

The Disconnected Mind

Unlocking secrets of healthy mental ageing

The Disconnected Mind aims to understand how changes in the brain's white matter – its connectivity – contribute to age-related cognitive decline in humans.

Newsletter 48: December 2019

Welcome to the Winter 2019 Disconnected Mind newsletter. This issue includes news about recent events the Disconnected Mind/Lothian Birth Cohorts (LBC) team have participated in, and details of our latest publications. The regular contribution from our colleagues at Age UK can be found on page 6. If you'd like more information about anything in this newsletter, or wish to contribute to a future issue, please get in touch: contact details are on page 8.

Lothian Birth Cohorts News



LBC Director, Ian Deary, opens the 2019 reunion

CELEBRATING 20 YEARS OF LBC!

On 7th September 2019, we held a reunion celebrating 20 years (to the day!) since the very first LBC1921 participant was tested. The team were delighted to welcome almost 300 guests to the Royal College of Physicians of Edinburgh; among them were many participants, research collaborators, friends and supporters, including Age UK Research Manager Susan Davidson, who you will hear more from on page 6.

The event kicked off with LBC Director, Ian Deary, showing some age-82 data, and giving a countdown of the cohorts' 'top 20 scientific reports' of the past 20 years. There were updates on health and brain imaging, including some exciting sneak previews of the LBC1936 age 82 results, and a series of quick-fire talks by LBC researchers and collaborators on the newest types of LBC1936 data collected during Wave 5: musical experience, financial capacity, 'omics, dietary information and longitudinal retinal imaging. Guests also had a chance to explore cutting-edge augmented reality (AR) brain displays, based on LBC1921 and LBC1936 data, showing 3D brain images -- with their anatomy and structural differences related to lifestyle and vascular risk factors -- floating in real space.

One of the highlights of the day came when LBC1936 participant, Mr Tom Sommerville, gave a wonderfully entertaining account of his trip to the House of Lords Select Committee on Science, for their newly launched Inquiry into Ageing. The remaining speakers had drawn the short straw following Tom! The event was very well received, and the team were touched by kind words and feedback from those who attended. Particularly appreciated were the positive words of Age UK Trustee, Stuart Purdy, who called the event 'remarkably successful', and noted the 'real enthusiasm and commitment from participants'. Thank you to all of our guests, speakers, and volunteers, for an enjoyable and memorable afternoon celebrating 20 years of LBC. Thanks also go to Douglas Roberston whose photographs beautifully captured the day and a few more of which you can enjoy on page 8.



Colin Buchanan (right) demonstrates AR Brains to LBC1936 participants

Don't forget to [download](#) our 20th anniversary brochure, which highlights the generous contributions of LBC1921 and LBC1936 members who have kindly volunteered their time to us over the last 20 years. It gives an overview of the many types of data we have collected since the studies began, and documents the continued influence that the LBCs have in the science of cognitive, brain, and general ageing, and beyond.

Lothian Birth Cohorts

Celebrating 20 years
of research into ageing



Scientific highlights

Since September, 16 LBC articles were accepted or published in scientific journals. Here we give a snapshot of two recent articles, and some other scientific highlights. The full publications list from this quarter is on page 8, or visit our [website](#) for the complete LBC back catalogue.

COLLECTION | 15 JULY 2019

Top 50: Life and Biological Sciences

We are pleased to share with you the 50 most read Nature Communications life and biological sciences articles published in 2018. Featuring authors from around the world, these papers highlight valuable research from an international community.



[Browse all Top 50 subject area collections here.](#)

nature communications

Article | Open Access | Published: 29 May 2018

Study of 300,486 individuals identifies 148 independent genetic loci influencing general cognitive function

LBCs named in Top 50 'Most Read'

We were delighted to discover that research led by LBCs' Dr Gail Davies was named fourth 'most read' in the *Nature Communications* Top 50 Life and Biological Sciences papers of 2018. At the time of publication, Gail's study was the largest-ever of the genetic contributions to general cognitive function. It combined cognitive and genetic data from the CHARGE and COGENT consortia (including LBC1921 and LBC1936 data) and UK Biobank, with a sample size of over 300,000 individuals. Read the paper [here](#).

Childhood intelligence attenuates the association between biological ageing and health outcomes in later life

Anna J. Stevenson, Daniel L. McClelland, Qian Zhang, Allan F. McRae, Tara L. Spector, E. Mariani



Childhood IQ and 'Biological age' in the LBCs

Available now as a [pre-print](#) on bioRxiv, and recently accepted for publication in *Translational Psychiatry*, is a new LBC1936 article by PhD student, Anna Stevenson et al. They report that a new measure of DNA methylation-based biological age is associated with a number of blood, cognitive, physical fitness and lifestyle variables at age 70, and with mortality. Notably, the measure was also associated with childhood cognitive ability at age 11, and with educational attainment. The majority of the later-life associations were no longer significant when analyses were adjusted for childhood IQ. These results highlight the importance of early-life factors on healthy ageing.

Research paper

Physical frailty and decline in general and specific cognitive abilities: the Lothian Birth Cohort 1936

Catharine Gale^{1,2}, Stuart J Ritchie³, John M Starr⁴, Ian J Deary¹

Physical frailty is associated with adverse outcomes including disability, hospitalisation, and mortality, but it is unclear what impact it has on 'normal' cognitive ageing. In a paper recently accepted by the *Journal of Epidemiology and Community Health*, Catharine Gale and colleagues used four waves of LBC1936 data to investigate relationships between physical frailty and cognitive function. Being frail was associated with lower levels of general cognitive ability at 70, and lower scores in the domains of visuospatial ability, memory, and processing speed. Frailty was also associated with more decline in general cognitive ability, and in all cognitive domains, between ages 70 and 79. The results suggest that physical frailty may be an important indicator of age-related cognitive decline. Read the [paper](#) and an associated [editorial](#) online now.

IN CASE YOU MISSED IT...

Disconnected Mind/LBC researchers designed and produced the cover image, based on UK Biobank data and their work featured in the associated editorial, for *European Heart Journal* [issue 40](#) in July. They also contributed to a new UK Biobank paper, published in *Alzheimer's & Dementia*, on the predictive ability of short cognitive tests in dementia. Read it [here](#).

Alzheimer's & Dementia

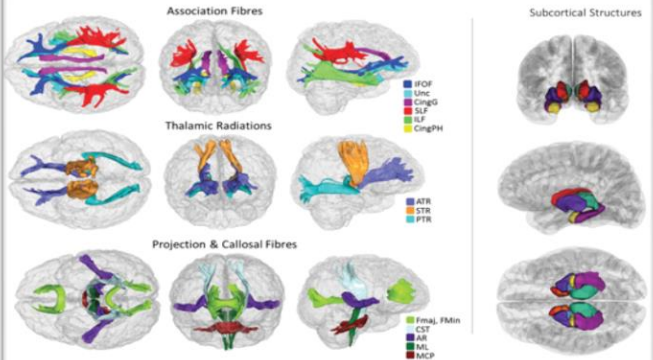
Available online 13 October 2019

In Press, Corrected Proof

Featured Article

Predicting incident dementia 3-8 years after brief cognitive tests in the UK Biobank prospective study of 500,000 people

Cover image



Associations between vascular risk factors and brain MRI indices in UK Biobank

Simon R. Cox^{1,2,3*}, Donald M. Lyall^{3,4}, Stuart J. Ritchie^{1,2,5}, Mark E. Bastin^{1,3,6}, M

Knowledge exchange and Impact

Autumn has been particularly busy for the LBC team. Read on for a whirlwind tour of our scientific and public engagement activities. A special thanks to the School of Philosophy, Psychology and Language Sciences for their Knowledge Exchange funding support for some of the activities included in this section.



From left: Simon Cox, Adele Taylor, Audrey Mackie, and Ian Deary at Apothecaries Hall, London

A long LBC day at Age UK!

“Blimey!” said Professor Ian Deary. “That was about nine hours almost continuous talking about the LBCs. It was exhilarating and encouraging to get so much positive feedback.” Ian was enthusing about a day that he, Dr Simon Cox, Adele Taylor, LBC1936-er Audrey Mackie (and her husband Ron) spent in and around Tavis House, the Age UK HQ on September 12th. Ian gave a 45-minute talk and half-hour Q&A on the LBC1936/Disconnected Mind project’s background, progress, and findings to about 100 Age UK staff. They also heard super things from Mrs Mackie about being an LBC1936 participant. The audience enthusiasm was terrific. Ian then met with one of the foundations that has loyally supported the project. Then, there was a quick transfer to Apothecaries Hall in the City of London for a meeting with present and prospective supporters of the LBC1936/Disconnected Mind. “This evening meeting was stunning,” said Ian. “The location was old, elegant, and impressive. There was a great turnout from Age UK’s staff—including many senior officers—and from interested supporters. They heard from me about how the project was going and why the next stages are so important. They also got to talk with Mrs Mackie and with Simon and Adele, including seeing and walking round some holographic LBC brains”. So, was it a tiring day? “Not that I noticed,” said Ian. “I walked back from Apothecaries Hall to Euston station for the Caledonian Sleeper with a spring in my steps. I just thought: what great funders and supporters we have, and what a wonderful group of participants and research team.”

BBC Music Day: Ageing, Dementia & Music

The team jumped at the chance to join in with celebrations for **BBC Music day** on 26th September. In coordination with hundreds of other organisations across the UK, the Reid School of Music’s Dr Katie Overy hosted a special event at Saint Cecilia’s Hall. It was an engaging mix of short talks and interactive fun. The LBC team were there with their latest teaching tool - the 3D AR brain display; it was a hit with guests, who tried it out while exploring the museum’s unusual and historical musical instruments. Prof Ian Deary opened the session of short talks with a brief history of the LBCs and their key findings. Katie followed with news about her exciting new collaboration with LBC, being led by Dr Judy Okely, investigating lifetime musical experience and cognitive ageing. Katie also introduced the Reconnect workshops, which bring together musicians and dementia patients. Three Scottish Chamber Orchestra (SCO) musicians were on hand to give a heart-warming demonstration of the interactive sessions they take into hospital dementia wards, and audience members were encouraged to join in singing and playing instruments with them throughout. A few closing words from the panel and audience members showed clear enthusiasm for further research into the benefits of musical activity in older age.



Above (from left): SCO’s Kirsteen Davidson Kelly, Katie Overy and Ian Deary at St Cecilia’s Hall on BBC Music Day. Below: Ian with SCO musicians



LBCs on BBC Brainwaves

The LBC team were delighted to welcome BBC Radio Scotland's Pennie Latin and Dan Holland to the department, to record a special episode of *Brainwaves*, ahead of the LBCs' 20th anniversary in September. Pennie and Dan met with Ian Deary, cognitive testers Alison Pattie and Danielle Page, and artist Fionna Carlisle (who painted a collection of LBC participant portraits) to hear about the history of the project, and some of the artistic endeavours that it has inspired. LBC1936 and LBC1921 participants were also interviewed for the show which aired in September and is available to download [here](#). Because the *Brainwaves* team recorded many fascinating stories, they appeared in a further two (!) BBC Scotland shows: the first, a slot on *The Afternoon Show*, featured a discussion with portrait artist Fionna Carlisle; the second, *Our Lives with Michelle McManus*, included a fascinating interview with an LBC1936 participant in which she recounts her earliest war time memories. The latter show is available to listen to online [here](#).



From left: Dan Holland, Danielle Page, Fionna Carlisle, and Pennie Latin, with Fionna's portrait of Professor Ian Deary

LBC at the Midlothian Science Festival

From 7th to 10th October, the team took part in the Midlothian Science Festival Schools programme. We spent our mornings with seven Primary 4 classes in four Midlothian schools with our 'Brain Matters: Explore your Senses' workshop. Pupils and teachers joined in activities about our five main senses, designed to help children develop their investigative skills and scientific analytic thinking. Children were encouraged to formulate hypotheses and complete a series of five experiments to test these, and learn about their senses and how they send information to the brain in response to the environment. The team, pupils and staff all had a wonderful time and there was a lot of learning and laughter, especially when the teachers were asked to do a blindfolded taste test! By the end of the workshops, the pupils had learned all sorts of interesting facts about the importance of our 5 primary senses; as one pupil put it, our senses are 'like superhero powers, except we all have them'!



Dr Barbara Skarabela supervises a blindfold taste test at the Midlothian Science Festival

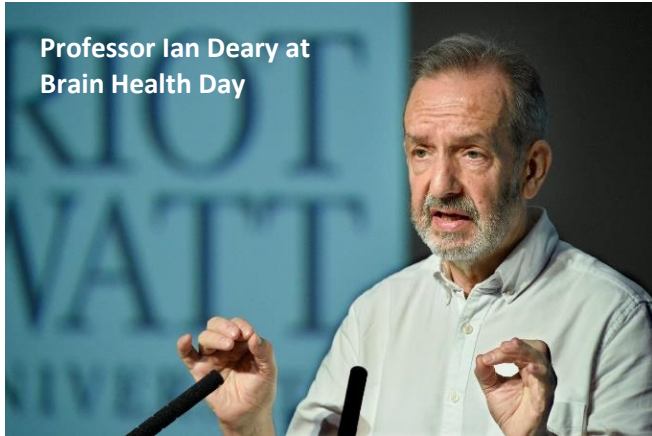
House of Lords Inquiry into Ageing

Drs Stuart Ritchie and Riccardo Marioni (co-investigator and collaborator, respectively, on the Disconnected Mind/LBC studies) were invited to Parliament in October to give evidence to the House of Lords Science and Technology Committee's Inquiry into Ageing. The Inquiry aims to explore ways to improve the health and wellbeing of older people. They contributed their expertise and findings from their work on the LBCs and other cohort studies, including on the biology and genetics of ageing. Asked about priorities for public health messages, Stuart spoke of there being a spectrum of variables which affect cognitive ageing, and many factors that add up to make differences between individuals in terms of cognitive ability and cognitive decline. He said, *"The message I would take away, and we've written about this in our cohort (LBC1936), is this idea of 'marginal gains' like you'd talk about in sport. Instead of there being one thing you can change, change lots and lots of different factors. Whether it is to do with education... smoking... physical fitness, or many other aspects."*



Dr Stuart Ritchie gives evidence to the House of Lords Science and Technology Committee

Brain Health Day at Heriot Watt



“This is a good development from, and complement to, the Lothian Birth Cohort studies,” said Professor Ian Deary in his invited talk to the Brain Health Day on 28th August at Heriot-Watt University. He described the insights that the Lothian Birth Cohorts had brought to understanding the differences in ageing of people’s brain structure and thinking skills. “The Brain Health Day brought together over 200 of Professor Alan Gow’s participants,” said Ian. “They took part in Alan’s team’s ‘Intervention Factory’ study of whether taking up a new activity could enhance some thinking skills. The participants have all been tested, and got a preview of some of the early descriptive results, though no findings are available yet. They also heard about the sorts of things that might help keep people sharp, and some local researchers gave brief talks.” Alan has been recently awarded ‘Runner Up’ in the [Nature Research Awards for Driving Global Impact](#) for his work on understanding the brain, with potential for a positive impact on society. Congratulations Alan!

Epigenomics of Common Diseases conference

Dr Riccardo Marioni and his research group attended the Epigenomics of Common Diseases conference in Cambridge in November. Two of the team gave poster presentations, and Anna Stevenson (whose work was covered in ‘Scientific Highlights’) was awarded best short presentation prize for her talk on inflammation and DNA methylation in relation to ageing and cognitive ability. Congratulations, Anna!



Riccardo Marioni’s Research Group at the conference (from left): Anna Stevenson, Eleanor Conole, Riccardo Marioni, Rob Hillary, Dan McCartney, and Jure Mur

Scottish Parliament Festival of Politics



The Festival of Politics ran at the Scottish Parliament from 10th to 12th October. During the festival, the Parliament opens its doors to allow the public, academics, MSPs, and commentators to engage in, and contribute to, current political issues. We were therefore delighted when Fionna Carlisle received an invitation to display a selection of her portraits of LBC participants and team members at the event. It was fantastic opportunity to highlight to the public and policy makers the team’s research and its important findings on cognitive ageing. Fionna said: “When Alan Rennie invited me to show a selection of portraits from my exhibition *The Art of Intelligent Ageing* during The Festival of Politics, I immediately contacted Professor Ian Deary. This project had always been a collaboration and I was sure he would be interested too ... This was a prestigious event with thousands of visitors able to access parts of the Parliament not usually available to the public, with lots of music, events and discussions ... once again this ‘organically grown’ mix of science and art was a real draw.”

Other events this quarter

- Disconnected Mind-funded PhD student, Miles Welstead, visited Age UK HQ in London to discuss progress on his project and meet Research Managers, Sujata Ray and Susan Davidson, and Senior Health Influencing Manager Tom Gentry.
- Riccardo Marioni spoke at Illumina's Genetics of Dementia Summit (Paris) and PREVENT Dementia General Assembly (Dublin), on how LBC methylation data are helping us better understand modifiable risk factors for AD and other dementias. He also presented on the link between blood-based DNA-methylation and cognitive function at a NeurEpiOmics workshop in San Antonio, Texas.
- Simon Cox gave a talk on Brain and Cognitive Ageing at Oxford’s Autumn School of Neuroscience.
- Judy Okely gave a talk on study design and open science at the Edinburgh Autumn School for PhD students.
- LBC collaborator, Dr Alixe Kilgour, gave a talk on sarcopenia measurement in the LBC1936 at the British Geriatrics Society Autumn meeting.

Age UK News

Happy Holidays! We are looking forward to winding down at the end of the month, and getting recharged and ready to face the New Year. Here are some treats, or at least food for thought, for you, starting with two new publications and two exciting recently launched campaigns.

What does Brexit mean for our older generations?

Whatever the outcome of the December elections, Age UK has posed 10 questions for the new government regarding how Brexit could impact older people. [Read](#) Age UK's concerns around rights, healthcare, and pensions, among others.

New Age UK report lays out truly frightening trends in social care

[‘The Health and Care of Older People in England 2019’](#) draws on many official statistics as well as new Age UK analysis to provide a comprehensive picture of how services are functioning today, for older people across the NHS and social care.

We Are Undefeatable

For the first time ever, 15 leading health and social care charities have launched a national campaign and movement to inspire and support people with long-term health conditions to be active. Age UK was pleased to develop the campaign on behalf of all 15 charities. The campaign is inspired by, and features, the real-life experiences of people with long-term health conditions getting active despite the ups, downs and unpredictability of their condition. “We Are Undefeatable” aims to support people living with health conditions to build physical activity into their lives, in a way that their condition allows, and to celebrate every victory big or small. A new website www.weareundefeatable.co.uk and social media channels will provide inspiration, reassurance and support.



Cadbury - donate your words



We've worked with Cadbury to produce a limited edition 'wordless' version of their Dairy Milk bar. You might start seeing some of these bars popping up in shops. Cadbury have 'donated the words' from their bars to raise awareness of the fact that 225,000 older people often go a week without speaking to anyone. While raising money for Age UK, the campaign encourages the public to 'donate their words' by committing to small acts of kindness to help lonely older people in their community.

Visit to the Disconnected Mind in Edinburgh

Six of my Age UK colleagues and I visited the Disconnected Mind team at George Square on 29 August, giving us a thoroughly absorbing and fascinating time. It's valuable and inspiring to us to hear about the amazing work they're doing across a wide variety of aspects of the project first-hand, and we're grateful to everyone for the time they all took to make that possible. Meeting the team in person and seeing the environment also help bring everything to life for us. Some words from the visiting team:

Our Fundraiser for Disconnected Mind - Helen Finch

As last year, it was fascinating to hear updates from Ian and the rest of the team. The time spent with them will definitely help me to communicate about the project with funders, and - although I wouldn't have thought it could have been possible - made me even more enthused about the project!

Our Policy lead in consumers, scams and fraud - Joel Lewis

Thank you to the whole team at the Disconnected Mind Project for hosting us. Really enjoyed meeting everyone and hearing about the great work taking place. With my particular interest in consumer decision making and financial capability, it was really good to hear about the testing that is being built into the next cycle. Hope to stay in touch with the team and see how future findings can support our influencing work.

Publications

In press

Hillary, R.F., Stevenson, A.J., Cox, S.R., McCartney, D.L., Harris, S.E., et al., (2019). An epigenetic predictor of death captures multi-modal measures of brain health. *Molecular Psychiatry*.
<https://doi.org/10.1101/703504>

Jia, T., Chu, C., Liu, Y., Dongen, J. van, Armstrong, N.J., et al., (2019). Epigenome-wide meta-analysis of blood DNA methylation and its association with subcortical volumes: findings from the ENIGMA Epigenetics Working Group. *Molecular Psychiatry*.
<https://doi.org/10.1101/460444>

Moodie, J.E., Ritchie, S.J., Cox, S.R., Harris, M.A., Munoz Maniega, S., et al., (2019). Fluctuating asymmetry in brain structure and general intelligence in 73-year-olds. *Intelligence*.

Wragg, D., Liu, Q., Lin, Z., Riggio, V., Pugh, C., et al., (2019). Using regulatory variants to detect gene-gene interactions identifies networks of genes linked to cell immortalization. *Nature Communications*.

E-published ahead of print

Altschul, D.M., Deary, I.J., (2019). Playing analog games is associated with reduced declines in cognitive function: a 68 year longitudinal cohort study. *The Journals of Gerontology: Series B* gbz149.
<https://doi.org/10.1093/geronb/gbz149>

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<https://doi.org/10.1136/jech-2019-213280>

Halachev, M., Meynert, A., Taylor, M.S., Vitart, V., Kerr, S.M., et al., (2019). Increased ultra-rare variant load in an isolated Scottish population impacts exonic and regulatory regions. *PLoS Genet* 15, e1008480.
<https://doi.org/10.1371/journal.pgen.1008480>

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<https://doi.org/10.1037/pag0000419>

Veluchamy, A., Ballerini, L., Vitart, V., Schraut, K.E., Kirin, M., et al., (2019). Novel Genetic Locus Influencing Retinal Venular Tortuosity Is Also Associated With Risk of Coronary Artery Disease. *Arterioscler. Thromb. Vasc. Biol.* ATVBaha119312552.
<https://doi.org/10.1161/ATVBaha.11>

Published

Clark, D.W., Okada, Y., Moore, K.H.S., Mason, D., Pirastu, N., et al., (2019). Associations of autozygosity with a broad range of human phenotypes. *Nat Commun* 10, 4957. <https://doi.org/10.1038/s41467-019-12283-6>

Corley, J., Cox, S.R., Harris, S.E., Hernandez, M.V., Maniega, S.M., et al., (2019). Epigenetic signatures of smoking associate with cognitive function, brain structure, and mental and physical health outcomes in the Lothian Birth Cohort 1936. *Transl Psychiatry* 9, 248. <https://doi.org/10.1038/s41398-019-0576-5>

Čukić, I., Gale, C.R., Chastin, S.F.M., Dall, P.M., Dontje, M.L., et al., (2019). Cross-sectional associations between personality traits and device-based measures of step count and sedentary behaviour in older age: the Lothian Birth Cohort 1936. *BMC Geriatr* 19, 302.
<https://doi.org/10.1186/s12877-019-1328-3>

McGrory, S., Ballerini, L., Okely, J.A., Ritchie, S.J., Doubal, F.N., et al., (2019). Retinal microvascular features and cognitive change in the Lothian-Birth Cohort 1936. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring* 11, 500–509.
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Okely, J.A., Deary, I.J., (2019). Longitudinal Associations Between Loneliness and Cognitive Ability in the Lothian Birth Cohort 1936. *The Journals of Gerontology: Series B*.
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Satizabal, C.L., Adams, H.H.H., Hibar, D.P., White, C.C., Knol, M.J., et al., (2019). Genetic architecture of subcortical brain structures in 38,851 individuals. *Nat. Genet.* <https://doi.org/10.1038/s41588-019-0511-y>

Sikdar, S., Joehanes, R., Joubert, B.R., Xu, C.-J., Vives-Usano, M., et al., (2019). Comparison of smoking-related DNA methylation between newborns from prenatal exposure and adults from personal smoking. *Epigenomics*. <https://doi.org/10.2217/epi-2019-0066>



Merry Christmas and Happy New Year from the Disconnected Mind Team!

Contact

You can contact the Disconnected Mind / LBC team by email, and keep up with our latest news on our website and on Twitter.

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Website

Stay up to date with the most recent Disconnected Mind events and publications at:
www.lothianbirthcohort.ed.ac.uk



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