Lifelong Health and Wellbeing Phase 3

Research Grants

Additional Information on each award, including a list of the co-investigators and an abstract of the proposal, can be found by clicking the name of the Principle Investigator.

Name	Institution	Award Title
Professor Ian Deary	University of Edinburgh	Lifelong health and wellbeing of the Scotland in Miniature : the 6-day sample of the Scottish Mental Survey 1947
Professor Brian Derby	The University of Manchester	Quantifying Age-related Changes in the Mechanical Properties of Tissues
Professor Klaus Peter Ebmeier	University of Oxford	PREDICTING MRI ABNORMALITIES WITH LONGITUDINAL DATA OF THE WHITEHALL II SUBSTUDY
Professor Deborah Anne Lawlor	University of Bristol	The menopausal transition and healthy ageing and wellbeing
Professor Gail Mountain	University of Sheffield	Lifestyle Matters
Professor James Nazroo	The University of Manchester	Inequalities in later life frailty and wellbeing: an interdisciplinary approach to causality
Dr Kai-Michael Toellner	University of Birmingham	Top Jabs - Improving vaccination responses in older adults

Lifelong Health and Wellbeing Phase 3 - Collaborative Grant Awards		
Grant Holder	Institutions	Title of Award
Professor Ian Deary	**University of Edinburgh**	**Lifelong health and wellbeing of the Scotland in Miniature : the 6-day sample of the Scottish Mental Survey 1947**
Co-Investigators		Abstract
Dr D Batty	(University College London)	We shall follow up the 1208 people born in 1936 who formed the 6-Day Sample of the Scottish Mental Survey 1947 (SMS1947). They were interviewed yearly from age 11 (1947) to age 27 (1963). There remain huge amounts of untapped stored information from their childhoods and early adulthoods. Now in their mid-70s, there is a time-limited opportunity to understand the life courses of this 'Scotland in Miniature'. This proposal will: (1) revitalise and extend the 6-Day Sample; (2) undertake and disseminate original research on the resource across many collaborating disciplines; (3) support the data and make them available to others. Existing data will be collated for analyses by statistical and non-statistical means: e.g., textual replies from respondents that have never been analysed will be coded for statistical analysis and transcribed for textual analysis. New data will be gathered from national databases both contemporaneous with the original data and (through data matching) subsequently gathered, and by contacting and interviewing the surviving participants. Methods will range from advanced quantitative modelling to qualitative analysis of life history interviews, as appropriate to the diverse, collaborating work streams, each led by an internationally-renowned expert. These are: (a) Life course social movements (lead: Dibben, social geographer); (b) Life-long educational experiences (lead: Paterson, sociologist); (c) Social and cognitive epidemiology (lead: Batty, epidemiologist); (d) Narratives of life transitions, social participation, health and well-being (lead: Elliott, sociologist); (e) Lifelong cognitive change (lead: Deary, psychologist); (f) Health and wellbeing in old age (lead: Starr, geriatric physician); (g) Stress and wellbeing in old age (lead: MacLullich, geriatric physician); (h) Sample selection (lead: Johnson, psychometrician and actuarial mathematician). The 6-Day Sample is a necessary addition to the other British cohorts because: it is representative of Scotland; the data on childhood home environments are detailed; the data from age 11-27 are detailed; data are available in detail on the characteristics and histories of the schools they attended; their age now mid-70s is important and not covered by other cohorts, and will allow time-series comparison with the other cohorts in due course. The study will be based in the University of Edinburgh Centre for Cognitive Ageing and Cognitive Epidemiology, which is funded under the LLHAW initiative. The project will provide transformational science for life-long health and wellbeing: new cohort resource; high-impact publications; a database for other researchers; and policy information. Knowledge Exchange activity will deliver impact on health and social policy, and international recognition
Professor P Boyle	(University of St Andrews)	
Dr C Dibben	(University of St Andrews)	
Professor B J Elliott	(Institute of Education)	
Professor B J Elliott	(University of London)	
Dr W Johnson	(University of Edinburgh)	
Professor A M MacLullich	(University of Edinburgh)	
Professor L Paterson	(University of Edinburgh)	
Professor J M Starr	(University of Edinburgh)	

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Professor Brian Derby	**The University of Manchester**	**Quantifying Age-related Changes in the Mechanical Properties of Tissues**
Co-Investigators		Abstract
Dr R Akhtar	(The University of Manchester)	Age-related changes in the mechanical properties of dynamic tissues within the pulmonary, cardiovascular and musculoskeletal systems profoundly affect human morbidity and mortality. Despite the immense clinical and economic burdens that result from disorders such as hypertension and low back pain, to date attempts to identify and localize the key molecular mechanisms which cause age-related loss of tissue compliance and elastic recoil have been limited by inadequate methods for measuring local mechanical properties of tissue. Therefore, we will develop nanoindentation techniques to map and quantify micrometer-scale changes in tissue mechanical properties to individual tissue components. Nanoindentation is routinely used in materials science to measure the mechanical properties of small volumes of engineering materials, with micrometre spatial resolution. Using this technique, we will determine how age-related changes in the structure of soft tissue cryo-sections influence local changes in mechanical properties and hence understand the mechanisms that lead to changes in bulk tissue behaviour. To achieve this we have specified a modified commercial nanoindentation platform, to include a high quality optical microscope that utilizes molecular auto-fluorescence and differential interference contrast to identify and then quantify the micromechanical properties of discrete tissue structures. Although we have successfully used nanoindentation to characterize tissue mechanical properties in Manchester, further development of the technique will be undertaken to develop constitutive laws that describe tissue mechanical behaviour and link it to tissue microstructure. In order to achieve these goals we have assembled a multidisciplinary team of materials scientists, life scientists and clinicians to apply this technique to research projects in three organ system where age-related mechanical change profoundly affect human mortality, morbidity and well-being. These are: 1) the increase in stiffness of the vasculature that occurs during both ageing and age-related disorders such as diabetes; 2) age-related degeneration of the intervertebral disc which is associated with low back pain; and 3) commercially important changes in the mechanical properties of ageing skin. A further advantage of the technology, is that by developing its use with standard histological specimens, we can provide mechanical analysis using very small quantities of tissue samples consistent with minimally invasive biopsies. Once these techniques are established and validated we will disseminate the details via scientific publications and invite the wider research community to utilise the approach.
Professor J K Cruickshank	(The University of Manchester)	
Professor C Griffiths	(The University of Manchester)	
Dr M Sherratt	(The University of Manchester)	
Dr R Watson	(The University of Manchester)	

Lifelong Health and Wellbeing Phase 3 - Collaborative Grant Awards		
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Professor Klaus Peter Ebmeier	**University of Oxford**	**PREDICTING MRI ABNORMALITIES WITH LONGITUDINAL DATA OF THE WHITEHALL II SUBSTUDY**
Co-Investigators		Abstract
Professor J R Geddes	(University of Oxford)	The programme will combine multi-modal imaging and cutting edge analysis of brain structure, brain perfusion, white matter integrity and brain function with a rich longitudinal data set, the Whitehall II cohort. Twenty-five year antecedent vascular and metabolic risk trajectories and morbidity, antecedent levels of physical and mental activity, baseline cognitive performance levels and 15-year slopes of memory decrement over time, history of depressed mood, genotype, and measured resilience will be used to model brain changes in 800 subjects. Hypotheses are predicated on the assumption that the brain responds adaptively to any age or illness-related lesion with compensating functional reorganization and repair that result in the restitution of cognitive and mental function and behaviour. Damage to this 'scaffolding structure', e.g. by widespread vascular damage to executive brain networks, will lead to decompensation of function, and result in clinical presentation with e.g. dementia or depression. We would thus predict that highly functioning individuals may show structural or functional lesions in e.g. hippocampal networks, associated with an increase in activity in scaffolding (e.g. executive) networks. We further predict that such active protective mechanisms will be dependent on such antecedents as vascular risk related behaviour and (mental) activity, in addition to other factors less amenable to treatment and prevention. The presence of detailed and frequently sampled cohort data in the Whitehall II study allows for a unique prospective analysis of the effects of socio-demographic, physical and behavioural factors on brain integrity, and a powerful study design strategy that makes it possible to compare the two extreme expressions of a clinical feature (e.g. depression with first onset in the 60s versus no depressive symptoms over at least 25 years), by controlling and stratifying for potential confounders, such as the conventional variables age, gender and occupational level, but also crucial mechanistic factors, such as vascular risk. Short of a prospective interventional study this will be the most effective and efficient way of establishing time directed associations between socially important variables and brain structure and function in older age. Considering the crucial importance that the growing group of active over 60 year olds will have in society, and the effect that a small shift from disabled to able people will have in this part of society, this is important research.
Professor M J Kivimaki	(University College London)	
Dr C E Mackay	(University of Oxford)	
Professor A Singh-Manoux	(The French Institute of Health and Medical Research)	
Professor S Smith	(University of Oxford)	

Lifelong Health and Wellbeing Phase 3 - Collaborative Grant Awards		
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Professor Deborah Anne Lawlor	**University of Bristol**	**The menopausal transition and healthy ageing and wellbeing**
Co-Investigators		Abstract
Mr I Beesley	(University of Bolton)	Unlike most physiological systems in humans, which age slowly and continue to function to some extent until death, in women reproductive function is lost abruptly and completely in middle-age. The menopause is a clear marker of the end of reproduction and has important biological, health and social implications for healthy ageing. Our hypotheses are that (i) the menopausal transition (MT) will be importantly related to changes in health, social and economic characteristics; (ii) some of these changes will be temporary and some will be beneficial to long term health and well-being and others detrimental to it; (iii) health related changes will be influenced by lifestyle changes, menopausal hormonal changes and the influence of menopausal hormonal changes on DNA methylation and (iv) that lifestyle, social, economic and health related changes over the MT will influence body image, family relations, employment and income, and vice versa. Because of the complex interplay of lifestyle, molecular genetic, hormonal, health, social and economic outcomes that are likely to influence how the MT influences healthy ageing and wellbeing it is essential that a multidisciplinary and large-scale approach is used to address our hypotheses. Our proposal is unique in that it will be the largest study to date to explore changes over the MT (2800 women will be studied) and will be the only study with a wealth of previously collected (over 20 years) early adulthood data on reproductive health, general health and lifestyle before the menopause, existence of genome wide data and prospectively collected data on offspring and partners. Our research will clarify the relationship between MT changes and healthy ageing and wellbeing in women and how these relate to health and wellbeing in their partners and children.
Professor G Davey Smith	(University of Bristol)	
Professor J Donovan	(University of Bristol)	
Professor D Kuh	(MRC Unit for Lifelong Health and Ageing)	
Professor S Nelson	(University of Glasgow)	
Dr A Owen-Smith	(University of Bristol)	
Professor C Propper	(University of Bristol)	
Dr C Relton	(Newcastle University)	
Dr S M Ring	(University of Bristol)	
Professor N Sattar	(Glasgow Royal Infirmary)	
Professor N Sattar	(University of Glasgow)	
Professor S L Smith	(University of Bristol)	
Dr K Tilling	(University of Bristol)	
Professor J Tobias	(University of Bristol)	

Lifelong Health and Wellbeing Phase 3 - Collaborative Grant Awards		
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Professor Gail Mountain	**University of Sheffield**	**Lifestyle Matters**
Co-Investigators		Abstract
Professor J E Brazier	(University of Sheffield)	The research being proposed is a population based clinical and cost evaluation of an intervention which aims to assist older people to make positive changes to their lifestyle and by doing so avoid the decline associated with poor mental health and low quality of life. The intervention 'Lifestyle Matters' is recommended in NICE guidance but has not been robustly evaluated. It is delivered weekly to the same group of older people in a local community venue by facilitators who are trained using an existing resource and then supervised throughout. The intervention involves using a range of techniques to enable individuals to learn new activities and/or re-engage with neglected activities in a supportive atmosphere. The group intervention extends over four months and is supplemented by monthly individual sessions for each participant as described in the published manualised programme. The research will involve recruiting people aged 65 years and over to the study from local communities in Bangor and Sheffield. Those who meet the study inclusion criteria will be randomised to either receive the intervention or to participate in data collection for the purposes of the study. The aim is to recruit 268 older people, with 134 being randomised to receive the intervention. All those recruited will be asked to complete a range of measures in questionnaire format at the outset, immediately following cessation of intervention delivery (4 months later) and once more 12 months after baseline measurement. They will all be asked to record their use of health and social care services. The primary study outcome is improved mental health. Secondary outcomes include overall quality of life, resilience and self efficacy, experience of loneliness and depressive symptoms and costs of involvement in the intervention compared with use of other existing services. Data will be analysed to determine whether the intervention has positive effect upon mental well being as well as the other factors mentioned above, and if there is a positive effect, to examine if it is maintained over time. We also wish to explore the possibilities that this intervention might have for others with different needs and at various stages of the life course and will consult locally and nationally to identify the best populations to work with. We will then test the feasibility of Lifestyle Matters with the identified populations in each location by recruiting and delivering the programme and interviewing both facilitators and participants about their experiences.
Dr S Cook	(Sheffield Hallam University)	
Mrs C Craig	(Sheffield Hallam University)	
Mrs C Craig	(Sheffield Hallam University)	
Dr D Hind	(University of Sheffield)	
Dr S J Walters	(University of Sheffield)	
Dr G Windle	(Bangor University)	
Professor R Woods	(Bangor University)	

Lifelong Health and Wellbeing Phase 3 - Collaborative Grant Awards		
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Professor James Nazroo	**The University of Manchester**	**Inequalities in later life frailty and wellbeing: an interdisciplinary approach to causality**
Co-Investigators		Abstract
Professor A Burns	(The University of Manchester)	The challenges posed by the ageing of populations have been repeatedly documented, with recognition of the need to minimise dependency and to maximise social engagement and wellbeing. The proposed research is concerned with examining causal processes relating to frailty and wellbeing (both broadly defined) at older ages. It will use an interdisciplinary approach, bringing together key findings and innovative methods from across disciplines, will be comparative, using similarities and differences across national contexts to get a clearer understanding of policy influences, and will engage a full range of users in the conduct and dissemination of the research. Core data sources will be the English Longitudinal Study of Ageing (ELSA), sister studies in the US and mainland Europe, and a similar study in Canada. ELSA is a multidisciplinary study involving repeat surveys with a representative sample of people aged 50 and older, giving six sets of interview data (each two years apart), three sets of biological data (collected four years apart) and a detailed life-history interview. Data coverage includes: stored DNA and serum suitable for additional genetic, metabolic and biomarker analysis; already analysed biomarkers; direct assessments of cognitive and physical function; direct assessments of physical health; and a range of self-reports covering demographics, economics, health, participation in social, civic and cultural activities, and social networks. These data will be used to: develop measures of frailty and wellbeing; model life-course trajectories; examine the influences of genetics, socioeconomic position, social factors, and gene-environment interactions; explore the relationship of these factors with markers of metabolic processes; and identify factors relating to resilience and vulnerability to adverse events. Key hypotheses to be tested cover: the relationships between life-course trajectories, later life socioeconomic position and frailty and wellbeing; that socioeconomic effects will operate through the hypothalamic pituitary adrenal axis connected to processes relating to anabolic function and inflammation; that resilience and vulnerability can be identified and will result from environmental factors, genes, and gene-environment interactions; and that a detailed study of gene-metabolite-phenotypic interfaces will lead to the discovery of novel pathways to frailty and wellbeing. Traditional statistical approaches will be supplemented with innovative methods to handle missing data (selection models; pattern mixture models; shared parameter models; sensitivity analysis), longitudinal data (multilevel multistate competing risks models; growth mixture and structural equation modelling of trajectories; sequence analysis and optimal matching) and data from different national contexts (Integrative Data Analysis; latent variable approaches; and anchoring vignettes).
Professor A Burns	(The University of Manchester)	
Professor T Chandola	(The University of Manchester)	
Professor R Goodacre	(The University of Manchester)	
Professor M A Horan	(The University of Manchester)	
Dr N Pendleton	(The University of Manchester)	
Dr N Pendleton	(The University of Manchester)	
Dr G Tampubolon	(The University of Manchester)	
Dr G Tampubolon	(The University of Manchester)	
Professor F Wu	(The University of Manchester)	

Lifelong Health and Wellbeing Phase 3 - Collaborative Grant Awards		
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Dr Kai-Michael Toellner	**University of Birmingham**	**Top Jabs - Improving vaccination responses in older adults**
Co-Investigators		Abstract
Professor M Drayson	(University of Birmingham)	Older adults are more susceptible to bacterial and viral infections than young people and the national vaccination programmes against influenza and Streptococcus pneumonia are the primary preventive measure aimed at reducing incidence of these infections. However, the decline in immune function in old age reduces the ability of older individuals to mount successful vaccination responses, with less than half of over 65 year olds producing a protective response to influenza. With age both the quantity and quality of antibody produced is reduced, which will reduce the efficacy of vaccination in older adults. Many older adults are therefore not benefitting from the protection provided by vaccination. There is an urgent need to understand why the vaccination response is compromised in old age and to develop interventions to improve vaccination responses in elders. We plan to address several aspects of the immune response to vaccination in older animals and humans to determine why there is a failure to develop good humoral immune responses in older adults. T cell memory and B cell differentiation are directed by adult lymphoid tissue inducer (LTi) cells. We will test if and how their reduced function impacts on reduced antibody responses in old age. In addition, immune complexes have been used as adjuvants in old mice, and we will study how antigen-masking changes selection and affinity maturation of B lymphocytes in lymphoid tissues in older animals. Crucially, we will test whether antigen-masking can be used as an efficient and novel vaccine adjuvant in older animals. Age related hormonal and metabolic changes also contribute to reduced immune responses. The study will test whether insulin sensitivity is related to vaccination responses, and will test in a small pilot study in animals whether a pharmacological intervention (metformin treatment) can improve vaccine response. Finally, a simple behavioural intervention will be used to modulate efficiency of vaccination responses: Our preliminary data show that diurnal variations in older adults lead to changes in the quality of humoral vaccine responses. We will repeat this in a larger randomised trial and test whether diurnal changes in responsiveness are due to variations in stress hormones or cytokines. If proved effective, this observation will lead to a simple intervention by manipulating the timing of immunization to improve the response to vaccination in older adults.
Professor P J Lane	(University of Birmingham)	
Professor J M Lord	(University of Birmingham)	
Dr A C Phillips	(University of Birmingham)	
Dr J W Tomlinson	(University of Birmingham)	