parents all you can}\\
\textit{And have some cheerful kids yourself.}\textsuperscript{17}

\textbf{References}

\textsuperscript{1} P Larkin. This be the verse. In: High Windows. Faber and Faber, London, 1974.

\textsuperscript{2} Modin B, Fritzell J. The long arm of the family: are parental and grandparental earnings related to young men’s body mass index and cognitive ability? \textit{Int J Epidemiol} 2009;\textbf{38}:733–44.


\textsuperscript{6} Knopik VS. Maternal smoking during pregnancy and child outcomes: Real or Spurious Effect? \textit{Developmental Neuropsychology} 2009;\textbf{34}:1–36.

\textsuperscript{7} Davey Smith G. Assessing intrauterine influences on offspring health outcomes: can epidemiological findings yield robust results? \textit{Basic and Clinical Pharmacology and Toxicology} 2008;\textbf{102}:245–56.


\textsuperscript{17} Adrian Mitchell. This be the other verse – http://www.confessingevangelical.com/?tag=adrian-mitchell.