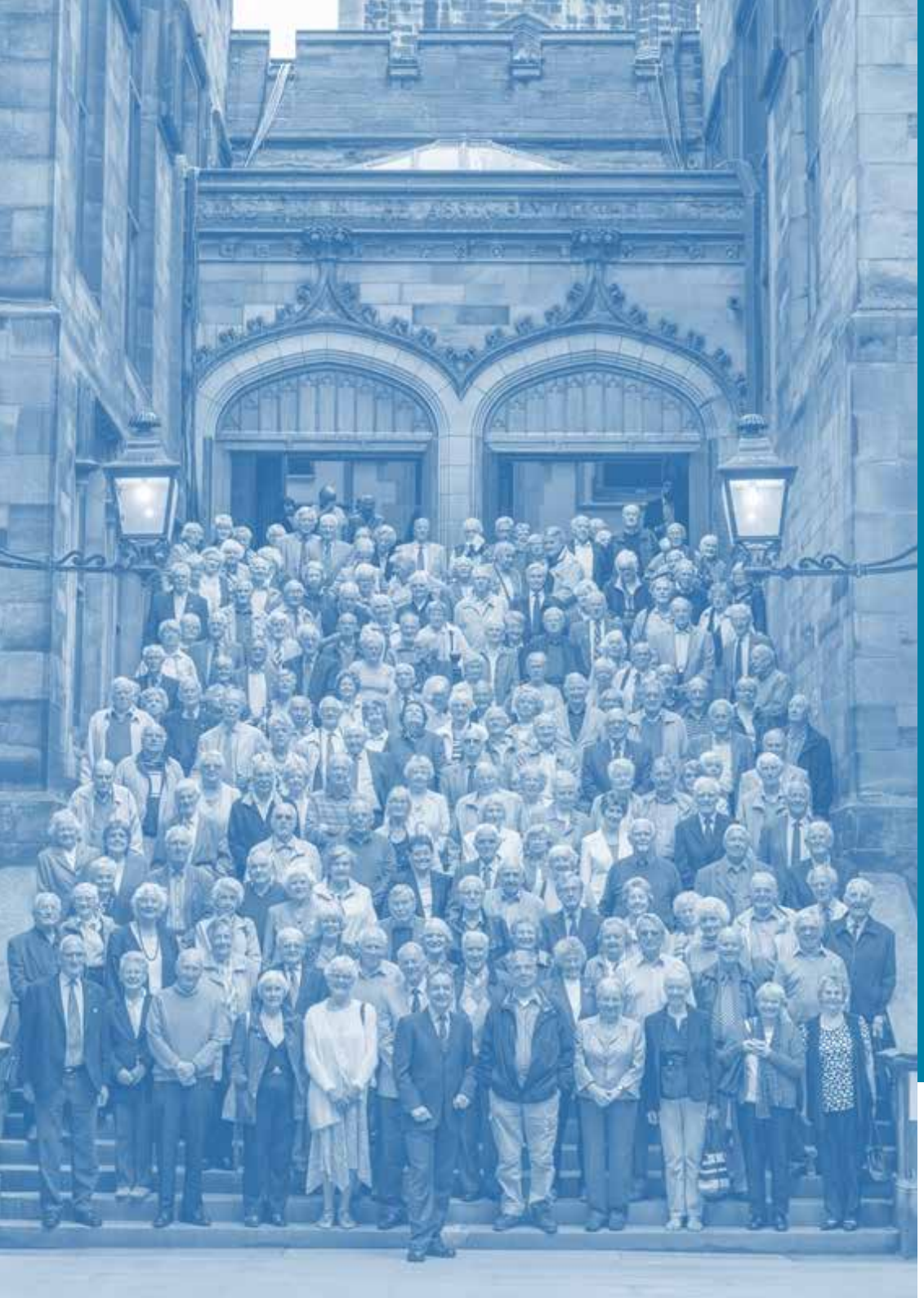
Lothian Birth Cohorts

Celebrating 20 years of research into ageing



Lothian Birth Cohorts

Celebrating 20 years of research into ageing

"The Lothian Birth Cohorts are unusual and extremely valuable groups of participants who permit us to understand the association between early life experiences and late life outcomes of health and disease. Their generous gift of their time and information, and the superb team at Edinburgh that has been able to leverage these data expertly and creatively has resulted in many new insights into brain aging in health and disease."

Professor Sudha Seshadri
Director of Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases
University of Texas Health Sciences Center, San Antonio, Texas, USA

LBC 1921

THE UNIVERSITY of EDINBURGH
Lothian Birth Cohorts

LBC 1936

Introduction: The LBCs at 20

On the 7th September 1999 we tested the first participants of the Lothian Birth Cohorts. On the 7th September 2019, the studies are exactly twenty years old. The main thing I and the LBC research team celebrate is the commitment of our participants. They have done a lot for us. We hope they will do more.

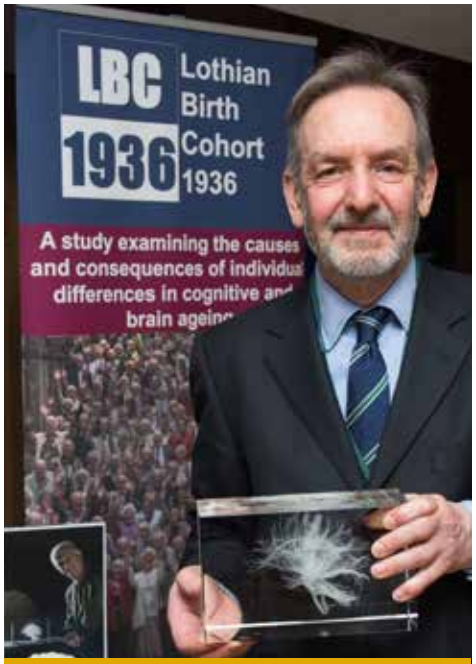
The LBC-ers generously submit to tests, surveys, and examinations, too numerous to mention. They provide data for: several hundreds of research reports; collaborators world-wide; and lots of young scientists' PhDs. They have taught us much about the hows and whys of healthy cognitive and brain ageing. Their data has also proven valuable for understanding many other aspects of ageing, including health, illness, mortality, psychological and social wellbeing, personality, and more.

When we began in 1999, the investigators were me, John Starr, and Lawrence Whalley. The others in the 'team' at that time were just Martha Whiteman and Alison Pattie who, between them, tested all of the original LBC1921-ers. Alison was with us until spring this year, and had worked for over 20 years on the LBCs. LBC1936 began in 2004, and this brought the hiring of more staff, including Janie Corley, who has been with us now for over 15 years.

There has never been core, guaranteed funding for the LBCs. Every few years, I and my co-investigators have to make a case and bid for continued and increased funding. Today, with funding secured up to at least 2022, we have direct funding for the LBCs from Age UK, the Medical Research Council, the USA's National Institutes of Health, and the University of Edinburgh. The investigators are me, Joanna Wardlaw, Tom Russ, Mark Bastin, Simon Cox, and Stuart Ritchie. There are 14 team members employed on this funding, most of whom you will meet in subsequent pages. They are busy running the LBCs, collecting and checking data, analysing data, publishing reports on their new discoveries, providing data for collaborators, and making sure the data are put to practical use.

Ian Deary

Lothian Birth Cohorts' participants at the 2017 reunion, 70 years after the LBC1936 participants sat the Scottish Mental Survey 1947 test.

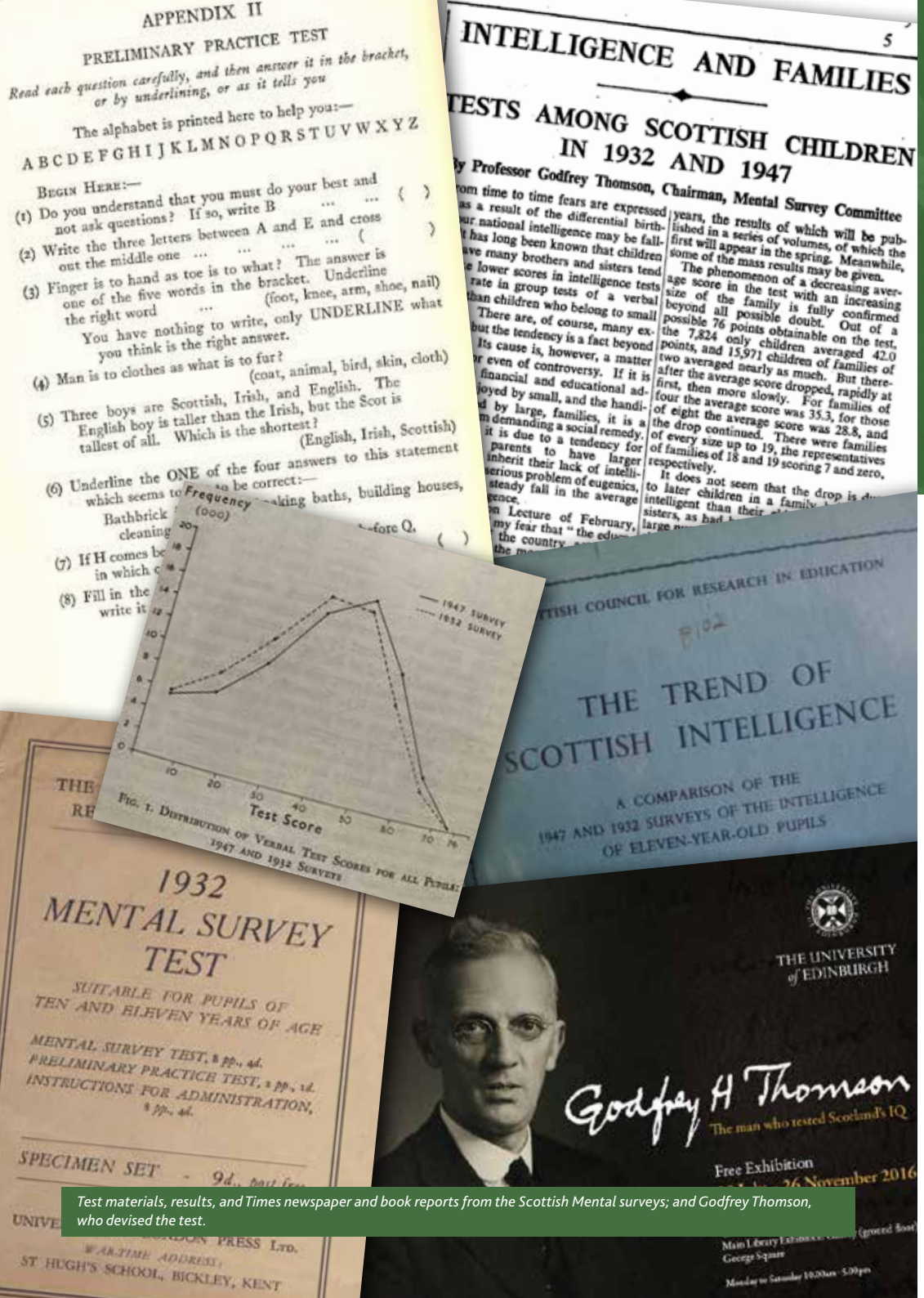


Professor Ian Deary, Director of the Lothian Birth Cohorts.

2001 First Lothian Birth Cohort 1921 reunion.

2017 Lothian Birth Cohort reunion.

The Scottish Mental Surveys of 1932 and 1947



Test materials, results, and Times newspaper and book reports from the Scottish Mental surveys; and Godfrey Thomson, who devised the test.

These Surveys are the foundations of the Lothian Birth Cohorts of 1921 and 1936, respectively. They were conducted by the Scottish Council for Research in Education (SCRE). The intelligence test used was devised by Professor Sir Godfrey Thomson (1881–1955). He was Professor of Education at the University of Edinburgh from 1925-1951. His life's mission was to try to help every child obtain the education that was best for them, irrespective of their background.

The Scottish Mental Survey 1932. On the 1st of June 1932 almost every child born in 1921 and attending Scottish schools sat Godfrey Thomson's Moray House Test of general intelligence. It tested 87,498 children. The aim was to examine whether intelligence testing could help with the, "problems of curricula, school equipment, and teaching technique".

The Scottish Mental Survey 1947. On the 4th of June 1947 almost every child born in 1936 and attending Scottish schools sat the same Moray House Test. It tested 70,805 children. Godfrey Thomson was the Survey's Chairman. Its Preface begins, "The inquiry reported in this volume was begun in the hope that it might throw light on the causes of a remarkable quantitative social fact, namely, that the results of intelligence tests show that the average scores of members of large families is less than that of members of small families. It was feared that this might be leading to a steady fall in the national intelligence…" The result: It wasn't.

The Surveys were once world famous. They became obscure. In 1997 Professor Lawrence Whalley and I found out about the Surveys. The data were held confidentially by the SCRE. We thought: if we trace, recruit, and re-test some of the participants, they could make a rare and valuable contribution to understanding how thinking skills change across the life course. We applied for research funding. The Lothian Birth Cohorts were conceived.

Ian Deary

10 reasons to love the Lothian Birth Cohorts

The Lothian Birth Cohorts of 1921 and 1936 began in 1999 (age 79 years) and 2004 (age 70), respectively. LBC1921 had 550 people to begin with, and LBC1936 had 1091 people.

The LBCs' history and data are described here: edin.ac/2P77GmR
Taylor (2018) International Journal of Epidemiology, 47, pp 1042-1042r.

A summary of our hundreds of research reports is here: edin.ac/2PbOjsW
Corley (2018) Psychological Medicine, 48, pp 187-207.

One of the world's top journals, Science, wrote a feature on the LBCs, here: edin.ac/2PbPdWm
Underwood (2014) Science, 346, pp 568-571.

Here are our top reasons to love the LBCs.

Lothian Birth Cohorts' participants at the 2007 reunion.

1.

Almost all of the LBC participants have intelligence test scores at age 11. This means that we can study factors that relate to 'lifetime' cognitive ageing, which is rare.

2.

The LBC1921 is the longest follow-up study of cognitive ageing in the world.

LBC1936 participants at the 2007 reunion with their 1947 school class photograph.

3.

The LBC cognitive test battery is one of the most extensive carried out on an ageing cohort.

4.

Most of the LBC1936 participants have repeated brain scans, which offers a rare and large-scale opportunity to track the age-related changes in their brains and to find causes and consequences of people's differences in brain ageing.

5.

Almost every 1921-er and 1936-er has been 'whole-genome-sequenced'; each person's 3 billion DNA bases are known. They were the first large cohorts in the world to have this done.

6.

Many LBC1936 participants signed up to provide post-mortem brain tissue. This is valuable to scientists looking at how brain cells relate to lifetime cognitive and brain scan data.

The Herald describing the beginnings of the Lothian Birth Cohort 1936 study in 2007; actor Richard Wilson sat the 1947 test.

7.

The LBC1936-ers provided blood samples for stem cell production, which can be converted into brain and other types of cells for investigation.

8.

The LBC-ers are world famous in science, and more generally. They appear on TV and radio, and in the newspapers. They and their data influence policy-makers on ageing.

9.

The LBCs have inspired artists as well as scientists. There is a book, a film, a play, a photo/video exhibition, and an exhibition of portraits about them.

10.

The LBCs have been the training ground for many young scientists, many of whom are now professors and senior academics in the UK and abroad.

Ian Deary

Lothian Birth Cohorts' Data

After 20 years, the LBC1921 and LBC1936 studies have completed 5 'waves' of attendance. The data, collected at each wave, can be classified as Phenotypic, Imaging, and Genetics.

Phenotypic

The phenotypic data are the observable traits, such as scores from cognitive tests, measurements from blood samples, answers in questionnaires, and individual physical attributes such as height, weight and grip strength. At each wave, participants spend several hours, one-on-one, and with breaks, with the LBC testing team. During each attendance, at least 400 items are collected: around 200 from cognitive scores, 50 from the physical exam, 50-100 blood test results are obtained, and another 100+ items on demographics and health. For a participant who attended all 5 waves, this would account for around 2000 items, although the actual number is much higher due to other sources such as the questionnaires and imaging.

Imaging data

We have collected brain scans since wave 2 of the LBC1936. Each scan produces hundreds of images which are used to calculate further data, including volumes of brain regions, and measures of brain white matter health. We have Doppler-scanned the carotid arteries, and we have taken retinal photographs to measure the eyes' blood vessels.

Genetics and epigenetics

Genetics and epigenetics data are obtained from blood samples donated at the clinic visits. We use the data for home research and to participate nationally and internationally in numerous genome-wide association studies and epigenetic analyses. We used to count the genetics data in millions of points; whole genome sequencing boosted that to billions per person.

Processing imaging and genetics data

Genetics samples undergo analysis and sequencing to generate some of the largest datasets held in Edinburgh, if not the UK. These complex and intensive analyses are carried out on our in-house, LBC-dedicated computer cluster, including our main processing workstation ("Mons Meg"), the largest single workstation within the University. Brain scans are processed to generate some of the most in-depth brain mapping data available internationally. We are leading in 3D data visualisation, and generating holograms showing changes in brain structure and function.

Paul Redmond, Adele Taylor, Danielle Page, and David Liewald

Some of the many types of data collected in the Lothian Birth Cohorts.

Ledgers containing childhood test scores from the Scottish Mental Surveys, used in the Lothian Birth Cohorts.

Part of the LBCs' giant computer cluster, including 'Mons Meg'.

LBC1936 participant taking a spatial ability test.

Lothian Birth Cohorts' cognitive tests

The Lothian Birth Cohorts are world-famous for many things, but the top of the list is their cognitive tests. They have been tested repeatedly in later life on a large range of mental abilities – their reasoning skills, their memory, their speed, and their knowledge – but the LBCs have a jewel in their crown: intelligence test scores from age 11.

The first question that comes to mind when you have cognitive scores from both early and later life is: "are the smartest people as children still the smartest in later life?" The answer is: to a large extent, yes. People who tended to be at the top in school were much more likely to be at the top in older age; but, also, there was a lot of movement. We try to find why some people move up or down in the cognitive rankings across their lives.

Since the Lothian Birth Cohort participants have been tested multiple times, we can also chart the trajectories of their cognitive skills within older age. Because they've been tested on so many different abilities, we can compare which tests change the most, and the least.

Some abilities are well-preserved, on average: tests of vocabulary knowledge are very stable across the years. However, participants' reasoning skills tend to decline, and their so-called 'processing speed' drops off even more steeply. We know that performance on these tests matters: it's related to real-world abilities like reading medicine labels, sorting out finances, and driving. Importantly, some people's cognitive declines are steeper than others.

The work that we have done so far suggests that there is no magic bullet; it appears that 'healthy' cognitive functioning is the result of an accumulation of many different influences across the life course, including: genetics; education; health and lifestyle; and psychosocial factors. But, while many of these things are related to one's level of cognitive ability, we are still investigating which factors reliably lead to cognitive change over time.

Understanding these differences in later-life cognitive ageing is a top priority of the LBCs. Can we uncover the parts of the brain that are most important for cognitive ageing? What about the lifestyle choices that might help us hold on to our thinking skills? Or the genetic factors that might predispose us to healthier ageing? With so much detailed cognitive data, there are no better studies for answering these questions.

Stuart Ritchie

Lothian Birth Cohorts' Brain Imaging

LBC1936 participant having an MRI brain scan at age 82 years.

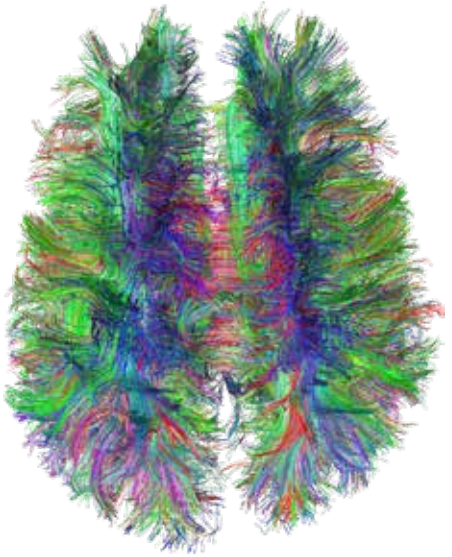
Our brain supports our thinking skills, which we hope will stay as sharp as possible as we grow older. Many LBC participants undergo a detailed brain scan to help us understand the relative importance of many facets of this vastly intricate organ. Knowing which aspects of brain ageing are important for which aspects of cognitive ageing and general health can offer unique insights into the ageing process. For example, if we discover a lifestyle or genetic association with brain connectivity only, and specifically on connections important for memory function, it focuses subsequent lines of enquiry on why this factor might exert tissue-specific effects (why white matter, but not grey?), and why only in certain parts of the brain.

Brain structure is well known to show decline ('atrophy') with advancing years. We have found that the degree of the brain's structural decline with age is highly variable between LBC1936 individuals. We discovered that even though our participants have approximately the same chronological age, some brains look younger or older than their time since birth. People who had younger 'brain ages' tended to have better physical functioning and cognitive functioning, and to live longer.

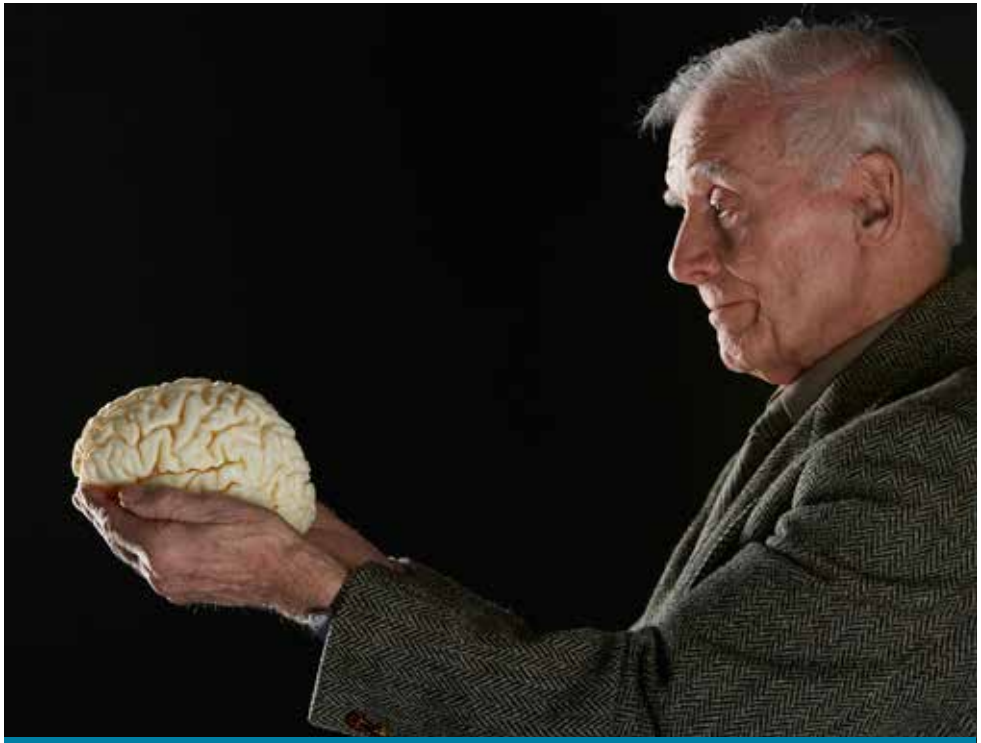
We identified specific areas of the LBC1936's brains' grey matter that are related to better lifetime cognitive ageing, and to a variety of possibly causal factors. Those who showed less relative decline in cognitive function between age 11 and later life showed less damage to their brain connections ('white matter') and less overall atrophy; this was strongest in brain areas related to more complex thinking skills. Some areas of the brain's grey matter are thinner with cigarette smoking; these are, again, regions mainly linked to more complex thinking skills.

Our ongoing work focuses on much more detailed evaluations of the brain's structure, including a measure of the brain's 'connectome'. This detailed approach maps the collective wiring of many trillions of nerve fibres across the brain as a network, and allows us to identify complex patterns of structural connectivity. These new methods offer even greater insights into how the brain ages, how different sub-networks are important for different thinking skills, and how they may be susceptible to different lifestyle and genetic factors.

Simon Cox, Susana Muñoz Maniega, and Colin Buchanan



One person's white matter pathways from the MRI brain scan.



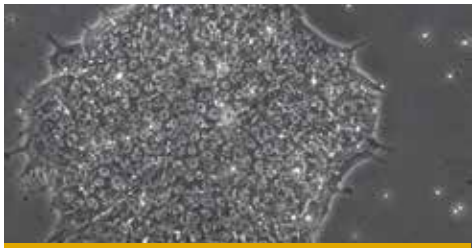
LBC1936 participant holding a 3D printed copy of their brain.

Lothian Birth Cohorts' Genetics, Epigenetics, and other 'Omics'

Blood being drawn from LBC1936 participant.

Loading the last samples at the Roslin Institute to complete the LBCs' whole genome sequencing.

LBCs' blood plasma samples.



Induced pluripotent stem cells (iPSCs) from LBC participant.


SCOTTISH DAILY EXPRESS
FREE KITE
FREE CHURCHILL DVD
FREE INSIDE Weight Watchers RECIPE CARD
FOUND: KEY TO LONGER LIFE
Andy's girl gets death threats

LBCs are first to find that people with a younger 'epigenetic clock' live longer.


Half your intelligence (or lack of it) is genetic
The rest is down to your education and how you use it

LBCs are first to use DNA to estimate genetic and environmental contributions to cognitive function.

Genes influence how well individual brains and bodies age. Twenty years ago twin studies told us that approximately 50% of the differences in cognitive ability was due to inherited genetic influences, but we knew little about which genetic variants were involved. Using genome-wide genetic data from the LBCs and others, we found that thousands of genetic variants, spread throughout the genome, influence life-long cognitive function and cognitive ageing. Many of these genetic variants influence health. The *APOE* gene that influences susceptibility to Alzheimer's disease also influences the amount of age-related cognitive decline in the LBCs, in the absence of dementia. In the LBCs, we showed that approximately 24% of people's differences in cognitive ageing is due to common genetic variation. We are currently running the world's largest study to identify specific genetic variants associated with cognitive ageing. With whole-genome sequencing data in the LBCs we investigate rare variants associated with cognitive ageing.

We have measured epigenetic markers in the LBC. These are non-DNA-sequence changes that influence gene expression. Epigenetic markers are influenced by genetic and environmental factors, and change as we age. The LBCs' data were the first in the world to show that people with an older 'epigenetic clock' tended to have poorer cognitive ability and die younger than those with a younger 'epigenetic clock'.

We have contributed genetic and epigenetic data from the LBC to over 20 international consortia studying the genetic contributions to numerous age-related and other phenotypes.

We have generated induced pluripotent stem (IPS) cells from the blood of some LBC participants. IPS cells can be converted into any cell type including brain cells and we will be using them to study 'brain ageing in a dish' in the laboratory.

In the LBCs we are investigating how levels of the following change with age, and relate to cognitive and brain ageing: gene expression for more than 1000 genes (transcriptomics); hundreds of proteins (proteomics); and hundreds of lipids (lipidomics). By combining genetics, epigenetics, and other 'omics we hope to identify biological pathways altered during the ageing process. This might help those seeking targets for medical intervention to alleviate the detrimental effects of ageing.

Sarah Harris, Gail Davies, and David Hill

Lothian Birth Cohorts' Lifestyle and Health

A wide range of lifestyle and health factors have been suggested that may boost thinking skills in older age, or buffer cognitive ageing. It is important to study these factors, as many of them might be modifiable by individuals, and therefore they are potential targets for those planning interventions to help ameliorate cognitive ageing.

In the LBCs, we found that being physically active, avoiding daytime naps, and not smoking or quitting smoking, are related to healthy cognitive function, albeit in small ways. Being physically fit and healthy, measured by things like walking speed, lung function, and grip strength, are related to better cognitive function in later life, even when taking into account age 11 IQ, sex, social class, and genetics.

Other factors turn out to be not directly protective once cognitive ability from age 11 is accounted for; these include moderate alcohol intake, moderate caffeine intake, lower body mass index, a healthy diet, a healthy cholesterol profile, and doing intellectual activities. These latter findings suggest that people who have higher intelligence in youth make healthier lifestyle choices, and have better health and cognitive functioning later in life.

We found that certain psychosocial factors from across the life-course are related to cognitive efficiency. These include more years of education, being bilingual, a complex occupation, having more social support, and being less lonely. Depressive symptoms were not related to cognitive changes; rather, those who experienced cognitive decline were at a higher risk for depression.

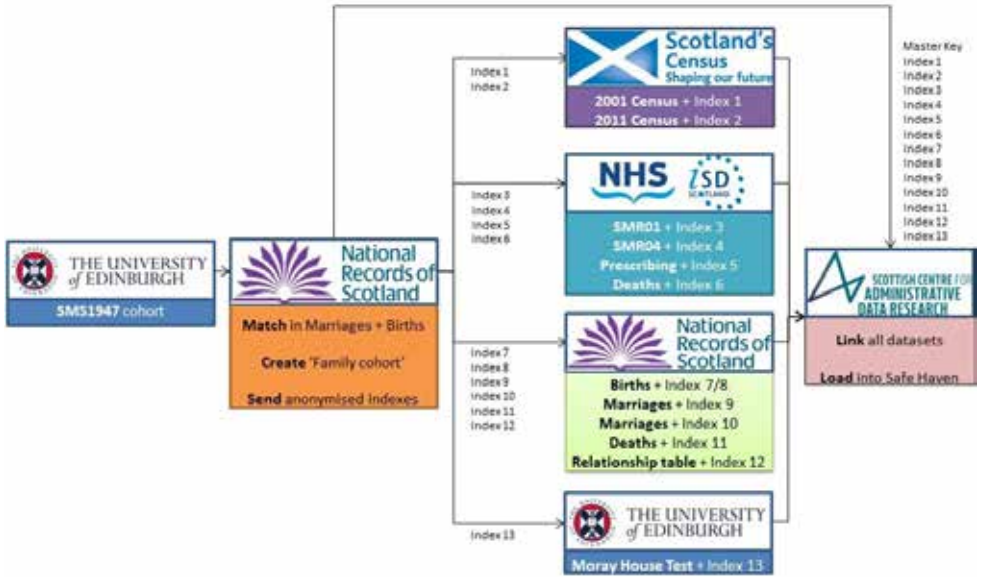
Now, we are examining how diet, financial capacity, and musical experience relate to life-long mental abilities. Our future plans include more long-term analyses of the lifestyle data, and how particular nutrients such as vitamin D, and biological processes such as chronic inflammation, relate to cognitive ageing. We will examine how life-long interactions between genetic make-up and environmental factors, influencing, for example, how our bodies' metabolism of alcohol or blood-glucose control, relate to cognitive and brain ageing.

Janie Corley and Judy Okely

Keeping active, at the 2017 LBCs' reunion.

Measuring height in a LBC1936 participant.

Measuring grip strength in a LBC1936 participant.



Plan for anonymous and secure data linkage for health research, including the Scottish Mental Surveys.

Scottish Mental Survey 1947 ledgers.

Linkage Studies

On the 4th of June 1947, almost all 11-year old children living in Scotland took part in the Scottish Mental Survey 1947 (SMS1947 ledgers pictured overleaf). Some of us in the team follow-up most of these 70,000+ SMS1947 individuals and their lives by anonymously linking together routinely-collected national records, such as NHS health records and Census records. We look at what sort of circumstances they lived in as children, whether they're still alive, whether they've been to hospital, whether they're in good health in older age, and more.

Although not as detailed as the Lothian Birth Cohort studies, following up all of the participants of the SMS1947 remotely means that we have reconstructed the life-courses of some 68,000 individuals, including those who don't typically volunteer for research studies.

Linkage of routinely-collected records involves data from lots of different organisations, each of which has its own procedure. Great care is taken to ensure that the privacy and anonymity of individuals is maintained. Identifying information such as names and addresses are removed before records are seen by researchers; data can only be accessed from within a specially-designed, secure and monitored room.

We've used data linkage to identify early-life risk factors contributing to poor health and wellbeing: e.g. childhood deprivation, education, and family circumstances. Children with good thinking skills tend to live healthier, longer lives and to be able to work in later life. This advantage is separate to the benefits of growing up in a wealthy household or spending a longer time in education. We're now examining how early-life circumstances might predict recovery from stroke, the need for long-term care in older age, and the risk of mental ill-health across the life course.

By investigating the lasting impact of childhood circumstances on health and wellbeing we hope to better predict problems before they arise and to help support healthy ageing.

Matthew Iveson and Drew Altschul

Knowledge Exchange and Impact

The project and its people have drawn the attention of the public, inspired artists, and established a firm presence on various communication outlets. We hear about the LBCs on the radio, on TV, and when we visit museums, science festivals, and art exhibitions.

Let's highlight just a few of the public events showcasing the LBCs. The LBC1936 study was featured on the BBC1 *Breakfast* show. Stories of both LBCs were captured in *Lifetimes*, a book by Ann Lingard. They were the subject of Anne Milne's film, *The Living Brain*. They were the subject of a successful play – *Still Life Dreaming* – at the Edinburgh Festival Fringe. They were the subject of the *Transformations* photograph and video exhibition by Linda Kosiewicz Fleming. They are on permanent display at the National Museum of Scotland (edin.ac/2P8dxs0). The LBCs were on the BBC series *How to Stay Young*. There are more newspaper, radio, and TV appearances than we can name.

LBC portraits, by Fionna Carlisle, formed the major *The Art of Intelligent Ageing* exhibition in 2018, and they will be on display in October 2019 at the Scottish Parliament's *Festival of Politics*. BBC Radio Scotland have a special episode of *Brainwaves* about the LBCs as the participants and researchers gather for a 20th anniversary reunion in September 2019.

Lewis MacDonald MSP views a LBC1936 participant's brain white matter connections etched in crystal.

LBC1936 participant, with portrait by Fionna Carlisle, at the Art of Intelligent Ageing exhibition.

BBC presenter Bill Turnbull and LBC1936 participants at filming for BBC1's 'Holding Back the Years'.

Our partnership with Age UK is essential for translating LBCs' findings to wider audiences. Through a co-produced impact plan, Age UK have helped to disseminate the LBCs findings to: older people and older people's groups; families and carers of older people; health and social care practitioners and policy makers; and other members of the general public. In 2017 Age UK launched the Staying Sharp web-pages (edin.ac/2MWQwU6). Based on LBCs' findings, these pages give top tips for staying sharp in later life and include a short animation of Ian Deary acting them out, watch here: edin.ac/2P9g7OG

The LBCs' story – reconnecting near-forgotten school tests of 11-year-old Scottish children with their grown-up versions decades later – is compelling. The impact of the findings on the public is undeniable. What resonates and inspires us all is the commitment and dedication of the participants to help scientists uncover secrets of healthy ageing for the benefits of future generations.

Barbora Skarabela

LBC team member explains DNA methylation game at Edinburgh International Science Festival 2018.

Artwork from the 'Transformations' video and photography exhibition held in 2010.

Words from a few of the LBCs' University of Edinburgh collaborators

"I would like to affirm again how immensely useful the Lothian Birth Cohorts have been for our work in cancer genetics. The genotyping and sequencing data has allowed us to compare large numbers of cases with the controls from LBC and thereby allowed us to discover over 100 genetic variants that are associated with risk of cancer of the large bowel (a common cancer in the Scottish population). Because you have generated such excellent data, we can predict gene expression in LBC participants from genetic models developed in subjects in whom we have sequenced the lining of normal bowel in an approach called TWAS. This then leads us to the actual gene that we believe is causing cancer. We can then look at ways of mitigating the effects of defects in this gene expression in new treatment for bowel cancer and potentially other cancers. Many thanks indeed to the participants and to Professor Deary and his team for making the data available to such a wide community of scientists."

Malcolm Dunlop
Professor and Group Leader
Colon Cancer Genetics Group, Institute of Genetics and Molecular Medicine

"We are interested to know how and why the places we live throughout our lives matter for our health later in life. By bringing together data from the LBC1936 alongside geographical information over the past 80 years we have for the first time been able to examine how our local environments in childhood and mid-life life affect health outcomes (such as cognitive ageing and mental health) later in life. We greatly appreciate working with the LBC1936 members."

Jamie Pearce
Professor of Health Geography
and
Catharine Ward Thompson
Professor of Landscape Architecture

"The Lothian Birth Cohorts have been particularly valuable for the investigation of factors related to mental wellbeing, where it has been possible to map out how these effects emerge over the full life course. There are other birth cohort studies, but it is the length and depth of the LBCs that makes them an unsurpassed resource for mental health research."

Professor Andrew McIntosh
Department of Psychiatry

"Our group collaborates with the LBCs to find why some people's brains are more resistant to age-related degeneration and Alzheimer's disease pathology. We use small post-mortem brain samples generously donated by LBC participants and their families. These samples are used to study synapses, the tiny connections between brain cells. We are looking at whether preservation of these synaptic connections is associated with better cognitive skills in ageing and protection from Alzheimer's disease. The LBC samples are particularly valuable because we can examine whether the changes we see are truly age-associated or whether they can be explained by childhood cognitive ability. Many thanks to all of you for your participation in these important studies!"

Professor Tara Spires-Jones
Deputy Director, Centre for Discovery Brain Sciences
UK Dementia Research Institute Programme Lead

"It's hard to emphasise how appreciative we are that the participants keep coming back and donating health information and, in particular blood samples! My group are particularly interested in DNA and chemical additions to DNA that can be added and removed over time and are a partial archive of your life history, e.g. if you smoked and how much you smoked! LBC has the best characterised set of these data between the ages 70-90. The LBCs lets us find out how people change and how this relates to healthy ageing."

Riccardo Marioni
Centre for Genomic and Experimental Medicine

"I am thrilled to be working with LBC participants as we begin to investigate the possible benefits of musical engagement across the lifespan. This is an extremely rare research opportunity and I look forward very much to the insights it will bring to the field."

Dr Katie Overy,
Director, Institute for Music in Human and Social Development (IMHSD)

Words from a few of the LBCs' UK collaborators

"The LBC data and Prof Deary's team have proven invaluable for our research on retinal biomarkers for systemic conditions and cognitive decline. VAMPIRE project team is delighted to count LBCs among our top collaborators."

Professor Emanuele Trucco
NRP Chair of Computational Vision, Computing, School of Science and Engineering
University of Dundee

"It's been a privilege to collaborate with the University of Edinburgh to work with the invaluable LBC1936 dataset. The unique data available in the LBC1936 means that we've been able to test how brain ageing relates to epigenetic ageing, physiological ageing and cognitive ageing, providing new insights into the complexity of the ageing process. There are no other datasets with this rich combination of information, which underscores the importance of the LBCs for present and future research into ageing."

Dr James H. Cole
Department of Neuroimaging, Institute of Psychiatry, Psychology & Neuroscience
King's College London

"Working with the LBC participants for our work on sedentary behaviour within the 'Seniors USP – Understanding sedentary patterns' was not only an enjoyable experience for the research associates involved in data collection, but has led to new knowledge on associations between prolonged sitting and health (physical, mental and social). So far, 10 research papers have been published with at least 3 more in progress. Continued collaboration with the LBC1936 means we can look further than associations into potential predictors of health based on activity behaviour. Importantly, this collaboration has helped shape future research into sedentary behaviour by publishing recommendations on the most accurate and reliable way to ask people about sitting time in large national health surveys, how much change in sitting time would denote a meaningful change, and recommendations on how to develop sedentary behaviour interventions that resonate with older people and will have the best chance of changing behaviour. More than a thousand researchers and health professionals have watched videos and taken part in seminars and workshops covering methods of collecting accurate and useable research data on the views and experiences of older people on sitting and when/how they might be willing to change behaviour. We have produced an 'Intervention Manual' for researchers wanting to develop future intervention studies which has been downloaded over 300 times. So far we are aware that our recommendations for the most sensitive and accurate sedentary behaviour questions have been taken up by 6 organisations/ research trials/service level data. They have recently been recommended by the Surveillance and Communication Panel of experts, as part of the update of the Chief Medical Officers Physical Activity Guidelines for Health, to be used in National Health Surveys. Importantly the work with the cohort has led to more funded studies which have allowed the creation of education leaflets for the public and moving on to studies on ways in which we can help older people reduce sitting time or break up long periods of sitting regularly."

Dawn Skelton
Professor of Ageing and Health, School of Health and Life Sciences
Glasgow Caledonian University

Words from a few of the LBC's international collaborators

"The LBCs have been a fantastic group to collaborate with for large scale international genetic studies aimed at deciphering the mechanisms of brain aging. The richness of investigations conducted with very high quality assessments and also the homogeneity of the study populations in terms of geographical origin and age are remarkably helpful. Having the Cohorts and the outstanding scientists leading LBC derived research on board of our European JPND project and of many other international collaborative research projects within the CHARGE consortium has been a fabulous asset, and many high profile projects have been spearheaded and published a the highest level under the leadership of LBC investigators."

Professor Stephanie Debette
Inserm center U1219, Department of Neurology, Bordeaux
University Hospital
University of Bordeaux, France

"The Lothian Birth Cohorts and DNA methylation data are a very useful resource for us to explore the aging epigenome in the older population. We are very thankful to your excellent supports and guidance in our joint effort in mining the highly valuable data and enjoy the success we have achieved together. Cheers!"

Professor Qihua Tan
Department of Public Health
University of Southern Denmark

"Participants in the Lothian Birth Cohort studies provide some of the most unique and important data in the world for understanding the specific patterns of brain aging that are linked with impairments in memory and other thinking abilities that arise with age. I am very fortunate to be collaborating closely with researchers at the University of Edinburgh to analyze data from the LBCs to gain important insights into cognitive aging."

Elliot M. Tucker-Drob, Ph.D.
Associate Professor
Department of Psychology, Population Research Center
The University of Texas at Austin, USA

"We have had the privilege and pleasure of working with Ian Deary and the Team in Edinburgh on a large number of research questions for which the Lothian Birth Cohorts have been a unique, valuable and essential resource.

A decade ago, we were quick to apply our newly developed statistical methods to genome-wide genetic data from the Lothian Birth Cohorts and showed that many genes contribute to intelligence (Davies et al. 2011, Molecular Psychiatry) and that cognitive function in childhood and old age are genetically correlated (Deary et al. 2012, Nature).

When a new genomics technology became available to measure DNA modifications (called methylation) in the genome that are associated with gene expression, we appreciated the advantage of birth cohorts to study the genetic control of DNA methylation, how it interacts with the environment and changes with age. We therefore provided seed funding to facilitate methylation profiling of the entire Lothian Birth Cohorts and this collaborative investment was handsomely repaid in a number of important discoveries. For example, we discovered that stability of methylation profiles across age in LBC participants is mostly due to genetic factors (Shah et al. 2014, Genome Research), and reported that methylation profiles are associated with subsequent mortality (Marioni et al. 2015, Genome Biology).

We wish all the LBC participants a happy 20-year anniversary. We would like to thank all participants for their generous contribution to scientific research. The Lothian Birth Cohorts are recognised worldwide as an important and unique research resource, particularly because of the comprehensive data collected longitudinally. We are confident that more important discoveries in medical, cognitive and ageing sciences will continue to be made in the next decade and beyond."

Peter Visscher, Naomi Wray, Jian Yang and Allan McRae
Program in Complex Trait Genomics, The University of Queensland, Australia

"The LBC of 1936 was among the most important and rich cohorts that I have had the opportunity to study in my career to date. This cohort was unique in having cognitive ability data from childhood and cognitive and brain data in older age. It allowed me to examine how cognitive ability in childhood accounted for brain and cognitive ability relationships more than 60 years later."

Dr Sherif Karama
Department of Psychiatry
McGill University, Canada

Professor James Watson – of 'Watson and Crick', who discovered the structure of DNA in 1953 – has made two whole-day visits over the last decade specifically to discuss the Lothian Birth Cohorts' results with the LBC research team.

Acknowledgments

We thank the participants of the Lothian Birth Cohorts.

We thank the present and past members of the Lothian Birth Cohorts research team.

We thank the staff at the Wellcome Trust Clinical Research Facility, Western General Hospital, Edinburgh.

We thank all the Brain Imaging staff at Edinburgh Imaging, and carotid Doppler imaging staff.

We thank our many collaborators in Edinburgh, the UK, and internationally.

We thank present and past funders of the Lothian Birth Cohorts.

We end by noting the sad loss of Professor John Starr at the end of 2018. He was the LBCs' 'research medic' from the start, and a close collaborator and friend to Ian Deary for over 20 years. We at the LBCs and our collaborators remember him fondly. See an appreciation of his life and works, here: edin.ac/2P9eT61

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