

Welcome to the Lothian Birth Cohorts (LBC) 2021 newsletter. The LBC team have been as busy as ever, and we want to take this opportunity to let you know about some of the things we've been up to this year. In this newsletter, we will update you on the latest study developments, our research and publications, and some scientific and public engagement events we've been involved in. It goes without saying that none of this would be possible without you; thank you for your continued involvement and support with the LBC studies. We hope you have a very happy festive season, and wish you and your loved ones all the best for 2022.

If you would like to get in touch, you will find our contact details on page 7 of this newsletter. Please let us know if any of your contact details have changed, or are about to, so we can update our records. We are always delighted to hear from you.

## Wave 6 of the LBC1936 study begins

It is an absolute pleasure to report that in October, we began the 6<sup>th</sup> wave of data collection with the LBC1936 cohort. Unfortunately, the pandemic put an 18 month hold on our plans to begin testing, so it is fantastic that we are now back at the Wellcome Trust Clinical Research Facility (WTCRF), seeing the first LBC1936 participants.



*An image of the first LBC1936 participant, Mrs Morrison, taking part in cognitive tests at wave 6; October 2021*



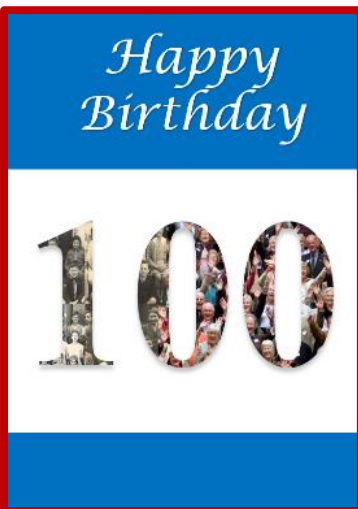
*LBC1936 participant Mrs Morrison with radiographers Maddy and Isla, taking part in the first MRI brain scan in October 2021*

We hope to see about 350 of you in total at mean age 86, and will be asking you to take part in some familiar thinking and memory tests and answer questions about your health and lifestyle. There will also be the option of having another brain scan. New to this wave, we are working closely with colleagues in the Alzheimer Scotland Dementia Research Centre (ASDRC), directed by Dr Tom Russ, one of the medics for the LBC studies. Tom's team are examining health records to determine important health outcomes in LBC1936 participants, including dementia diagnoses. This will be an invaluable resource for researchers trying to determine factors related to the development of dementia and other ageing-related outcomes.

At the time of sending you this newsletter in early December, 40 participants have attended a cognitive appointment at the WTCRF, and 14 have returned for an MRI brain scan at the new scanning facility at Edinburgh Imaging Facility (EIF), Royal Infirmary of Edinburgh. We're blown away by how keen everyone has been to come back for Wave 6, and we are all delighted to see you. The value of your generous contributions to the study only continues to grow each time we see you, and the data we collect holds tremendous promise for making important scientific discoveries in the coming years. We look forward to seeing many more of you in 2022 and beyond.

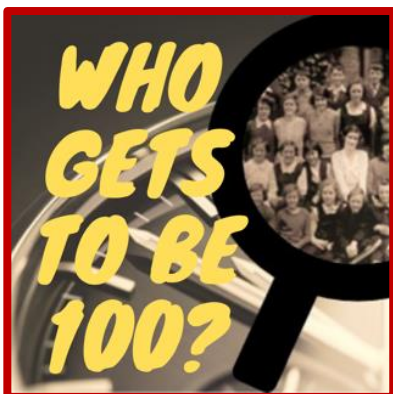
## A century of the LBC1921

This year marks an amazing milestone for our LBC1921 cohort, as they celebrate their 100<sup>th</sup> birthdays. We want to wish all of our cohort members a very happy birthday. Living to the age of 100 is a remarkable and rare achievement, and during 2021, study director Dr Simon Cox has been sending hand-written birthday messages to all of those in the cohort who are celebrating this marvellous milestone.



The LBC1921 study was established by Professor Ian Deary and the late Professor John Starr in 1998. At the time, 550 members of the cohort underwent cognitive and physical testing at mean age 79 years. Participants returned at up to four further occasions, with 59 participants tested at age 92 in the fifth and final wave of LBC1921 testing. Although data collection was completed in 2013, like their younger sister-cohort LBC1936, the LBC1921 have provided a lasting treasure-trove of data, which continues to contribute to scientific discoveries, particularly those focused on the genetics and epigenetics of ageing, up to the current day.

As well as the birthday cards, we marked this wonderful event in a podcast. We invited two of the LBC1921 to take part, and spoke to them about their upbringing, their experience of being involved in the LBC1921 study, and how they feel about reaching the age of 100. We also heard about how their contributions have helped us understand how to stay sharp in older age, from Founding Director Professor Ian Deary, study geneticist Dr Sarah Harris and current Director Dr Simon Cox. You can listen to the podcast on our website (web address on page 7).



## Welcome back, Mrs Alison Pattie!

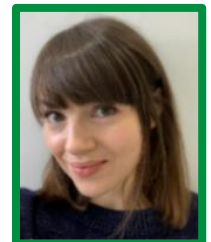


In September, we were thrilled to welcome back Mrs Alison Pattie to the LBC study team. Alison started her retirement in March 2019, having worked continuously with the LBC studies since they began in 1999. Given her vast expertise on the study, having tested LBC1921 and LBC1936 participants throughout all waves, she kindly agreed to come out of retirement in order to help the LBC1936 testing team with wave 6 data collection. Alison is an absolute asset to the team and we are thrilled to welcome her back. Some of you will see her at the WTCRF soon!

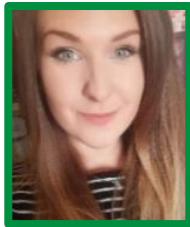
## LBC young researchers' achievements

The LBC study has a long history of attracting talented young researchers to the project, and we are proud to offer such fertile ground for important research training and future career preparation. Their work would not be possible without your generous contributions to the project; your data is an absolute treasure trove for new discoveries! In this special section, we wanted to highlight the many and varied successes of some of our brilliant young researchers in 2021. You will also find details of some of our young researchers' publications on page 8.

First, two of the LBC1936 testing team have been studying for MScs in addition to their full-time roles with the study. Study co-ordinator **Adele Taylor** passed her MSc in Psychology with distinction. She used LBC1921 and LBC1936 data to examine cohort effects: differences in certain attributes that occur between similar-aged groups of people, born at different times. Using a range of variables, measured using identical methods when both cohorts were age 79, she found that the more-recently born LBC1936 had better cognitive function and fewer symptoms of anxiety and depression than LBC1921, who were born 15 years earlier, but physical fitness results were more mixed. Cohort differences in later-life cognitive ability may reflect a lifelong continuation of cognitive ability differences that were evident when participants were first tested at age 11 as part of the Scottish Mental Surveys.



Research Assistant **Danielle Page** is awaiting her grade after completing an MSc in Human Cognitive Neuropsychology in October. Her thesis aimed to solve a theoretical problem that makes interpreting associations between brain structures and cognitive abilities in neuropsychological studies more difficult. By extracting scores for domains of cognitive ability such as processing speed, and a score for general intelligence or 'g', from LBC1936, she was able to map which structures in the brain are related solely to each domain, or solely to g, and which overlap.



**Dr Federica Conte** used LBC1936 data in her thesis to explore how cognitive abilities change across the lifespan from age 11 to 82, and how earlier change trajectories might be used to predict greater cognitive decline in older age. She said: *"I have a lot to look forward to next, but I especially hope there will be opportunities to keep working with the LBCs in the future."*



We hope you will join us in congratulating four of our PhD students who used LBC data in their theses in 2021. **Dr Emily Wheeler** spent some of her PhD analysing birth weight and brain structure in later life using LBC1936 data. She found that larger birth weight was associated with having a larger brain in late life, but was not associated with age-related change such as atrophy. She said: *"my examiners were really enthusiastic about this rare, historic data that allows us to delve a bit deeper into the early life origins of later life brain health"*.



We also have a number of current students working with LBC data. **Miles Welstead's** PhD thesis focuses on how and why frailty changes over time, often using LBC data. He has also helped to develop a valuable new measure of Mild Cognitive Impairment (MCI) using LBC1936 data, and published two papers examining the prevalence and predictors of MCI in LBC1936 participants.

**Danni Gadd** is using LBC biological data in her PhD to predict and better understand the onset of dementia and its associated comorbidities. With LBC1936 data, she recently created scores for protein levels in the blood, and used these to predict onset of Alzheimer's Dementia and other diseases including diabetes and stroke over a follow-up of 14 years, providing new insights into early markers of disease.



**Dr Olivia Hamilton** used LBC1936 data in her PhD to explore associations between vascular changes in the brain and cognitive abilities. One of her main findings was that dysfunction of the brain's small vessels is associated with declining ability in all major cognitive domains. She said: *"My work benefitted hugely from the range of brain and cognitive data available in the LBC studies and from the support of the LBC team."*

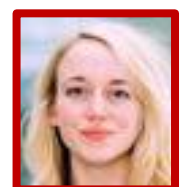


**Jure Mur** has been exploring environmental factors associated with health and disease in later life in his PhD. He is currently working on researching anticholinergic drugs, which block the action of neurotransmitter acetylcholine in the brain, and their relationship with health-related outcomes.

**Dr Robert Hillary** tested whether biomarkers in our blood can predict our risk of developing dementia with LBC data. He found a number of blood proteins that might cause us to have an increased risk of dementia, which might point towards new drug targets if his findings are replicated using other research techniques. He said: *"My work was made possible by the vast array of molecular and cognitive data available in the LBC studies and the amazing contributions of the LBC participants as well as support from our funders."*



**Eleanor Conole** is interested in the impact lifestyle has on brain structure. In LBC1936, Eleanor showed that a DNA methylation proxy for the marker of inflammation, C-Reactive Protein (CRP), was up to 6-times more strongly associated with brain structure and cognitive functions than a blood-based CRP measure. Eleanor's study suggests that DNA methylation-based predictors could be used as proxies for chronic inflammatory status.



## Simon Cox awarded Sir Henry Dale Fellowship

We are sure you will join us in congratulating Study Director Dr Simon Cox, who was awarded a prestigious Sir Henry Dale Fellowship from Wellcome and the Royal Society this year. The fellowship will provide nearly a million pounds of funding over 5 years to support his research project 'Factors of biological ageing – does it all go together when it goes?'. The project aims to use large datasets, including the LBC1921 and LBC1936, to better understand the nature of the ageing process by integrating information collected about different aspects of ageing, such as cognitive, brain, physical, and genetic. Identifying the degree to which these different facets of ageing change in parallel over time could help us identify different dimensions along which people decline, or stay stable, and in turn, we might uncover how different facets are linked with different risk factors.



Dr Simon Cox presents at the LBC reunion event, September 2018

As part of Simon's grant, he received funding for a new post-doctoral researcher to join the team. We were delighted to welcome Dr Joanna Moodie to the team in May. Joanna first used LBC data during her MSc to explore associations between brain asymmetry and cognition; her project was later published in the journal *Intelligence*. She aims to characterise connections between biological, brain and cognitive ageing, and is currently investigating links between cortical gene expression and brain correlates of cognition, using LBC1936 data alongside other cohorts.



## Ian Deary: An update from retirement

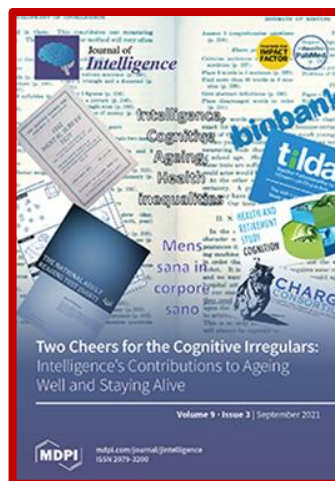
We are sure you are all curious what our former director, Professor Ian Deary, has been up to in his first year of retirement. And you will not be surprised to hear that he has not stopped!



Ian has been an author on over 40 papers in 2021, and was the lead author on 4 of these, including one high-profile commentary published in journal *Molecular Psychiatry*, titled 'Genetic variation, brain, and intelligence differences'. With new study director Dr Simon Cox and LBC geneticist Dr David Hill, Ian undertook the difficult task of summarising the last decade of research on the underlying origins of intelligence, including new contributions from studies of molecular genetics, brain imaging, and studies combining both.

The paper is a cornerstone commentary in our mission at the LBC studies, which is to apply our understanding of genes and the brain to understand why our thinking skills change, and why they change more for some people than others, with age. Ian drew on many key LBC findings to explain the genetic and brain bases of intelligence differences, and noted the gaps in current research, many of which can be addressed using the LBCs valuable data.

Ian also authored an article titled 'Two cheers for the cognitive irregulars', which was featured as the cover story in *Journal of Intelligence* in their autumn edition. Here, Ian described how the thinking and memory tests taken by the LBCs offer highly useful assessments of brain functioning, and explained how these tests can be used to contribute to research which helps people stay sharp, remain healthy, and live longer.



Now professorial fellow of differential psychology, Ian remains an active member of the LBC investigator team. We're delighted to continue to benefit from his experience and expertise, and look forward to updating you on his fantastic research.

## Scientific Highlights

We are grateful to all LBC1921 and LBC1936 participants for giving their time and effort, and providing an amazing range of data. Here are just a few highlights of the many amazing discoveries our LBC researchers and collaborators have made in 2021, using LBC data:

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### The Edinburgh Lifetime Musical Experience Questionnaire (ELMEQ): Responses and non-musical correlates in the Lothian Birth Cohort 1936



**Author:** Judith Okely et al

**Journal:** PLOS ONE

At wave 5, LBC1936 participants completed a new questionnaire designed by Dr Katie Overy (Reid School of Music) and the LBC1936 team. Judy used the data collected to identify some non-musical correlates of greater lifetime musical experience, including a more affluent childhood environment, more years of education, a higher childhood cognitive ability, female sex, and higher scores on the personality trait extraversion.

Judy has led a number of online events to explain her findings, as well as getting the public involved in musical activities like singing workshops and learning about unusual instruments (see our website; link on page 7).

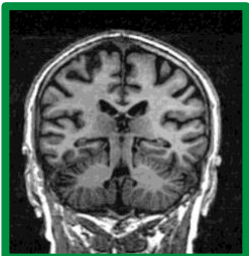
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### Life Course Air Pollution Exposure and Cognitive Decline: Modelled Historical Air Pollution Data and the Lothian Birth Cohort 1936

**Author:** Tom Russ et al.

**Journal:** *Journal of Alzheimer's Disease*

Tom's paper is the first to examine exposure to air pollution across the life course in relation to cognitive decline; this has not been possible up to now due to a lack of data on air pollution before the 1990s. Tom used estimated pollution levels and LBC1936 lifetime residential history data to model exposure to air pollution levels at multiple time points between 1935-1990. Higher air pollution levels in 1935, when LBC1936 participants would have been in utero, were associated with greater decline in cognitive abilities from age 11 to age 70, but not with change in cognitive ability *within* older age, from age 70 to 79.



### Comparison of structural MRI brain measures between 1.5 and 3T

**Author:** Colin Buchanan et al.

**Journal:** *Human Brain Mapping*

This paper reports the results of our carefully-planned transition from the older 1.5T brain MRI scanner to a newer 3T scanner (T stands for Tesla, which are the units of magnetic field strength). At wave 5, 105 LBC1936 participants kindly took part in scans at both scanners to help us uncover any brain image differences to expect, and account for, between scanners. Colin found differences in many brain measurements depending on the scanner used. For example, grey and white matter tissue volumes from the 3T scanner were measured as 6-11% higher than the 1.5T scanner. However, we also showed that these differences could be eliminated statistically, meaning that results can be reliably matched between scanners. These are also highly valuable findings for other researchers who use multiple MRI scanners.

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### Dietary patterns and trajectories of global- and domain-specific cognitive decline in the LBC1936

**Author:** Janie Corley & Ian Deary

**Journal:** *British Journal of Nutrition*

Healthy dietary patterns may protect against age-related cognitive decline but results are inconclusive, and few have had extensive longitudinal follow-up. Janie and Ian examined two dietary patterns: a healthy Mediterranean-style pattern, and a traditional processed-food pattern. Neither dietary pattern was associated with cognitive change over time, with the exception of a slightly steeper decline in verbal abilities in those with a more Mediterranean-style diet at age 70. Overall, dietary patterns were not associated with general cognitive ageing, or with decline in visuospatial-, processing speed- or memory- abilities over 12 years of follow-up.

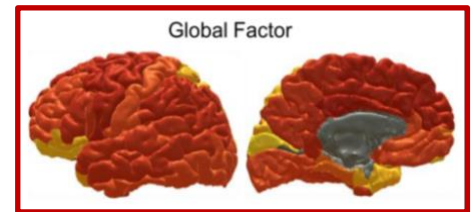


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## Three major dimensions of human brain cortical ageing in relation to cognitive decline across the 8th decade of life

**Author:** Simon Cox et al.      **Journal:** *Molecular Psychiatry*

Many brain imaging studies use cross-sectional data, meaning scans take place at just one time point, rather than longitudinal data across multiple time points like in LBC1936. Cross-sectional data makes it difficult to distinguish whether some patterns we observe are due to changes in the brain over time due to ageing, or if they are present throughout the whole lifetime. Simon used 1376 scans of LBC1936 participants from age 73, 76 and 79 to characterise brain ageing. He found changes in the grey matter on the outer layer of the brain (where many of our brain cells are) occur mostly in a general and fairly concerted fashion: one major dimension of brain atrophy which explained 66% of longitudinal changes in brain volume. People who showed more brain ageing in the aspect also showed corresponding cognitive ageing. Changes involving just the front or just the back of the brain explained an additional 20% of brain ageing. These findings weren't observed in cross-sectional data, which highlights the value of our longitudinal LBC1936 brain scans.



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Many of you will remember taking part in the LBC1936 COVID-19 survey during the national lockdown in May 2020. The team's hard work launching the questionnaire, promptly using the data to write the papers described below, and contributing to an article about older peoples' experience of the pandemic in The Times, led to them being shortlisted for the University of Edinburgh's 'Adaptation to Change' award at the College of Arts and Humanities Teaching Awards. We summarise our 3 COVID-19 publications next.

### Impact of COVID-19 lockdown on psychosocial factors, health, and lifestyle in Scottish octogenarians

**Author:** Adele Taylor & Danielle Page et al.

**Journal:** *PLOS ONE*

The team examined responses to the questionnaire including experience and knowledge of COVID-19, adherence to government guidance, and the impact of lockdown on day-to-day living, social contact, physical and mental health, loneliness, and lifestyle. They also examined which participant characteristics, measured previously at age 82, were associated with outcomes during lockdown at age 84. Overall, characteristics such as lower occupational social class, poorer self-rated general and mental health, and lower cognitive ability level were related to risk of poorer psychosocial and physical outcomes.

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### Home garden use during COVID-19: Associations with physical and mental wellbeing in older adults



**Author:** Janie Corley et al.

**Journal:** *Journal of Environmental Psychology*

Janie examined whether home garden usage was associated with self-reported mental and physical wellbeing. Spending more time in the garden during lockdown, compared with before lockdown, was associated with better self-rated physical health, emotional and mental health, and sleep quality, but specifically 'doing' garden activities or using the garden for relaxation purposes were not significantly associated with wellbeing.

Spending time in a home garden might be a potential health resource during the pandemic for older people.

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### Change in Physical Activity, Sleep Quality, and Psychosocial Variables during COVID-19 Lockdown

**Author:** Judith Okely, Janie Corley, Miles Welstead et al.

**Journal:** *International Journal of Environmental Research and Public Health*

The team examined changes in physical activity, sleep quality, loneliness, memory problems, neighbourhood cohesion, and psychological wellbeing. Some characteristics predicted change in aspects of participants' lockdown experience: personality traits (intellect, emotional stability, extraversion) and higher general cognitive ability were associated with more positive changes. History of cardiovascular disease, more anxiety symptoms, and living alone were associated with more negative changes. In combination with other studies, this might help identify individuals who may particularly benefit from extra support during the pandemic.

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## LBCs at virtual conferences in 2021

The continued restrictions on social gatherings hasn't slowed the LBC researchers, who attended a huge number of virtual conferences, summits, society meetings and exhibitions in 2021. Presentation topics included: protein biomarkers of cognitive function, characteristics associated with lifetime musical experience, new methods to identify white matter in brain scans, and lifestyle factors associated with living to be 100.

Of particular note in 2021, Study Director Dr Simon Cox was invited to deliver a Plenary Address at the Society of Biological Psychiatry 2021 Annual Meeting. At this global meeting, attended by more than 1,000 delegates, Simon presented some core LBC1921 and LBC1936 findings, and described cutting-edge contributions LBC data will continue to make, to help us understand why some people's brains and thinking skills age better than others'.

Here, we will tell you about just a few of the other activities and events the team have been involved with in 2021, to share our scientific discoveries from the LBCs with the public and beyond.

## Ian Deary featured in British Neuroscience Association Bulletin

Professor Ian Deary was featured in the Spring Bulletin of the British Neuroscience Association, a publication circulated to over 2,000 BNA members. The article, with the fitting title 'Never too old', dedicated three pages to Ian and his contribution to the field of cognitive ageing. It describes his unorthodox journey to medical training and later academic career in the Department of Psychology at the University of Edinburgh, and the discovery of the LBCs data that would change his life and form the foundation of cognitive epidemiology with the longest study of cognitive ageing in the world. In his interview, Ian acknowledged the dedication of the LBC1921 and LBC1936 participants, the commitment of his team, and the fantastic collaborators and expertise available on our doorsteps at the University of Edinburgh.



## LBCs featured in University magazine



The LBCs have been prominently featured in 'Edinburgh Impact', an online magazine about how the University of Edinburgh community is making its mark upon the world through its research, innovation, ideas and actions. The article, 'The Brain Boosters', highlights the study's invaluable contribution to the field of cognitive ageing, and in finding ways to keep our minds sharp into old age. The article was also included in 'Edit', the annual magazine for alumni of the University of Edinburgh. We are delighted and honoured that the LBCs were included, reaching alumni all over the world.

## Keep your brain sharp from age 11 to 85

In the summer, team members Danielle Page and Barbora Skarabela delivered a workshop as part of Edinburgh University's Widening Participation team's 'Primary Initiative', which aims to address educational inequalities and patterns of under-representation in Higher Education. Danielle led 60 11-year-old children from Craighour Park Primary School, Edinburgh, through an online session designed to get them excited about Psychology.



Danielle delivers the LBC Primary School workshop

Danielle explained why LBC1936 participants are so interesting, and what your data has taught us so far about the brain and how to keep our thinking skills sharp. The children made hypotheses about whether their thinking skills would be better or worse than an 85-year-old, and took part in some of the same cognitive tests we give you at the Wellcome Trust clinic to test their hypotheses. This started some lively debates: particularly about whether an LBC participant would have better memory because they had had more years of practice, or worse because their thinking skills had gotten a little slower since they were 11!

## Thank you from the LBC team

As a member of the LBC1921 or LBC1936 cohort, your contributions are helping to further our knowledge and understanding of cognitive, brain, and general ageing. You are also helping to train talented new researchers, such as those described in this newsletter. Thank you for your continued interest and involvement; we look forward to seeing you in 2022 and beyond.

For a digital copy of this newsletter, a complete list of LBC publications, or for further information about anything you have read, visit our website: [www.ed.ac.uk/lothian-birth-cohorts](http://www.ed.ac.uk/lothian-birth-cohorts), and stay up to date with our most recent LBC activities at: [www.twitter.com/EdinUniLBC](https://www.twitter.com/EdinUniLBC)

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## LBC publication highlights 2021

- Buchanan, C.R. et al. (2021) 'Comparison of structural MRI brain measures between 1.5 and 3 T: Data from the Lothian Birth Cohort 1936'. *Hum Brain Mapp.*
- Conole, E.L.S. et al. (2021) 'DNA Methylation and Protein Markers of Chronic Inflammation and Their Associations With Brain and Cognitive Aging'. *Neurology.*
- Corley, J. & Deary, I.J., (2021). 'Dietary patterns and trajectories of global and domain-specific cognitive decline in the Lothian Birth Cohort 1936'. *British Journal of Nutrition.*
- Corley, J. et al. (2021) 'Home garden use during COVID-19: Associations with physical and mental wellbeing in older adults'. *J. Environ. Psychol.*
- Cox, S.R. et al. (2021) 'Three major dimensions of human brain cortical ageing in relation to cognitive decline across the eighth decade of life'. *Mol Psychiatry.*
- Deary, I.J. et al. (2021) 'Genetic variation, brain, and intelligence differences'. *Mol Psychiatry.*
- Deary, I.J. et al. (2021) 'Intelligence, health and death'. *Nat Hum Behav.*
- Deary, I.J. (2021) 'Two Cheers for the Cognitive Irregulars: Intelligence's Contributions to Ageing Well and Staying Alive'. *Journal of Intelligence.*
- Deary, I.J. & Sternberg, R.J. (2021) 'Ian Deary and Robert Sternberg answer five self-inflicted questions about human intelligence'. *Intelligence.*
- Gadd, D.A. et al. (2021) 'Epigenetic predictors of lifestyle traits applied to the blood and brain'. *Brain Commun.*
- Hamilton, O.K.L et al. (2021) 'Associations between total MRI-visible small vessel disease burden and domain-specific cognitive abilities in a community-dwelling older-age cohort'. *Neurobiology of Aging.*
- Hamilton, O.K.L., et al. (2021) 'Cerebral small vessel disease burden and longitudinal cognitive decline from age 73 to 82: the Lothian Birth Cohort 1936'. *Transl Psychiatry.*
- Hillary, R.F. et al. (2021) 'An epigenetic predictor of death captures multi-modal measures of brain health'. *Mol Psychiatry.*
- Mur, J. et al. (2021) 'Increase in anticholinergic burden from 1990 to 2015: age-period-cohort analysis in UK Biobank'. *Br. J. Clin. Pharmacol.*
- Okely, J.A., Deary, I.J., Overy, K., (2021) 'The Edinburgh Lifetime Musical Experience Questionnaire (ELMEQ)'. *PLoS ONE.*
- Russ, T.C. et al. (2021) 'Life Course Air Pollution Exposure and Cognitive Decline: Modelled Historical Air Pollution Data and the Lothian Birth Cohort 1936'. *Journal of Alzheimer's Disease.*
- Taylor, A.M., Page, D., et al. (2021) 'Impact of COVID-19 lockdown on psychosocial factors, health, and lifestyle in Scottish octogenarians: The Lothian Birth Cohort 1936 study'. *PLoS One.*
- Welstead, M. et al. (2021) 'Predictors of Mild Cognitive Impairment Stability, Progression, or Reversion in the Lothian Birth Cohort 1936'. *JAD.*
- Welstead, M. et al. (2021) 'Prevalence of Mild Cognitive Impairment in the Lothian Birth Cohort 1936'. *Alzheimer Disease & Associated Disorders.*
- Wheater, E. et al. (2021) 'Birth weight is associated with brain tissue volumes seven decades later but not with MRI markers of brain ageing'. *NeuroImage: Clinical.*