



Please accept the season's greetings from the LBC1921 study team. We welcome you to the LBC1921 newsletter for 2017. We hope you have had a good year and would like to send warm wishes for a happy Christmas and New Year. Professor Deary would like to begin by updating you, in the message below.

Director's Report

We began the Lothian Birth Cohort 1921 (LBC1921) study in early 1999, so it's almost 19 years old. And it is still going strong. The information, measurements, and data that you provided have made you famous world-wide. You have been, and still are, the subject of hundreds of reports in prestigious international scientific journals. Scientific reports of your results are used by government, charities, universities, and older people's organisations to give the best advice about healthy ageing.

I sometimes get a letter from one of the Cohort that suggests that, because we no longer see you in the clinic, the LBC1921 study is finished. Not so! Your data are still used in lots of scientific reports; sometimes they are used on their own, sometimes they are used for comparison with the LBC1936, and sometimes they are combined with other datasets from the UK and beyond. In all these combinations, you are still making valuable contributions. Medical data still arrive about LBC1921 participants, and these are incorporated as they arrive. There are still many researchers who discover new ideas to test among your rich data.

So, as we wish you a Merry Christmas and Happy New year again this year, you must consider yourself a continuing member of one of the world's most respected studies of human ageing: one that is alive and highly productive. As evidence for that, just look at that list of new scientific studies you have produced, at the end of this newsletter. If, for any reason, you'd like to contact the study office, please do so. I and Alison, and other team members, are still here and keen to hear from you.

Again, with my best Christmas and New Year wishes,

Ian Deary

LBC1921 Study Director

If you wish to get in touch for any further information, our contact details can be found at the end of the newsletter. Please do let us know if you have moved house, or are about to, so that we can update your address and are able to keep in touch. Thank you again for your continued interest in the LBC1921 study. We hope that you are proud to be part of the longest cognitive ageing study in the world.

As usual, we would like to take this opportunity to update you on the progress and goings-on in the research and events that have occurred in the last year. Everything you read about in this newsletter is a result of your involvement in the LBC1921 study.

LBC reunion 2017

We were delighted to see a number of you at the Lothian Birth Cohorts' reunion event in June. The team were delighted to welcome about 400 LBC1936 and LBC1921 participants and their guests to an exciting afternoon of talks from the Principal Investigators and collaborating researchers. Participants also had an opportunity to speak to members of the research team, including the cognitive testing team and those who analyse the data collected. During the event, Libby Archer, Research Manager at Age UK, recorded a series of interviews with the LBCs'

participants and researchers for Age UK's radio station, The Wireless. A selection of the interviews are available to listen to at: <http://www.thewirelessradio.com/listen-again/>



We are already planning a future reunion in 2019 which will be the 20th anniversary of the Lothian Birth Cohorts being established.

The Lothian Birth Cohorts in demand by scientists, industry, and the public

“Three talks I've given about the Lothian Birth Cohorts' (LBCs) results and resources in the last wee while represent how they are valued by different sectors,” said Professor Ian Deary, the LBCs' Director. In September, Ian gave a talk at the Roslin Institute (where Dolly the sheep was invented) on the whole genome sequencing data and other 'omics' data available on the LBCs. “The meeting was for scientists,” said Ian, “and was organised by the company Illumina who made the array that tested 3,000,000,000 genetic locations on every person in the LBCs. There was wonder in response to the range and depth of the LBCs' data, and there was more academic collaboration as a result that will address genetic contributions to ageing well”.

In November, Ian gave a packed-out talk to the University of Edinburgh Retired Staff Association on the Lothian Birth Cohorts' findings. “I last talked to them about the LBCs

in February 2010,” said Ian, “so it was fun, then, to be able to tell them that I was about to summarise the results of about 400 research papers. Just kidding. They were an attentive and appreciative audience, with lots of good questions. Also, among this supposedly 'lay' group were two innocent-looking retired women who came up to speak to me afterwards, and turned out to have been lab technicians working on epigenetics and telomeres!, both of which we examine in the LBCs. So, however simple one makes things one also has to think what expertise there is out there.”

Also in November, Ian gave an invited plenary lecture at the Royal Society in London to the Galton Institute's conference on 'Surveying (Sir Francis) Galton's Legacy'. Galton was a prolific Victorian genius--a noted explorer and geographer, inventor of fingerprinting, discoverer of the anticyclone, highly original statistician, pioneering geneticist, and much more.

“The aspects of Galton's work that were relevant to the LBCs,” said Ian “were his interest in human cognitive function, and his enthusiasm for collecting longitudinal health and psychological data. If you look at what and how Galton collected data from thousands of the public in the 1880s, his work predates and resembles the data we are collecting these days in the LBCs and other large surveys, such as UK Biobank.

He saw, before anyone else, how valuable it could be serially to assess the body and the mind, and it was a pleasure to remind the audience what Galton did and urged, and how the Lothian Birth Cohorts' superb serial data confirmed Galton's judgement about the usefulness of such longitudinal data.



Dementia's Hidden Voices, Luminate Festival of Creative Ageing

"Using a combination of modern classical and minimalist influences, John McHugh has composed a piece that elevates the voices of people with dementia and their carers. It is beautiful as a piece in itself, it brings attention to dementia, and seeing and hearing the piece's origins brought tears to many eyes in the audience." These are Ian Deary's first reactions after hearing *Hidden Voice* performed in the University of Edinburgh's St Cecilia's Hall as part of the 2017 Luminate Festival of Creative Ageing on 1st October.

The musical piece developed its themes from the comments made by people with dementia and their carers. John McHugh heard melodies and rhythm in their natural speech prosody. He composed a piece for a quartet in which he played piano and three members of the Royal Liverpool Philharmonic Orchestra played strings; samples of the voices appeared in the piece. Ian Deary joined John McHugh and Dr Katie Overy (from the Reid School of Music at the University of Edinburgh) to discuss the performance and answer questions from the audience. "I was still savouring the beauty and poignancy of the piece when I was cast back into professional mode," said Ian. "However, alongside using the discussion to explain how the Lothian Birth Cohorts were contributing to understanding cognitive ageing, I also discussed the music with John, and others' artistic attempts to reflect on dementia and cognitive ageing." A video of the Hidden Voice can be viewed here: <https://www.youtube.com/watch?v=ZdDf3HrxJfA>

LBC1921 Portraits

You might remember our collaboration with the renowned artist Fionna Carlisle who has been painting and drawing portraits of the LBC research team and participants. Fionna is hoping to organise an exhibition of LBC portraits sometime next year and is also keen to expand her portfolio of LBC1921 portraits. Previous sitters have enjoyed the experience and looked forward tremendously to the

sessions. Please contact Alison if you would like to sit for Fionna.

What Keeps You Sharp?

In October, Dr Alan Gow was invited to speak at the ROAR-Communities for Life AGM in Linwood. His presentation focused on lifestyle factors associated with cognitive ageing. Alan used the 'What keeps You Sharp?' survey from his own lab as the basis for audience discussions, with many LBC examples then being used to explain how certain lifestyle factors might be good (or bad) for the ageing brain.



Presidential Award at the European Stroke Conference

Professor Joanna Wardlaw, Principal Investigator for neuroimaging on the LBC studies, has been honoured with the Presidential Award, at the European Stroke Conference, May 2017, in Prague. Speaking on this international recognition of her contributions to stroke research, Professor Wardlaw said "This award is for all the people who have ever worked together with me to improve the diagnosis, prevention and treatment of cerebrovascular disease. Such improvements rely on collaboration and contributions from many many people, especially those at a risk of, or those who have already suffered, from stroke and its other effects of the brain. It is a great honour to receive the award."

Brain Structural differences between 73- and 92-year olds matched for childhood intelligence, social background, and intracranial volume (*Neurobiology of Aging*)

One recent study, led by Dr Stuart Ritchie and Dr Simon Cox, who a number of you saw at the clinic during the last wave of assessments, used the unique data in the Lothian Birth Cohorts to match participants aged 73 (from LBC1936) and 92 (from LBC1921) who were similar in cognitive ability and social background in early life, and produced a detailed map of brain ageing.

As you know, a unique feature of the members of the Lothian Birth Cohorts of 1921 and 1936 is that they completed the same intelligence test at age 11 (in 1932 and 1947, respectively). Stuart and his colleagues took advantage of this test data by matching LBC1936 participants (at the time aged 73) to LBC1921 participants (aged 92) with similar age-11 intelligence scores, and then comparing their brain health. They made a map of where the largest differences were in the brain in terms of volume, surface area, and cortical thickness, and found that a substantial portion of the cognitive differences between the samples—with the older LBC1921 members scoring lower on a number of cognitive tests—were due to these specific differences in the brain.

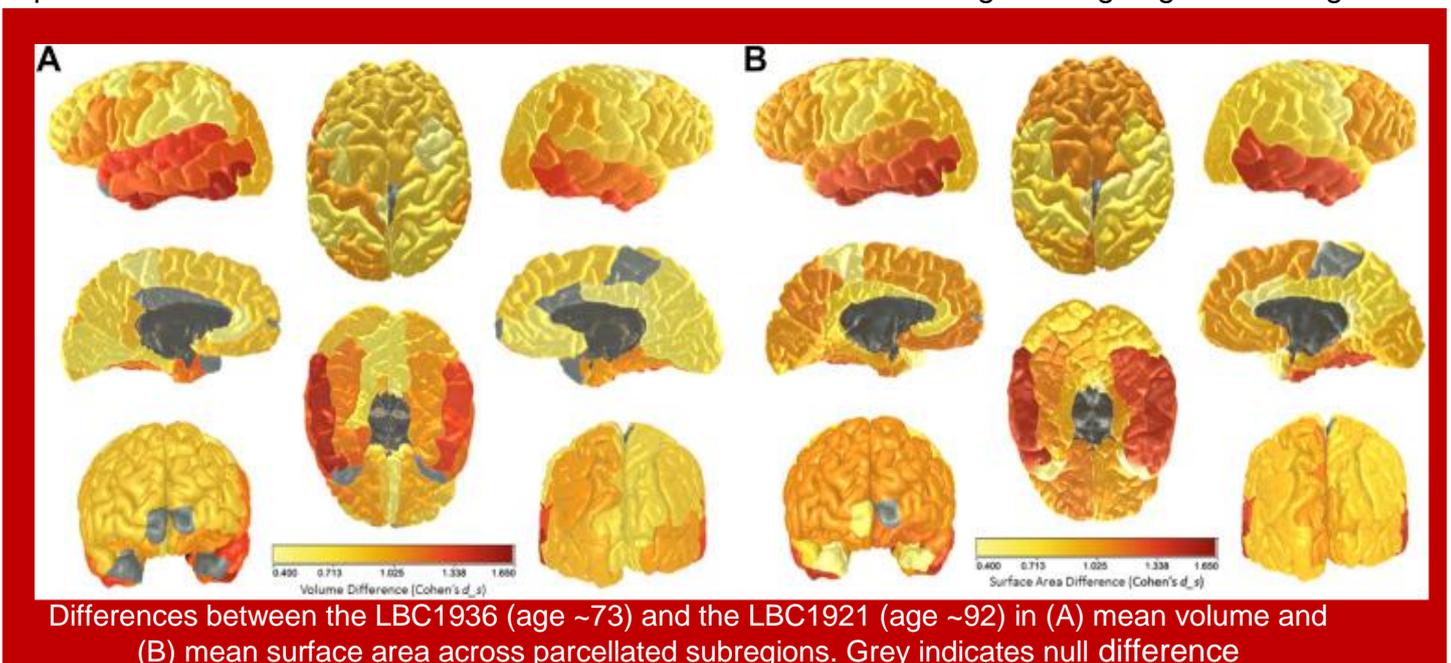
The detailed map of brain ageing produced can be compared to maps from studies of dementia to highlight the differences between normal and pathological ageing. The paper has been accepted by *Neurobiology of Aging* and is currently in press.

Healthy cognitive ageing in the Lothian Birth Cohort studies: marginal gains not magic bullet (*Psychological Medicine*)

In an invited review of almost 20 years of cognitive ageing research from the Lothian Birth Cohorts of 1921 and 1936, Dr Janie Corley and Dr Simon Cox, and Professor Deary, summarised key results from more than 300 Lothian Birth Cohorts studies' publications to date. The paper focussed on reports of cognitive and brain ageing in relation to genetics, early life and demographics, lifestyle and psychosocial factors, health, and biomedical factors.

Some of the key findings from the LBC studies include that individual differences exist in cognitive ageing, such that some individuals will age better and some worse than predicted by their childhood IQ, and individuals with higher childhood intelligence are more likely to be healthier and more cognitively able in older age.

Some factors which may be particularly beneficial for cognitive ageing are: having



particular genetic characteristics, being in good physical condition, being active, being more intelligent in childhood, speaking more than one language, not smoking, and having more education.

Assessing the results in context of one another, and in relation to existing findings from the field, Dr Corley and team concluded that, though there are many associates of cognitive ability *level* in older age, many effects are small, are not independently predictive, and, crucially, few predict cognitive ability *change*. In light of this, they suggest that a useful concept for summarising their findings is that of marginal gains, whereby the small incremental improvements brought about by lifestyle and health-related factors may act cumulatively as an aid to healthy cognitive and brain ageing, but no single factor provides the *magic bullet*. The Scottish Herald covered the review and the LBC reunion in an article which can be read here: http://www.heraldscotland.com/news/15328423.Landmark_ageing_study_marks_70_year_anniversary_with_Edinburgh_reunion/

Identification of a novel locus on chromosome 2q13, which predisposes to clinical vertebral fractures independently of bone density (*Annals of the Rheumatic Diseases*)

Another paper hot off the press by Alonso and others, looked at genetic determinants of susceptibility to clinical vertebral fractures, which is an important complication of osteoporosis. This genome-wide association study included data from the LBC studies and identified a significant association between a marker on chromosome 2 and clinical vertebral fractures in postmenopausal women. This may help us to try and gain new insights into this important and poorly understood clinical problem.

With the data from five waves of the study now available to analyse and publish on, 2017 has been another highly productive year. Some of the most recent publications are listed at the end of the newsletter.

Thank you, again

As a member of the LBC1921 you are furthering our knowledge and understanding of how our thinking skills change over time, and helping to inform others about how to maintain thinking skills along with brain health and a healthy lifestyle. Far beyond that, your data are proving valuable for many aspects of human ageing. Your data are rare and highly valued. We hope you are pleased about how well your generosity in helping with the project has paid off. From all of the LBC1921 research team, we send a big thank you.

Yours sincerely,



Professor Ian J. Deary,
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Mrs Alison Pattie,
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Mr Paul Redmond,
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The LBC Team: Paul Redmond, Alison Pattie and Ian Deary

Would you like to talk to us?



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Some of your publications from this year *In press*

Kraja, A., et al. (in press). New blood pressure associated loci identified in meta-analyses of 475,000 individuals. *Circulation: Cardiovascular Genetics*.

Linner, R. K., et al. (in press). An epigenome-wide association study meta-analysis of educational attainment. *Molecular Psychiatry*.

Liu, S. J., et al. (in press). Exome-wide association study of plasma lipids in >300,000 individuals. *Nature Genetics*.

Ritchie, D. J., et al. (in press). Brain structural differences between 73- and 92-years olds matched for childhood intelligence, social background, and intracranial volume. *Neurobiology of Aging*.

Wain, L. V., et al. (in press). Novel blood pressure locus and gene discovery using GWAS and expression datasets from blood and the kidney. *Hypertension*.

E-published ahead of print

Alonso, N., et al. (2017). Identification of a novel locus on chromosome 2q13, which predisposes to clinical vertebral fractures independently of bone density. *Annals of the Rheumatic Diseases*.

Corley, J., et al. (2017). Healthy cognitive ageing in the Lothian Birth Cohort studies: Marginal gains not magic bullet. *Psychological Medicine*.

Laukka, E. J., et al. (2017). Effects of between-person differences and within-person changes in symptoms of anxiety and depression on older-age cognitive performance. *Psychological Medicine*.

In print

Ben-Avraham, A. J., et al. (2017). The complex genetics of gait speed: genome-wide meta-analysis approach. *Aging*, 9, 209.

De Vries, P. S., et al. (2017). Comparison of HapMap and 1000 Genomes reference panels in a large-scale genome-wide association study. *PLoS One*, 12, e0167742.

Gow, A. J., et al. (2017). Life course activity participation from early, mid and later adulthood as determinants of cognitive ageing: The Lothian

Birth Cohort 1921. *Journal of Gerontology: Psychological Sciences*, 72(1), 25-37.

Hedman, A., et al. (2017). Epigenetic patterns in blood associated with lipid traits predict incident coronary heart disease events and are enriched for results from genome-wide association studies. *Circulation: Cardiovascular Genetics*, 10, e001487.

Li, A., et al. (2017). Identification, replication and characterization of epigenetic remodelling in the aging genome: a cross population analysis. *Scientific Reports* 7, 8183.

Mandaviya, P. R., et al. (2017). Genetically defined elevated homocysteine levels do not result in widespread changes in DNA methylation in leukocytes. *PLoS One*, 12 (10), e0182472.

Marouli, E., et al. (2017). Rare and low- frequency coding variants alter human adult height. *Nature*, 542(7640), 186-190.

Mendelson, M.M., et al. (2017). Association of body mass index with DNA methylation and gene expression in blood cells and relations to cardiometabolic disease: A Mendelian randomization approach. *PloS Medicine*, 14(1),e1002215.

Russ, T. C., et al. (2017). Childhood cognitive ability and incident dementia: follow up of participants in the 1932 Scottish Mental Survey into the tenth decade. *Epidemiology*, 28(3), 361-364.

Shenkin, S. D., et al. (2017). Improving data availability for brain image biobanking in healthy subjects: Practice-based suggestions from an international multidisciplinary working group. *Neuroimage*, 153, 399-409.

Valves Hernandez, M. C., et al. (2017). Metric to quantify white matter damage on brain magnetic resonance images. *Neuroradiology*, 59, 951-962.

**Merry Christmas, and
best wishes for a happy
New Year.**

