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Q1 What led you to pursue a career focusing on life course epidemiology?

After leaving Cambridge University, UK, with a degree in economics, in 1975 I became a research scientist at Exeter University, Devon, UK. I first joined the Operational Research Unit, where I used mainframe computer models to help allocate healthcare funds, which was sometimes frustrating. I then joined the Paediatric Research Unit, studying the unmet needs of adolescents and young adults with disabilities, which was a big learning experience. There, I heard about the Medical Research Council (MRC) National Survey of Health and Development (NSHD), the oldest of the British birth cohort studies, following 5,362 participants since their birth in March 1946. I was lucky enough to become an MRC scientist on that birth cohort study at University College London (UCL), UK, in 1987, and eventually the Scientific Director of the study, and Founding Director of the MRC Unit for Lifelong Health and Ageing from 2007–2017.

One of the first analyses I undertook was for a paper led by the late Professor David Barker, at a time when there was a revival in the early origins of cardiovascular and respiratory diseases. David's hypothesis focused on exposures in foetal life. It was a wonderful period for using data from birth cohort studies to investigate this intriguing hypothesis. This became the focus of my PhD and various articles, which turned me into an epidemiologist. With Yoav Ben-Shlomo, I co-edited 'A Life Course Approach to Chronic Disease Epidemiology',[1,2] persuading our colleagues to contribute chapters reviewing the evidence for lifetime risk factors on later life chronic diseases. This book was the founding text for life course epidemiology, which studies how biological, psychological, and social factors across life affect adult health, ageing, and chronic disease risk. This led to a series of life course books (I co-edited one on women's health in 2002 and one on healthy ageing in 2014), as well as over 500 peer-reviewed articles. The second edition of 'A Life Course Approach to Women's Health', co-edited with Gita Mishra and Rebecca Hardy, is due out in July 2023, and a third edition of 'A Life Course Approach to The Epidemiology of Chronic Diseases and Ageing' has just begun!

Q2 As a world-leading pioneer within the field of public health, what initially sparked your specific interest in women's health?

The study members were 41 years old when I joined the NSHD research team, and I saw an opportunity to ask women participants about their gynaecological health in 1989, at age 43, when nurses interviewed them at home. Back then, there were few longitudinal studies of the menopausal transition, and none with prospective data from birth, so with Rebecca Hardy, and later with Rachel Cooper and Gita Mishra, we sent out postal questionnaires every year between ages 47–54 years to capture the timing of perimenopause and natural or surgical menopause, symptoms, and healthcare, including a full hormone replacement therapy history. Because of the high response rates, we were able to look first at a range of lifetime risk factors for timing of menopause, and

other related experiences. We showed how early life exposures, such as better childhood socioeconomic circumstances, higher childhood cognitive ability, and breastfeeding, were associated with a later menopause, even after accounting for adult risk factors. Once we had collected further data at 60–64 and 69 years, we then showed how the menopausal transition was associated with later health, such as adult bone density, and cognitive and cardiovascular function.[3-5]

Q3 Focusing on menopause, do you believe healthcare professionals lack awareness, and what can be done to combat this?

Not all health professionals have sufficient training in, or time to devote to, the menopausal transition, so some may lack awareness of the full range of experiences associated with the transition and its implications. For example, they may not recognise the symptoms presented by women in their early 40s as being consistent with early menopause, or that some women may still experience vasomotor symptoms for more than a decade post-menopause. Women from culturally and linguistically diverse backgrounds may face difficulties in describing or expressing their menopausal symptoms, such as sexual difficulties caused by vaginal dryness. Well informed general practitioners and staff at menopause clinics, where they exist, can make all the difference to women's healthcare. We look forward to assessments of the new 'women's health hubs' proposed by NHS England, as currently there are insufficient services for all aspects of women's reproductive life.

Q4 Could you briefly summarise the main findings of the paper you co-authored, entitled, 'Is there a link between infertility, miscarriage, stillbirth, and premature or early menopause? Results from pooled analyses of 9 cohort studies.'?

This paper was led by Chen Liang and Gita Mishra as part of Gita's successful InterLace consortium, which has harmonised data from women participating in cohort studies worldwide (including NSHD), so has the power to investigate premature menopause (<40 years) and early menopause (40–44 years). In a pooled analysis of nine cohort studies, including 303,594 postmenopausal women, the median age at natural menopause was 50.0 years (interquartile range: 47.0–52.0). The percentages of women with premature and early menopause were 2.1% and 8.4%, respectively. The relative risk ratios (95% confidence interval) of premature and early menopause were 2.72 (1.77–4.17) and 1.42 (1.15–1.74) for patients with infertility; 1.31 (1.08–1.59) and 1.37 (1.14¬–1.65) for women with recurrent miscarriages; and 1.54 (1.52–1.56) and 1.39 (1.35–1.43) for women with recurrent stillbirths. The risks for Asian women with these histories were higher. The paper discusses the possible biological mechanisms underlying these associations, and suggests that women with such a reproductive history would benefit from early care and advice about its implications for menopause timing.

Q5 You are due to publish a second edition of your book, entitled, 'A Life Course Approach to Women's Health'.[6] What can the reader expect to learn?

I co-led the first edition with Rebecca, and Gita is the leading editor of the second edition, which we are excited to see published in July. The second edition updates and reviews the tremendous amount of new research evidence and advances in life course methods, examining the long-term influence of foetal and childhood experience in the development of chronic health conditions. We focus on conditions that are common or unique to women, and that typically impact physical and mental health in midlife and beyond. There are new chapters on lifetime factors associated with endometriosis and lung function in women; on the role of integrative omics in understanding chronic conditions; and on the impact of violence on women's long-term health. The chapter on knowledge translation describes how we can translate all the epidemiologic evidence to inform better health policy, practice, and promotion. This is particularly important, as the life course approach is increasingly adopted around the world as a framework for developing national strategies for women's health.

Q6 You have also applied your career in life course epidemiology to ageing and cognitive development, establishing and directing the MRC Unit for Lifelong Health and Ageing, and acting as Scientific Director of the MRC NSHD. What have been the most exciting developments in this field in recent years?

There have been many exciting developments, and I give an example in my response to question 7. Increasingly, life course and ageing researchers can use repeated measures within a cohort study to investigate different aspects of functional change at the individual, and increasingly the system and cellular levels, and identify lifetime risk factors, mediators, modifiers, and consequences of functional trajectories. Cross-cohort studies have proliferated in recent years, enabling, data permitting, the whole life course to be investigated, to check whether findings are replicated, and vary by age or birth cohort. Intensive biology is providing multiple omics measures, and the relatively new field of exposomics is providing more detailed environmental exposures over time, to incorporate into cohort studies. Advances in life course and longitudinal methods are being used to analyse these data. The COVID-19 pandemic accelerated the development and use of remote data capture within cohort studies, which will persist, but needs to be carefully evaluated. More cohort studies are taking place in middle- and low-income countries, and increasingly the challenge is to translate the growing body of evidence into intervention studies to improve population health, as well as into practice and policy-relevant guidelines.

Q7 Returning to the NSHD birth cohort study, what have been the most interesting findings from the 1946 cohort?

Overall, the key message from the thousands of papers based on NSHD is that childhood matters for adult health, emphasising the importance of each new generation having the best start to life. In broad terms, we showed that early socioeconomic disadvantage; poor childhood physical, cognitive, and emotional development; and prior ill-health adversely affected musculoskeletal, cardiometabolic, cognitive, and reproductive function in midlife and long-term survival, even accounting for adult lifestyle and socioeconomic conditions. In turn, midlife functional performance identified individuals, before symptoms were manifesting, who had a higher risk of chronic disorders in later life. Repeat measures of function across adult life showed, in some cases, that early life disadvantage also affected functional change, and led to accelerated ageing. Identifying individuals at risk earlier would enable timely preventive action to be undertaken.

Taking musculoskeletal ageing as a specific example, in the 1990s, my colleagues and I published papers showing that patterns of physical growth, motor and cognitive development, and childhood adversity were differentially associated with grip strength and other measures of physical performance at age 53 years. Two decades later, after two more assessments of grip strength, we showed that parameters of physical growth, such as birthweight and height tempo; attainment of motor milestones; and childhood cognitive ability remained persistently associated with adult grip strength, and that higher childhood cognitive ability was also associated with a slower decline

in strength, even after taking account of adult factors.[7] Then, after collecting intermediate markers of heart and kidney damage in midlife, we went on to show that lower levels of N-terminal pro-B-type natriuretic peptide and IL-6 were independently associated with better physical performance up to 9 years later.[8] The associations were meaningfully stronger than those observed for conventional risk markers, including lipids, blood pressure, and glycaemia, and were not explained by the onset of cardiovascular and kidney disease or diabetes. Findings like these help design interventions across life to maximise muscle development and maintain strength as people grow older.

Q8 Your research paper, entitled, 'Worldwide Trends in Body-Mass Index, Underweight, Overweight, and Obesity from 1975 to 2016' is considered to be among your most cited publications. Why do you believe it was so impactful?

This paper, by the NCD Risk Factor Collaboration, is an excellent example of team science. It pooled together 2,416 population-based studies with measured height and weight data on almost 130 million participants from 1975–2016. I was privileged to be part of that collaboration, having contributed NSHD data, and along with all the other co-authors, I had the opportunity to comment on the draft manuscripts. It has been heavily cited because in children and adolescents (5–19 years), the sophisticated global analysis shows rising trends in mean BMI and in prevalence of obesity over 42 years in many regions of the world, even as underweight remains stubbornly high in some regions.

Of my other publications where I made a more substantial contribution, I am delighted that our original life course book,[1,2] the editorial on life course epidemiology with Yoav Ben-Shlomo,[9] and the glossary of life course epidemiology[10] remain highly cited.

Q9 Are there any publications or innovations on the horizon within the field of life course epidemiology that you are particularly excited about?

I was recently commissioned to do a third edition of our original life course book with Yoav Ben-Shlomo, Ezra Susser, and Joanna Blodgett as co-editors. This third edition of the life course book, two decades since the second edition, and a quarter of a century since the first edition, includes new chapters that address the value of life course epidemiology in the context of increasingly urgent global challenges, such as pandemics and climate change. Jo and I have a chapter on the life course and COVID-19 coming out soon, and we will develop our ideas further in the third edition. We have a wonderful group of 52 contributors who will bring together climate and life course epidemiology; assess recent developments, including COVID-19 and other contextual factors, that shape birth cohorts and other life course studies; review new life course research for specific chronic diseases, multimorbidity, and the underlying mechanisms of ageing; and address how a life course approach informs what can be done, and is being done, in low-, middle-, and high-income countries to develop policies and interventions to improve population health. I feel very privileged to work with so many wonderful colleagues who are experts in their fields.

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