



Understanding lives –
now and for the future

‘Life after Life Study’

Report of a Scientific Meeting

held at

The Royal College of Physicians

14th January 2016

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Acknowledgements

This work was supported by the Economic and Social Research Council [Grant numbers ES/J007501/1, ES/L002507/1, ES/L002353/1, ES/L012871/1, ES/N007549/1]

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ISSN 2398-1652. DOI: 10.14324/000.wp.1485681

URL: <http://discovery.ucl.ac.uk/1485681/>



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Executive Summary

The purpose of this meeting was to consider the challenges that Life Study encountered and their implications for birth cohort studies. The meeting noted the major achievements of Life Study and the lessons learned, discussing opportunities for taking forward key elements of Life Study, and identifying the implications for future birth cohort studies, and how to manage those implications. The meeting was structured around two themes: (i) achievements, challenges and opportunities, and (ii) what next for birth cohort studies.

During the course of the day, the unique value of the integrated and interdisciplinary nature of Life Study was emphasised by presenters and participants. It was recognised that Life Study's carefully considered pilot studies had generated data with wider relevance and that data dissemination should be a priority. Life Study has catalysed interdisciplinary approaches to the life course and achieved significant scientific momentum and direction, leaving a strengthened community of scientists from across medical, social and physical sciences as an important legacy from which to take forward future studies.

Discussion focussed on the design of future birth cohort studies, in the light of experience in Life Study and other birth cohorts. Clarity on the purpose of future birth cohort studies was essential at the outset, notably whether their development should be driven by interdisciplinary scientific and policy questions, or by the desire to create a multipurpose data resource. It will be important to identify where future birth cohorts can add most value, and to exploit the exciting potential for understanding heterogeneity in early life using innovative exposome and phenotypic data capture alongside rapidly developing 'omics technologies.

The design of a future birth cohort will need to take into account representativeness, available sampling frames, scale required, and feasibility of innovative measures in diverse settings and populations. In particular, a review of access to sampling frames derived from birth registration records for research is urgently required. At present, NHS registration records provide the only feasible approach for a national probability birth cohort in the UK, given the selective eligibility and timing of registration for child benefit payments. NHS records and linked birth registration records have the added advantage of enabling integration between representative and clustered samples.

A greater understanding of barriers to participation in birth cohort studies and of how to address these using modern social networking, communication technology and public partnerships is required. Clarity is needed on the ethical considerations regarding incentives that can be offered to encourage participation – particularly within a NHS setting. The involvement of parents and families in the design and conduct of future birth cohort studies is critical. Participant burden may be increased by the aspirations inherent in interdisciplinary innovative studies, requiring careful prioritisation of the breadth, depth and timing of information to be collected.

A number of strategic considerations emerged as crucial to the future planning and development of birth cohort studies – an essential element of the UK’s data infrastructure and contributor to the global standing of UK science. Enabling science to innovate at a population level was seen as a strategic priority, and the limitations of the current funding and governance infrastructure for supporting multidisciplinary innovative science should be reviewed and addressed. Continuity of funding and resilience to variations in funding availability are essential if the UK is to maintain its world-leading position in life course research and sustain a new birth cohort study. The time taken to realise impacts of a new UK birth cohort study will vary according to the nature of those impacts and this requires recognition and a long term sustainable strategy on the part of funders. Funders should consult and work with the scientific community in order to understand the scientific options and impacts before reaching decisions to stop the funding for studies that are in progress and to avoid loss of hard-won funds to this area of science. Consistent and sustained commitment by funders to birth cohort studies and to life course research is crucial: the scientific community needs to communicate their benefits and impact to the public, policy-makers and funders more widely.

The UK still needs a new birth cohort study, particularly one that speaks to interdisciplinary science, as well as to the major social and public health challenges facing children, families and society today. A focus on pregnancy and the first year of life remains key, reflecting the ambition and continued potential of the interdisciplinary science identified and developed within Life Study.

The need for a birth cohort study of the scale, ambition and science of Life Study remains if we are to understand and address some of the most pressing social, economic and public health issues confronting the lives and life chances of current and future generations of children and their families, and ensure that science is funded and used for their benefit.

The purpose of this meeting was to consider the challenges that Life Study encountered and their implications for birth cohort studies, by noting the major achievements of Life Study and the lessons learned, discussing opportunities for taking forward key elements of Life Study, and identifying the implications for future birth cohort studies and how to manage those implications.

The programme for the meeting and a list of attendees is attached at Annex 1. This report provides short summaries of each presentation and the related discussion. The presentations are listed in Annex 2 and can be downloaded from the Life Study website¹. The main body of this report should be read alongside these presentations.

More than 60 individuals attended, from diverse disciplinary backgrounds including the social, statistical, life, clinical and population sciences and from UK universities, fieldwork and other research organisations, the NHS, and UK statistical authorities. Most are members of the Life Study Scientific Research Investigator Network, and have contributed their expertise to the development and operationalising of the Life Study protocol through membership of scientific working groups as well as attendance at previous Life Study scientific and consultative meetings held in 2011, 2012, 2013 and 2014.

The meeting was structured around two themes: (i) achievements, challenges and opportunities and (ii) what next for birth cohort studies. Key points from discussions about these two areas are summarised in Box 1 to Box 4 below.

¹ www.lifestudy.ac.uk

Box 1: Achievements

- Life Study has catalysed inter-disciplinary approaches to the life course and achieved significant scientific momentum and direction.
- It has created a strong interdisciplinary community of scientists from across medical, social and physical sciences as an important legacy for future birth cohort studies.
- The impressive outputs of Life Study's innovative methodological developments and pilot studies should be widely disseminated.
- Life Study protocols, standard operating procedures and questionnaires represent an asset for future birth cohort studies.

Box 2: Design of future birth cohort studies

- Clarity about the purpose of future birth cohort studies is essential, notably whether their development should be driven by interdisciplinary scientific and policy questions, or the desire to create a multipurpose data resource.
- It will be important to identify where future birth cohort studies can add most value and how they can best exploit the exciting potential for understanding heterogeneity in early life using innovative exposome and phenotypic data capture alongside rapidly developing 'omics technologies.
- The design of future birth cohort studies needs to take into account representativeness, available sampling frames, scale required, and feasibility of innovative measures in diverse settings and populations.
- The involvement of parents and families in the design and conduct of future birth cohort studies is critical.
- Greater understanding of barriers to participation in birth cohort studies, and of the contribution that social networking, communication technologies and public partnerships can make to this, is required. Clarity on ethical aspects of incentives to encourage participation is needed, especially in a NHS setting.
- Participant burden may be increased by the aspirations inherent in interdisciplinary innovative birth cohort studies, requiring careful prioritisation of the breadth, depth and timing of information to be collected.

Box 3: Strategic considerations

- Consistent and sustained commitment by funders to birth cohort studies and life course research is crucial.
- Enabling science to innovate at a population level through birth cohort studies is a strategic priority: current funding and governance infrastructures need to change.
- The time needed to realise impacts of a new UK birth cohort study will vary according to the nature of those impacts and this requires recognition as part of a long term sustainable funding strategy.
- Funders should consult and work with the scientific community in order to understand fully the scientific options and impacts before reaching a decision to stop the funding of birth cohort studies that are in progress, and to avoid loss of hard-won funds.
- The scientific community needs to communicate clearly and widely about the critical importance of innovative birth cohort studies and life course research to the public, policy makers and funders.
- A review of access to sampling frames derived from birth registration records for research is urgently required. At present, NHS registration records appear to provide the only feasible approach for a national probability birth cohort, given the selective eligibility and timing of registration for child benefit payments.

Box 4: The need for a new UK birth cohort study

- The UK still needs a new birth cohort study capable of bringing world leading science to populations and populations to science from a life course perspective.
- A new birth cohort study is essential if we are to understand and address some of the most pressing social, economic and public health issues confronting the lives and life chances of current and future generations of children and their families, and ensure that science is funded and used for their benefit.
- A prospective focus on pregnancy and the first year of life remains a key priority for such a birth cohort study, reflecting the continued relevance of this ambition for interdisciplinary science developed within Life Study.

Introduction and Welcome

Purpose of the Meeting

Professor Hilary Graham and Professor David Leon, both members of the Life Study Scientific Steering Committee (SSC), opened the meeting and chaired Sessions 1 and 2. They noted that the purpose of the meeting was to consider the challenges that Life Study encountered and their implications for birth cohort studies, by:

- Noting the major achievements of Life Study and the lessons learned
- Discussing opportunities for taking forward key elements of Life Study
- Identifying the implications for future birth cohort studies, and how to manage those implications

It was noted that the aim of the meeting was not to look backwards other than in acknowledging the achievements and challenges, but rather to look forwards to the lessons learned and implications for future birth cohort studies. The primary focus of the meeting was on the science (although it was recognised that it may also flag up other considerations), and it was considered likely that this meeting would begin, rather than conclude, the process of considering the achievements, challenges, and lessons learned.

Report of the Meeting

The Session Chairs noted the Research Councils'² requirement that a report of the meeting be published on the Life Study legacy website. They highlighted that information considered inappropriate for the public domain (for example intermediate research findings) would be redacted in published versions of the presentations³ so as not to compromise the intellectual property of the speaker. Furthermore, and in order to allow free discussion, the published report would not attribute comments to named individuals and would present a summary of the discussion only. This final report of the meeting has been validated by the Session Chairs and the SSC.

Life Study Scientific Steering Committee

The Session Chairs noted that this meeting had been arranged at short notice to fit within the Research Councils' notice period. While the majority of SSC was present, some members (including Professors Vignoles and Kiernan) had been unable to attend. As a consequence, discussion of the important work on non-resident fathers (funding awarded to Professor Kiernan by the Nuffield Foundation and ESRC on 31st March 2015) had not possible to arrange and a report of this work would be published on the Life Study website.

² The Economic and Social Research Council (ESRC) and the Medical Research Council (MRC)

³ Presentations 3,6,7 and 8 were redacted

Session 1: Achievements and Challenges

Life Study: Sampling and Recruitment during Pregnancy

Professor Dezateux gave an overview of the main events and decisions taken since the last Scientific Research Investigators Network scientific meeting in June 2014, prefacing her talk by a reminder of the integrated design of Life Study. She noted that Phase 1 of the Study – the Innovation Phase - was designed to evaluate recruitment methods in the Pregnancy Component and to test whether an assumed recruitment rate of 50% was realistic. It had been agreed that Phase 1 would run from January 2014 to October 2017. Funding for the first part of this Phase had been released up to mid-2016, when a further Office of Government Commerce Gateway review⁴ to assess progress and to inform the scope and content of Phase 2 had been planned.

Outlining the design and experience of the Pregnancy Component (participants recruited during pregnancy), Professor Dezateux highlighted the lessons learned in the first Life Study Centre (opened on 12th January 2015); these had been used to inform the establishment of the second Centre (opened on 28th September 2015).

The ESRC and MRC formally notified UCL of their decision to close Life Study on 12th October 2015. This inevitably brought to a close Phase 1 of the Study before its planned-for completion in October 2017. Unfortunately and in consequence, there had been insufficient opportunity to test and refine the recruitment strategies in the first Centre or to gain any experience of recruitment in the second Centre. These strategies included different approaches to recruitment that had been or were being implemented and tested when the decision to close the Study was taken.

Professor Dezateux summarised the partnerships established, the community engagement, and development work undertaken, as well as experience with recruitment of pregnant women and their partners to date. She highlighted and reflected on the challenges experienced and the lessons learned regarding recruitment in pregnancy.

In the first Life Study Centre these included: midwife shortages and difficulties in their recruitment impacting on contact with and recruitment of mothers initially; difficulties in re-contacting mothers to confirm appointments following initial contact with them in scan clinics; participant burden related to questionnaire length and complex consent for

⁴ See <https://www.gov.uk/government/publications/major-projects-authority-assurance-toolkit>

three contacts as well as multiple record linkages; and challenges in engaging deprived and difficult-to-reach communities.

It was noted that, although experience was limited as a consequence of the abrupt closure of the Study, these challenges were not evident to the same degree in the Leicester Life Study Centre where recently initiated recruitment had been progressing well, reflecting regional differences in, *inter alia*, the availability and engagement of midwives as well as the ability to apply at the outset some of the lessons learned in the first Life Study Centre.

Life Study: Sampling and Recruitment after Birth

Professor Elias outlined the design of the Birth Component (participants recruited when the babies were approximately six months old), stressing that the key principle guiding the design was the potential for integration with the Pregnancy Component. This integration was a unique and innovative approach – the value of this integrated study design is substantially greater than the sum of the two individual components. He noted a number of other innovations within the Birth Component, for example the use of a SQL⁵ database to reduce errors and increase the efficiency and accuracy of the complex process of scripting the questionnaires. In addition, the recruitment process – via the UK statistical authorities and birth registrations – allowed a comparison of the characteristics of all registered births in England and Wales to the Life Study sample. This contrasts with traditional approaches which have not hitherto allowed the comparison to take into account such a rich range of characteristics of those not taking part or otherwise approached. Professor Elias stressed the interdisciplinarity of the Life Study, and the potential benefits for the social science communities of accessing the planned integrated sample.

Professor Elias summarised the development and results of the Birth Component pilot. This was a purposive pilot, designed not to be representative but to test recruitment procedures using linked NHS records and birth registrations, and to pilot questionnaires and interview procedures. The UK statistical authorities required the initial Life Study pilot to use an opt-in approach. This entailed the statistical authorities contacting all sampled mothers of babies whose births had been registered, offering them an opportunity to participate in Life Study. Participants in the pilot were recruited from among those who had responded positively to this invitation. The percentage of mothers opting in to

⁵ Structured Query Language

further contact using this method of recruitment was exceptionally low and unlikely to generate a representative national probability sample.

A linked dataset, containing both birth register data and NHS 'spine' data for England and Wales, had been placed in the Office for National Statistics (ONS) 'Virtual Microdata Laboratory' (VML) for analysis by Life Study staff who had been granted ONS 'approved researcher' status. These data are enhanced with a flag indicating the mothers' responses to the invitation to opt-in to Life Study. Further work had been planned to analyse the VML dataset of all 4000 births/mothers contacted (linked to their birth registration and NHS 'spine' records) and to conduct a detailed analysis of recruitment and response rates. This would have allowed a detailed and innovative exploration of the statistical characteristics of both respondents and non-respondents, leading to a nuanced understanding of any biases in recruitment and willingness to opt-in to the study, as well as serving as a model for future analyses of response bias. This work had not been completed as funding had been withdrawn.

Professor Elias summarised the implications of the pilot for future birth cohort studies recruiting after birth:

- An opt-in approach had not proved feasible.
- NHS/ONS birth registrations, accessed via an opt-out procedure, provided the best sampling framework for future birth cohort studies.

He noted that while the Life Study team had taken steps to provide the Confidentiality Advisory Group with the information required to amend Life Study's existing Section 251 (NHS Act 2006) approval to include approval for an opt-out approach, a formal application under Section 251 to test this opt-out model had not been pursued. This was because, once Life Study funding was withdrawn, there would have been no prospect of participant follow-up to justify testing this method of recruitment.

Discussion

There was a general discussion about whether a future UK-wide birth cohort study recruiting in pregnancy and / or after birth was feasible. It was noted that:

- Local community engagement and ownership are of fundamental importance. Although Life Study had a comprehensive programme of community engagement, the population around the first Centre in London presented particular challenges. It was rapidly changing and had seen large increases in recent years, especially with respect to young families from ethnic minorities and under-5s.

- These challenges had not been evident to the same degree in the second Centre which served a more stable population. Hence uncertainty about recruitment in pregnancy remained as, following closure of Life Study, the testing of recruitment in two Centres in Phase 1 of Life Study has not been able to proceed as planned.
- A strong local study identity fosters commitment and, along with the stability of the population, is a key feature of the UK's existing regional birth cohort studies. Engaging local community doctors and other healthcare professionals is also essential when embarking on recruitment to regional birth cohort studies. Scaling up these aspects for a national birth cohort study presents significant challenges and requires proper resourcing.
- Recruitment to a large scale birth cohort study commencing in pregnancy is only feasible through the NHS as there is no national or UK-wide sampling frame of pregnancies.
- Recruitment of a representative sample after birth in time to capture the rapid changes in health and development occurring during the first year of life is only feasible using NHS registration data in England and Wales, given those elements of the Statistics and Registration Service Act 2007 governing the use of birth registration data for research.
- Using child benefit records as a sampling frame (as was the case in the previous Millennium Cohort Study) is unlikely to allow recruitment of a representative sample as this is no longer a universal benefit. Furthermore, the timeliness of registration for this benefit may be too late to enable sampling to achieve initial contact at the target age of six months.

Session 2: Innovations

Integrating representative and clustered samples in birth cohort studies

Professor Harvey Goldstein outlined the statistical approach to achieving integration of the Pregnancy and Birth Component data. The intention in this approach had been to present Life Study data to users as a single dataset and to avoid complex weighting procedures. He noted that the value of the Pregnancy Component lay in its contribution to understanding differences within the population, for example, using the purposively sampled ethnic diversity within this component to contrast different ethnic groups and then relate this back to the national population through integration with Birth Component data.

Discussion

During discussion, it was noted that one of the key methodological innovations of the Life Study design had been to enable data from a nationally representative birth sample to be integrated with rich data from clustered purposive samples of pregnant women.

Measuring environmental exposures in pregnancy

Professor Frank Kelly summarised the design and results of pilot work to investigate the acceptability to pregnant women of sampling methods and new technologies for the measurement of air pollutants and other environmental factors such as temperature and noise. Measurements taken in homes were tested using new mobile and non-invasive devices that pregnant women could carry. The impact and improved efficacy of this newly available technology is high, allowing measurements to be made at an individual level of exposures over the course of several days, irrespective of the location of the person, as well as noting e.g. periods of activity or sleep.

Discussion

During discussion, it was noted that:

- The Life Study environmental pilot had used cutting-edge technologies.
- The closure of Life Study meant that it had not been possible to evaluate these techniques in a larger sample of pregnant women in whom outcome measures could be collected.

- The results of the pilot will be useful to other studies, including European studies. Professor Kelly is already involved in the EU Exposomics programme, and the findings of the Life Study pilot will be of value to this programme as well as to future birth cohort studies.
- It was recognised that these techniques will also be valuable more widely, for example, in studies collecting detailed phenotypic information of adult chronic obstructive pulmonary disease.

Placenta sampling in Life Study

Professor Neil Sebire summarised the development work that he had carried out as a collaboration between Life Study and the National Institute for Health Research Biomedical Research Centre at Great Ormond Street Hospital for Children NHS Foundation Trust and University College London. This has enabled examination of the sampling, storage, and analysis of Life Study placenta samples, including a particular focus on 'omics technologies. Data on the stability of factors including biomarkers and sample consistency were presented and the importance of this emphasised. These novel findings are relevant not only for the collection and storage of placental samples but as a 'proof of principle' for the collection, storage and analysis of other biological tissue samples.

Discussion

During discussion, it was noted that:

- With the closure of Life Study, an important opportunity had been lost to combine ground-breaking methodological work with socioeconomic and biomedical data to investigate using placentas to understand the complexities and phenotypes of heterogeneous conditions, including for example intra-uterine growth restriction.
- There were important scientific benefits of this work for other studies collecting tissue samples, particularly placenta samples.
- Publication of this innovative work is important so that researchers could access the detailed findings to inform their own studies, as well as future birth cohort studies.

Session 3: Opportunities

Session 3 was chaired by Professor Diane Reay (member of the Life Study Scientific Steering Committee) and Professor Anne Ferguson-Smith (UK member of the Life Study International Scientific Advisory Board). These talks focused on the scientific opportunities for taking forward key innovative areas following the closure of Life Study.

“Babyomics”: Infection, Immunity and the Microbiome

Professor Peter Brocklehurst summarised the infection and immunity enhancement to Life Study – which is continuing and is now called the ‘Baby Biome Study’. This enhancement to Life Study, funded by the Wellcome Trust, aims to measure the extent to which early exposure of a newborn baby to microbes impacts on health outcomes in later life. This work includes exploring the impact of elective caesarean section, and of antibiotics given in pregnancy or labour, on the development of microbiota in a child’s gastrointestinal tract. This will help understand the development of a child’s immune system and how it relates to the subsequent development of childhood asthma, allergies and diabetes. It will also help to understand how antibiotic resistance develops. Professor Brocklehurst summarised the work accomplished to date, and future plans with national and international collaborators. It is planned to take this work forward despite the closure of Life Study. A key issue to address is the feasibility of scaling up the methods to recruit at scale.

Discussion

There was discussion about the potential for linking this work with work currently taking place in Europe and the US. During discussion, it was noted that elements of the Life Study questionnaires may also be useful for the continuation of the Baby Biome Study, where participant burden and funding permitted. Another important area for researchers to explore in future will be the impact of these key bacterial species in other areas such as cardiovascular health. Record linkage will allow a number of other areas to be explored.

Vision, Attention and Cognitive Development in Infancy

Professor Jugnoo Rahi and Dr Tim Smith gave this talk on behalf of other Life Study Neurodevelopment Group members - Professors Mark Johnson, Dale Hay, Alan Emond, Catherine Peckham and Tony Charman. The speakers noted that Life Study has provided an opportunity to develop a cross-disciplinary collaboration to explore the inter-

relationship of vision, attention, cognitive development and behaviour in infancy. Vision is important to learning and cognition, and provides a measure of neurodevelopment. This work comprises vision and ophthalmic measures developed at UCL, combined with measures of attention using eye-tracking developed at Birkbeck, and psychological tests of attention and behaviour developed in Cardiff. The Neurodevelopment Group is collaborating to take this work forward.

One aim had been to develop clinical quality measurements that could be administered by a team of non-clinical researchers in a non-specialist research setting. Life Study would have also provided an opportunity to test existing and novel measures at scale. A number of protocols had been developed and tested, bringing together measures intended for the Pregnancy Component visits to Centres planned for when cohort members were aged six and twelve months. Pilot data had been gathered, and some of the methodologies tested. A cutting edge and integrated programme of work had been developed but would not be implemented, given the closure of Life Study. The Group planned to obtain funding to take forward a smaller scale study, utilising Life Study questionnaires, standard operating procedures and equipment to facilitate this. This work and the research questions behind it would have important implications for policy and practice, and address an important gap in current birth cohort studies. Their inclusion in a future birth cohort study would enable longer-term outcomes relevant to children's social, emotional and cognitive development to be understood.

Discussion

There was discussion of the opportunities to examine intergenerational aspects of the dimensional measures proposed in this work as the Life Study protocols included some measures on parents. Realising these opportunities, now Life Study has been closed, would depend on what funding could be obtained, as well as the priorities of funding organisations. It was noted that a focus on vision and attention, as proposed, would allow researchers to examine infant development more broadly and identify factors that place children at risk of developmental trajectories associated with adverse health and educational outcomes, while at the same time enabling much needed research in infant ophthalmology and the visual sciences.

Session 4: Panel Discussion: What next for longitudinal and birth cohort studies?

Session 4 was chaired by Professor David Leon. The Panel comprised: Professor Diana Kuh (Director of the MRC National Survey of Health and Development), Sam Clemens (Research Director at Ipsos MORI), Helen Pearson (author of a forthcoming book on the UK birth cohorts), Professor Heather Joshi (founder Director of the UK Millennium Cohort Study), and Madeleine Wang (member of the Life Study Advisory Group on Ethics).

Panel members each briefly presented their thoughts and observations on ‘What next for longitudinal and birth cohort studies?’ This was followed by open discussion.

Summary of achievements, challenges and opportunities

The key points from the Sessions and the discussions on achievements, challenges, and opportunities were:

Learning from the development and implementation of Life Study

- Life Study comprised a unique, integrated and ambitious programme. A huge amount of work had been accomplished, and had led to a number of important achievements. A study of the scale, ambition and science of Life Study is much needed. Dissemination of the work achieved in developing the Life Study programme and the resulting opportunities was viewed as essential. Life Study would have an important impact on how studies of this type would be developed in future.
- Life Study intended to be, and became, inter-disciplinary and multi-disciplinary. This represented an enormous achievement, highlighting that time and trust is needed for collaborators from different disciplines to work together to clarify the optimal approaches to scientific questions that need a joint approach. There was strong endorsement of the need for this approach in future birth cohort studies and of the importance of maintaining the collaborative networks and resulting science developed through Life Study.

Impressive outputs from methodological developments and pilot studies.

- Life Study had generated exciting primary data in a number of areas, which the audience considered should be written up and shared in the widest possible way.

Significant scientific direction and momentum.

- New and productive collaborations and networks had been formed, especially across disciplines. Life Study had helped to catalyse and strengthen a community of scientists from across the medical, social and physical sciences. This achievement was recognised as one of Life Study's major legacies.

Strategies and infrastructure for future innovative studies and their funding.

- It was recognised that working with a single funder within the context of a multidisciplinary innovative study remains challenging given the breadth of science and experience of different settings needed. The limitations of existing models for funding and governance also remain and need to be resolved. Whilst dialogue with funders is important to streamline and rationalise the amount and content of reporting and monitoring, the audience also recognised the importance of a structure that enabled innovations to be properly tested. This is a strategically important issue to get right from the outset, for all parties.

Summary of Discussions on 'What next for Longitudinal and Birth Cohort Studies?'

Key points emerging from the Panel and subsequent discussion were:

Design of future birth cohort studies

- When developing a future birth cohort study, consideration must be given to whether it is a study whose development is driven by contemporary scientific challenges, or simply by a desire to create a data collection infrastructure (and - in the latter case- who is most appropriate to specify the data to be collected and how).
- As research and technology moves on, it creates pressure to measure more, but the participant burden becomes greater and may become too great.
- Issues of generalisability may become more of an issue where a national sampling frame is lacking (as is the case with pregnancies, for example) or where it becomes too expensive or is not feasible to collect certain types of data or samples from a nationally representative sample (based on household visits, for example). These tensions will need to be addressed at the outset; however Life Study's innovative design provides some methodological opportunities to integrate both clustered and probability based samples.

- Life Study addressed priorities across disciplines when determining which data and samples to collect across multiple sweeps. This required consideration to be given to the depth and breadth of the topics included in the questionnaires, and what was achievable and the participant burden that it imposed. A future birth cohort study will need to consider these issues.
- Life Study sought to address gaps in timing of assessments, diversity of the population included, and the information collected in earlier birth cohort studies. There is a need to balance collection of novel measures reflecting recent scientific advances with collection of information comparable to that in earlier cohorts to facilitate cross-cohort comparisons. The Life Study protocol included both elements and this aspect was explicitly considered when determining the protocol content. This remains a challenge for future birth cohort studies, especially with respect to participant burden. While record linkage can enable alternative sources of information and minimise respondent burden, the relevance, quality and completeness of routine data in pregnancy and infancy is acknowledged as insufficient to replace direct collection of this information from participants, especially in pregnancy and infancy.
- Future birth cohort studies should be better able to capture heterogeneity in early life, to capture data in real time with new technologies, and to make the most of the exciting opportunities offered by the rapidly-developing ‘omics technologies. It will be important to identify where birth cohort studies can add the most value, working with biobanks.
- During the post-war period, there was a spirit of optimism and parents felt that participation in birth cohort studies would improve the lives of their children. This may be less true of British society today. Modern social networking, communication technology and public partnerships could be better exploited to engage today’s participants.
- Regional infrastructure challenges will need to be overcome if recruitment in pregnancy through clustered centres is to be achieved. This might be achieved through a federation of studies, as was suggested in the original Longview report⁶ carried out for the funders before the tender for Life Study was developed. An alternative of recruitment of children born to members of existing birth cohort studies could be considered (as in the case of the Children of the Children of the 90’s, a study of children born to participants in the Avon Longitudinal Study of Parents and Children [ALSPAC]). This would have the advantage of adding an intergenerational dimension, as well as capitalising on the loyalty

⁶ See http://media.wix.com/ugd/df1448_449d3148bd8c4c919fd29edfffe897b5.pdf

already shown by the parents in encouraging their children to participate, however the dispersal in time and place of births to cohort members might limit feasibility.

- The governance of any future large study must learn from Life Study. Governance structures and reporting must be simplified and streamlined to ensure that the scientific leadership team can focus on developing and delivering the study.

Strategic considerations

- An opt-in recruitment model for a nationally representative birth cohort does not have a high enough response rate to be credible. There is evidence that response rates from studies using opt-out methods are higher and hence a more effective model would be to use NHS registration records as the sampling frame in an opt-out design with the potential for access to further information available in linked birth registration records.
- Child benefit records are not considered to provide a useful approach to creating a nationally representative sampling frame since they are no longer universal. In addition, the timeliness of registration for this benefit may not be adequate to allow a first home visit by 6 months of age which was the age many considered optimal, scientifically, to address information gaps from earlier birth cohort studies.
- ONS does not currently have a legal route whereby an opt-out sampling strategy can be pursued, in contrast to the exemptions afforded through section 251 of the NHS Act 2006. There was considerable support for a review of the provision of ONS data for research and survey work to assess how an opt-out approach to sampling might be enabled, given the wider implications for survey based research.
- Ethical considerations regarding incentives (financial or non-financial) that can be offered to encourage participation should be clarified - particularly within the NHS - so that researchers and funders are clear about what is acceptable.
- Historically there have been periods of feast and famine in the funding available for birth cohort studies. Clarity of purpose and function and resilience to variations in funding availability are essential if the UK is to maintain its world-leading position in life course research and also for the sustainability of any new birth cohort study.
- There is a strategic issue around the unity of the funders and the scientific community for this type of 'big science'. The importance of life course research has only recently become widely accepted. Life Study had been conceived and developed as a multi-

disciplinary venture, and by its nature would be a large study. Lessons could be learned from the physics community on how they garner support for large scientifically-driven facilities like the Large Hadron Collider. They communicate clearly and widely (e.g. via the national media) about the importance and benefits of such a venture. The importance of birth cohort studies needs to be articulated more clearly and more widely. Raising awareness amongst the public, policymakers and funders of the value of cohort studies would be a good way of increasing engagement and understanding.

- The decision to cease Life Study creates a further gap in the series of birth cohort studies for which Britain is famous (the last gap was created when the proposed 1982 birth cohort was turned down), leading to missing information for tomorrow's researchers and policy makers. Policy makers generally wish to use evidence from a nationally representative birth cohort study to inform policy changes and historically have been reluctant to generalise from findings in clustered or local birth cohort studies. However certain types of evidence could be robustly obtained from clustered studies with more intensive measures which could then be combined with 'representative' information to make generalisable inferences.
- Funders should consult the scientific community in order to understand the scientific options for going forward in the face of slower than anticipated recruitment. Funders should also assess the wider scientific impacts of a decision to cease funding for a birth cohort study such as this, and how those impacts might be mitigated, prior to considering such a decision. A number of attendees noted that it remained unclear precisely why Life Study had been closed, or what scientific evidence had been considered before reaching that decision.

The need for a new UK birth cohort study

- The UK still needs a new birth cohort study, particularly one that speaks to interdisciplinary science, as well as to the major social and public health challenges facing children, families and society today. The presentations and discussion at the scientific meeting illustrate that there remain many important questions to answer in childhood. A recent Unicef report⁷ has noted that the UK is 16th overall out of the 29 richest countries in terms of ranked child wellbeing measures. Absolute child poverty in the UK has plateaued and is increasing among working families.⁸

⁷ See http://www.unicef-irc.org/publications/pdf/rc11_eng.pdf

⁸ See <http://www.ifs.org.uk/publications/7880>

- It was noted that the earliest cohorts did not start as longitudinal or birth cohort studies, rather as cross sectional maternity surveys driven by concerns that focussed on maternal and perinatal health and which subsequently evolved into birth cohorts. The major UK birth cohorts which have recruited in pregnancy (ALSPAC, Born in Bradford) had not been funded by Research Councils at their inception.
- It was generally agreed that most of the major opportunities afforded by the design of Life Study, especially those with important impacts in the social sciences and which depended on the integration of data concerning social and biomedical sciences, would not now be realised as the Study has been closed. It was recognised that while the early impacts were most likely to be focussed on health outcomes, that valuable social science impacts would have emerged in the medium and longer term. Life Study would have provided important insights into social mobility, inequalities, child poverty, and education.
- The interface between social and biomedical research in Life Study was exciting, original and presented novel and potentially important opportunities. The importance of an inter-disciplinary approach to telling the full story about people's lives had become very apparent to those involved in developing Life Study. The questions that Life Study had been designed to answer remain. Inter-disciplinary interactions which enabled the gaps between the disciplines to be bridged must remain a key strategic and scientific priority for future birth cohort studies.

In concluding the meeting, members of the Life Study team were thanked by all for their hard work and dedication. Participants at the meeting recognised the very exciting scientific achievements and significant progress made in the short window of time for recruitment prior to the funders' decision to close the study, and the urgent need to mitigate the scientific impacts arising from this decision.

Annex 1 Programme and List of Attendees

Programme

Life after Life Study: achievements and scientific considerations for future studies

Royal College of Physicians, 11 St Andrews Place, London NW1 4LE

14th January 2016 10.30am-4.00pm

CHAIRS Sessions 1 and 2 - Hilary Graham and David Leon

10.30am **Coffee and registration**

11.00 **Welcome** **Chair**

Session 1 - Achievements and Challenges

11.05-11.45 Life Study: sampling and recruitment in pregnancy and after birth
Carol Dezateux and Peter Elias

Session 2 - Innovations

11.45-12.30 Integrating representative and clustered samples in cohort studies
Harvey Goldstein

Measuring environmental exposures in pregnancy
Frank Kelly

Placenta sampling in Life Study
Neil Sebire

12.30-1.15 *Lunch*

CHAIRS Session 3 - Diane Reay and Anne Ferguson Smith

Session 3 - Opportunities

1.15-2.15 “Babyomics”: infection, Immunity and the microbiome
Peter Brocklehurst

Vision, Attention and Cognitive Development in Infancy
Jugnoo Rahi, Mark Johnson, Dale Hay, Tim Smith

CHAIR Session 4 - David Leon

Session 4 - Panel discussion: What next for longitudinal and birth cohort studies?

2.15-3.30 Panel discussion
Diana Kuh, Heather Joshi, Helen Pearson, Sam Clemens, Madeleine Wang
Followed by general discussion

3.30 Summary and close (Chair)

Life after Life Study: achievements and scientific considerations for future studies
Royal College of Physicians, London 14th January 2016

Attendees:

Sarah Bailey - UCL	Jenny Kurinczuk – Oxford
Vikki Barry-Jackson - Life Study	David Leon - LSHTM
Stephan Beck - UCL	Marsha Lowe - Life Study
Helen Bedford - UCL	Peter Lynn - Institute for Social and Economic Research
Peter Brocklehurst - Life Study	Ronan Lyons - Swansea
Simon Burgess - Bristol	Barbara Maughan - KCL
Emma Butcher - UCL	Lynne Molloy - ALSPAC cohort
John Bynner - Longitudinal & Life Course Studies, and Institute of Education	Dele Olorunshola - BHRUT
Anne Carey - Life Study	Alison Park - CLOSER
Sam Clemens - Ipsos MORI	Dipesh Patel - UCL
Debbie Colson - Life Study	Helen Pearson – Author
Vanessa Cooke -Life Study	Catherine Peckham – UCL
Neil Dalton - KCL	Darina Peycheva - Life Study
Carol Dezateux -Life Study	Jugnoo Rahi - UCL
Liz Draper -Leicester	Diane Reay - Cambridge
Peter Elias - Life Study	Marcus Richards - NSHD (1946) cohort
Anne Ferguson-Smith - Cambridge	Helen Roberts - UCL
Nigel Field - UCL	Ian Scudamore – Leicester
Nicola Foster - Life Study	Neil Sebire - GOSH
Mark Gautrey - ONS	Francesco Sera -
Nick Gilby - Ipsos MORI Harvey Goldstein Life Study	Ana Silva - Birkbeck
Hilary Graham York	Tim Smith - Birkbeck
Rebecca Hardy - NSHD (1946) cohort	Leye Thompson – BHRUT
Dale Hay – Cardiff	Claire Thorne - UCL
Steven Hope - UCL	Stephan Tietz – Ipsos MORI
Mark Johnson –Birkbeck	Mireille Toledano – Imperial
Heather Joshi - Institute of Education	Diana Viscusi - Life Study
Frank Kelly – KCL	Suzanne Walton - Life Study
Rachel Knowles - Life Study	Madeleine Wang - Life Study Advisory Group on Ethics
Diana Kuh - NSHD (1946) cohort	John Wright - Born in Bradford cohort

Annex 2 Summary of Presentations available from website⁹

- 1 Dezateux: Sampling and Recruitment in Pregnancy
- 2 Elias: Sampling and Recruitment after Birth
- 3 Goldstein: Integrating Representative and Clustered Samples
- 4 Kelly: Measuring Environmental Exposures in Pregnancy
- 5 Sebire: Placenta Sampling in Life Study
- 6 Brocklehurst: Infection, Immunity and the Microbiome
- 7 Rahi and Smith: Vision, Attention and Cognitive Development

⁹ <http://discovery.ucl.ac.uk/1485679/>