

Book Review

History of the Avon Longitudinal Study of Parents and Children (ALSPAC) c. 1980-2000.

Overy, C., Reynolds, L.A., & Tansey, E.M. (eds.) 2012. Wellcome Witnesses to Twentieth Century Medicine, vol. 44. London: Queen Mary, University of London. 122pp. ISBN 9780 90223 878 7

John Bynner

Institute of Education, London

jbynner@slls.org.uk

There are many ways of writing the history of a research programme, project or research centre depending on author predilections, research team preferences and the aims of the exercise in terms of the messages that the sponsors want to get across to the target audience. The Wellcome Witnesses to Twentieth Century Medicine history series, compiled by the History of Modern Biomedicine Group at Queen Mary College, London use, as the source for the history, a recorded conversation between key actors involved in the project, lasting for some hours. The monograph devoted to the life history of the Avon Longitudinal Study of Parents and Children (ALSPAC) – the 44th in the series - comprises the edited version of such a conversation that took place in the Wellcome Trust headquarters in London in May 2011. Nineteen people representing a wide range of ALSPAC interests, expertise and experience took part, including the original director, Jean Golding and the current director, George Davey Smith.

ALSPAC's key role in the development of birth cohort study strategy makes such a conversation particularly worthy of attention, while recognising the limitations of the discussion method in providing a full account. Inevitably, even in the hands of such an excellent chairman as Professor Catherine Peckham, Emeritus Professor of Paediatric Epidemiology at the London Institute of Child Health, a conversation on this scale can be controlled only to a certain extent. Consequently, some topics such as genetics attract a great deal of attention while others such as the important "Children in Focus" sub-study is mentioned only briefly but never fully explained and survey response barely features at all. A conventional history will include within the text, a lot of relevant facts about the subject. In the monograph, such information is supplied in footnotes, along with explanations of key terms and concepts and

additional information about the affiliations and biographies of the speakers, and of others referred to in the discussion who played a crucial role. These are backed-up further by seven appendices and a bibliography.

The benefit of the method is the rich seam of personal reminiscences from key personalities in a major scientific venture revealing dogged perseverance, if not genius, in surmounting the obstacles that needed to be overcome. The weakness of the approach is a kind of lumpiness in the narrative, involving the reader in digging into footnotes that may or may not contain the information sought. If you are looking for measures of ALSPAC performance such as attrition rates, you will not find them here. Nor will you find much on the broader context of especially the British series of post-war birth cohort studies starting at 12 year intervals, 1946, 1958, 1970, 2000 and 2012 (listed in an appendix but not discussed). ALSPAC starting in 1991-92 is now seen as playing an important part in the series as the 'missing cohort'. We might assume the 1970 birth study, which grew up in the Department of Child Health in Bristol under the direction of Neville Butler, might have had some influence on ALSPAC planning, yet this survey similarly receives barely a mention.

But then maybe such an approach to understanding ALSPAC is not such a bad idea: technicalities and backcloths are the job of another kind of history e.g. Jean Golding's history of ELSPAC (Golding, 1989). The Wellcome discussion format is better seen as eliciting a collective oral history bearing comparison with such classics as the US 'Looking at Lives' (Phelps, Furstenberg & Colby, 2002) and closer to home the edited video transcript of a discussion in 1982 between the directors of the 1946, 1958 and 1970 birth cohort studies, James Douglas, Mia Kellmer Pringle and Neville Butler (Bynner & Goldstein, 1998). Personality emerges as a key factor in moving these pioneering studies along.

Few people who know about ALSPAC in general terms, or even use its data for their own research, have much idea of the saga involved in getting it going. This is why the period examined embraces only 10 years of the actual longitudinal survey, now in its 20th year, with the rest devoted to the preceding 10 years that it took to get the required funding together. Though talked about in the 1970s as Catherine Peckham recalls, the main driver for the project was actually the rejection in 1980, by the UK Department of Health, of a proposal by Jean Golding for a new national birth cohort study due to begin in 1982. Such a study would have continued the British birth cohort studies series of studies at 12 year intervals. Largely by chance, what emerged instead was an international commission from the World Health Organisation to test the feasibility of a comparative area-based birth cohort study focused on child health in a number of European countries. £5000 was made available for piloting a self-completion instrument in Greece, Russia and the UK. The comparative framework for the whole survey finally took substance in the form of the European Longitudinal Study of Parents and Children (ELSPAC), involving eight countries - and funded separately by each of them. This initiative provided the starting point for ALSPAC, the most successful of the individual studies that survived.

If WHO supplied the seed corn, inspiration for development arose more from a conversation between Jean Golding with geneticist Marcus Pembrey in 1988. Their idea was to break new ground by going beyond the scope of the earlier birth cohort studies in Britain that follow the developing child from birth, in favour of recruiting the individual cohort member from the first notification of pregnancy. In other words, the idea was to move away from the focus on the birth of a child and what followed, to the child's development from conception. And unlike the other ELSPAC studies, there was also to be much more emphasis in ALSPAC on the collection of biological samples early in the baby's life. The starting point was urine and blood samples from the mother during pregnancy and at the time of the birth, and storage of a sample of cord blood and the placenta. This was to be followed by the collection from the child, of blood samples for the extraction of DNA, and the regular collection of a range of genetic and non-genetic biological samples, and physical assessments throughout the child's development.

The idea attracted support across a wide range of interests leading to a bank of expert advice to draw upon. But, as David Gordon in the preface to the monograph makes clear, attracting funding for the study was a different matter. It required "a long memory, a conscience and willingness to work round mindless rules and regulations, and a disdain for action that is not backed by evidence". On the basis of what is reported I would add to that: "the need for: a clear vision of where the future lay, long before it was realisable in terms of scientific products, serendipity in taking advantage of everything that could possibly progress the work, and doggedness of a high order in resisting objections to what was being proposed". The record of 258 failed applications for grants and 176 that were successful is just one indication of the battles that had to be won.

The key problem in funding terms was a mismatch between the funding model customary in medicine, of a scientific project with hypotheses to be tested and data collected within a clearly defined analytic framework, and what amounts to setting up a small business. The birth cohort study needs to conserve resources not only to do the immediate research at hand, but to sustain the project on a long-term basis, so that the widest range of research rewards, some serendipitous, can be fully gained from it. Notably, it is not until relatively recently in the UK, that, as George Davey Smith observes, the recognition of the need to build the necessary infrastructure for a sustainable 'longitudinal resource' (as it is now called), has been endorsed by the Research Councils and Government, and has become the basis of the substantial joint funding now committed to it.

It would be difficult to overestimate the importance of the 'incurable optimism' of Jean Golding in sticking to her guns over the first 20 years of development, not least through building the right alliances. Without the support of the University of Bristol's Vice-Chancellor and Director of Finance, through effectively underwriting the study through dark times, when one month fixed-term contracts for staff were not uncommon, ALSPAC is unlikely to have begun, let alone survived. A degree of stability was finally achieved when first the Wellcome Trust then the Medical Research Council (MRC) started supplying core funding for genetic data collection.

The conversation brings these key challenges to centre stage and provides a vivid picture of the achievement in overcoming them. But as it emerges at the end, the key protection came ultimately from introducing charges as part of grant applications for access to ALSPAC data. First the MRC, then the Economic and Social Research Council (ESRC), agreed to accept such charges of up to £40,000 for the projects they agreed to fund.

Once the project was up and running with the first data collection scheduled for the period 1991-1992, the sample design and operational strategies for recruitment and retention of families to the study came into play. In the earlier birth cohort studies the sample was defined by all births in Great Britain in a single week. ALSPAC was based in the now defunct administrative area of Avon, comprising Bristol, Bath and surrounding areas in Gloucestershire and Somerset (population of 1 million individuals in the 1991 census) and extended the period of recruitment to a whole year, 1991-1992.

At this stage the advantage of an area study becomes obvious in the sense that the whole network of facilities and services that families are connected to in relation to the birth of a child can be tapped into as the means of making contact with expectant mothers. Such a network - extending to subsequent child care and schooling - supplies the foundations for continuing contact with the family, for the medical and other assessments of that the study demands. In the case of expectant mothers, general practitioners followed by midwives were typically the main point of first contact, with follow-up and filling of gaps by members of the team recruited especially for their inter-personal skills. Promotional literature in multiple translations, distributed through libraries, GP surgeries and other media was also used to recruit mothers who might have fallen through the net.

Retention techniques inherited from other birth cohort studies, such as birthday cards and regular feedback to parents, were also built into the study's approach. Much attention was also paid to child-friendly clinical procedures, to make the experience of assessment as enjoyable as possible. Another feature common to effective birth cohort studies is boosting the feeling of 'specialness', extending, in the case of an area study, to local 'ownership' of a project of much importance to medical and health service improvement.

The management of feedback also confronted the problem of what medical information to supply to families in the event of serious problems being identified in the child's development. It is at this stage that another initiative, widely copied elsewhere, comes into the picture - an ethics committee established specifically for the project, but also, unusually, covering legal advice and scientific advice alongside ethical rulings. In this respect, the committee served as a kind of interface with the officially established Local Research Ethics Committee (LREC) operated in the UK by the National Health Service to govern research involving human subjects.

LRECs can often be seen more as obstacles to rather than facilitators of research. The ALSPAC experience shows how an internally appointed committee can actually work most effectively in collaboration with a research team in solving problems. Members of the committee clearly became as committed to the success of the project as the scientific team running it, and this contributed in a major way to the success of the project that continues to the present day.

The central principle that emerged early on in the committee's work was that every consideration of what was scientifically desirable, and therefore might be permissible in the study, was secondary to the interests of the child. Thus it was mandatory to ask the child's permission, from as early an age possible, for the application of any medical assessment procedure in the course of data collection. Thus the procedure for collecting blood, for example, went through a number of iterations until the means was found of making the use of a syringe for this purpose virtually unnoticed. The collection of first (milk) teeth by parents, who posted them to the team for the reward of a badge for the child, was also aided by one of the team acting the part of 'tooth fairy' for the study.

Such sensitivity and consideration for the child's needs - of vital importance to long term participation in the survey - was carried over in the cohort's teenage years to collective consultation through the Teenage Advisory Panel (TAP) covering all aspects of the survey.

The committee's only notable failing was to decide against recruitment of fathers at the same time as the mothers in the study. As the team acknowledge, genetic data for the whole family would have offered much added value over that of

the mother and baby alone and would now be central to such a study's design. Apart from the acclaim attached to the work of the ethical committee, tribute is also paid to the massive technological effort that went into data entry, processing and labelling of especially the biological data. This included the use of robotics from industry at the storage and data preparation stages. It is hard to remember now that in the beginning stages of the project in the early 1980s, cohort studies were still a long way from the massive high-speed computing facilities that enable data processing to be carried out anywhere with relative ease. At the beginning of ALSPAC's development, survey research was barely past the era of punched cards, card sorting machines and batch processing through mainframe computers, all of which added time and cost to the data collection and analysis enterprise.

This account rightly ends with recognition of perhaps ALSPAC'S biggest achievement (as the last part of the discussion makes clear), namely the collection and use of the biological samples collected in pregnancy and after. This resource now underpins a major programme of leading edge genetic investigations. One of the key strengths of ALSPAC is that the individual genotype is embedded in a series of exposures to environmental influences in every domain of life over a period of what is now

20 years – an unsurpassed resource for epidemiological understanding.

To summarise twenty years' history in a few paragraphs does insufficient justice to a project that helped move birth cohort studies to a new level of scientific significance, paving the way for the large-scale cohort studies in the USA and UK targeting up to 100,000 pregnancies. The collective oral history that the monograph reflects is in no sense a complete picture of what a full appraisal of ALSPAC would encompass. That we may hope is still to come.

What such a history does is illuminate facets of experience that no other method could match. We learn what it was like to work on the project and how, and why, key decisions were taken. The insights gained provide guidance about the pitfalls, as well as how to avoid them, in a 'real life' context that text book descriptions often fail to get across. They also contribute to strategy for understanding the human condition in challenging established paradigms of scientific value and legitimacy in favour of a more holistic, life course-orientated approach to developmental science. Those who contributed to the ALSPAC endeavour and provided the where-with-all for its achievement deserve the gratitude of those who have reaped the benefit.

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