

ALSPAC activity aligned to Wellcome and MRC key science areas and strategic priorities.

Focus areas/Board	Funder for "focus area/board"	Strategic priority mapping (for MRC and Wellcome)	Example ALSPAC activity	Development and future work for ALSPAC
Understanding health and disease - Biomedical science (Genetic & genomics)	Wellcome	MRC - Research that delivers – Living a long and healthy life (molecular data sets and disease)	Over 20000 participants with GWAS data, 2000 with NGS data, 1000 mother child pairs with multi time point epigenetics and expression data on ~1000 cell lines combined with resources like multi-timepoint metabolomic data has yielded outputs able to define the genetic architecture of the phenome, but also to probe the specific signatures of disease <sup>1-3</sup> .	Not only is ALSPAC able to maintain an important contribution to the understanding of genetic and genomic contributions to complex traits, but the availability of specific samples allows for the screening and analysis of new important and as yet population-untested phenomena such as the frequency and impact of familial hypercholesterolaemia via germline mutation or myeloid leukaemia related haematopoietic changes through somatic mutation.
Understanding health and disease - Biomedical science (Infection & Immunity) MRC Infection and Immunity Board	Wellcome & MRC	MRC - Research that delivers – Resilience & repair (natural protection and immunity)	Previous analyses of infection data from self-report has allowed for the analysis of susceptibility and infection in light of genetic contributions <sup>4,5</sup> , the potential relevance of exogenous factors <sup>6</sup> and in terms of lifecourse patterning <sup>7,8</sup> .	New opportunities are now presenting with the availability of infection titre data (as called for by the recent MRC cohort review) and longitudinal data focused on life course exposures and health outcomes <sup>9</sup> .
Understanding health and disease - Biomedical science (Cell & developmental biology)	Wellcome	MRC - Research that delivers – Living a long and healthy life (molecular data sets and disease)	The availability of biosamples from birth to adulthood has presented opportunities to assess the molecular underpinnings of events which go on to shape development and later life health such as the epigenetic marks left in foetus/child as a result of exposure to cigarette smoke in utero <sup>10</sup> .	With the vast array of biosamples ALSPAC has available it is possible to consider the biological events that feed into the earliest stages of the life course (for example placental function and dynamics), but also to consider the utility of extremely detailed phenotyping (proteomic and metabolomic) of longitudinal samples able to characterise growth and development.
Understanding health and disease - Biomedical science (Physiology & non-communicable disease)	Wellcome	MRC - Research that delivers – Resilience & repair (tissue disease & degeneration) MRC - Research that delivers – Resilience & repair (mental health & well-being) MRC - Research that delivers – Lifestyles affecting health MRC - Research that delivers – Environmental health	Second to none, ALSPAC has an ability to comment on the antecedents of adult disease. There are clear precursors of later life health and with samples of early life and "peak" health participants it is possible to investigate the indolent biological features likely contributing to the rise of disease in the healthy <sup>11</sup> .	The multiple generations of ALSPAC each offer an opportunity to examine physiology and non-communicable disease. Whether it is the examination of cognitive decline in the original parents (now approaching 60 years old), the importance of early presentation of health (or later disease) in the young adults of ALSPAC (30 years) or the important cross-sectional or multi-generation derived experiences of the new born moving through childhood, each of these stages can be explored by the ALSPAC study.
Understanding health and disease – Population health research (Longitudinal population studies) MRC Population systems medicine Board	Wellcome & MRC	MRC - Research that delivers – Living a long and healthy life (life course perspective) MRC - Research that delivers – Lifestyles affecting health MRC - Research that delivers – Environmental health	ALSPAC is an exceptional longitudinal study and specifically a birth cohort. With an excellent track record and clear plans to be an enabling platform for others in the future, ALSPAC represents the ethos of Wellcome LPS and cohort studies from the MRC – yielding (now and in the future) high academic return on efficiently used support <sup>12,13</sup> .	The primary ALSPAC objective is maintain the study as the premier multi-generational birth cohort offering unrivalled access to existing data and samples - whilst providing new data and resources for science focused on the health and characteristics of families, young adults and mother & child through the lifecourse.
Understanding health and disease – Humanities & social science (Cultures, settings & health)	Wellcome	MRC - Research that delivers – Lifestyles affecting health MRC - Research that delivers – Environmental health	Often overlooked, ALSPAC has enormous potential as a generator of social science. Through a mixture of methods, ALSPAC has generated research output focused on modern lifestyle <sup>14,15</sup> , the impact of social behaviour on mental health <sup>16</sup> and the aetiology of social behaviour <sup>17</sup> .	There are substantial developments in this field that ALSPAC will take advantage of. Advanced linkage opportunities and the enhanced use of social media and linked data sets (such as transactional data bases or twitter feeds) present exciting opportunities. Research will not only better characterise the social characteristics ALSPAC, but also develop and test social science methods in the context of substantial retrospectively collected and contextual data sets. We are able to move towards a real opportunity to start quantifying <i>lifestyle</i> and considering which social aspects are policy worthy (see RESEARCH IMPACT 1 – suicide and internet

				use). Lastly, there is the study of ALSPAC itself. Ethnographic work on the ALSAPC study is an importance component of future research.
Understanding health and disease – Supporting research careers	Wellcome	MRC - Supporting scientists – Capacity & skills MRC - Supporting scientists – Research environment	ALSPAC and the data/sample based resource proved by it is a building block for training opportunities and career development. At a graduate level, schemes such as the Wellcome supported 4 year PhD programme Molecular Genetic and Life course epidemiology sees almost all students using the ALSPAC collection ( <a href="http://www.bristol.ac.uk/mgl-epidemiology/">www.bristol.ac.uk/mgl-epidemiology/</a> ). Furthermore, ALSPAC is an important resource for the development of first fellowships and more advanced awards where the quality and flexibility of the study makes it a valuable asset to those local to Bristol and outside.	We already support training activity at all levels through access to ALSPAC data and have been developing access routes for masters and undergraduate programme access in addition to optimising the use of ALSPAC as a resource for supporting research careers. We will look to maintain this, but also to develop an important line of support with the University of Bristol – the training of and development routes for staff members who may or may not come from traditional research backgrounds.
Improving health (public health interventions) Combined with Influencing policy	Wellcome	MRC - Research that delivers – Lifestyles affecting health MRC - Research to people – Securing impact from medical research MRC - Research to people – Ethics, governance & working with decision makers	A core challenge for ALSPAC (as a pregnancy cohort) is in the facilitation of research which is able to lead to intervention. Routes to policy include dedication to open and easy access to data and resources ( <a href="https://wellcome.ac.uk/news/used-effectively-your-research-can-improve-policy-and-practice">https://wellcome.ac.uk/news/used-effectively-your-research-can-improve-policy-and-practice</a> ) and an open and engaging relationship with key sites of policy formation (for example the National Institute for Health and Care Excellence and Parliamentary committees – as we have contributed to before)	ALSPAC will maintain an open and responsive approach to the development of not only policy, but directly to public health interventions. The study will continue to provide infrastructure which will enable intervention guiding science (i.e. using population based epidemiology to generate intervention targets), but will also work with groups such as CLOSER ( <a href="http://www.closer.ac.uk/">www.closer.ac.uk/</a> ) to develop new lines of translation for work undertaken in the study. We will also carefully align activity in the core components of the study to likely public health intervention relevant developments – for example our proposed work collecting cognitive data with collaborators Dementias Platform UK as coordinated with our own MRC PATHFINDER initiative with sister study Born in Bradford.
Engaging the public	Wellcome	MRC - Research to people – Engagement Wellcome - Science education	ALSPAC considers engagement to be a critical focus area. For ALSPAC, there is not only a responsibility to disseminate and promote science to those involved and the wider public, but there is an absolute need to engage in order to maintain the study. There is a constant flow of engagement activity as part of core ALSPAC management.	The key development for engagement is to harness the benefits of working with new Bristol city collaborators (We The Curious - <a href="http://www.wethecurious.org">www.wethecurious.org</a> ) to broaden the reach of the study and to reconnect with those who may have fallen away from the study or who are hard to contact. This is a challenge, but the combination of explicitly designed data collection strategies and multi-pronged outreach activity will be used to maximise general engagement and to ensure the success of the study.
Molecular and cellular medicine	MRC	MRC - Research that delivers – Resilience & repair (tissue disease & degeneration) MRC - Research that delivers – Living a long and healthy life (molecular data sets and disease)	Overlapping with the Wellcome focus on Cell & developmental biology and Physiology & non-communicable disease, there are clear opportunities which have been exploited and remain in terms of molecular and cellular medicine. Another example of the excellent opportunities in ALSPAC come from the study of molecular underpinnings of atopy and skin disease. Not only was the study a major contributor to the dissection of genetic underpinnings of this complex set of phenotypes <sup>18</sup> , but the availability of infrastructure, relevant omic data and contactable and engaged members of the population has allowed for the recruitment and running of detailed and demanding followup work (e.g. punch biopsies).	Strategically the opportunities to continue the omic dissection of the ALSPAC collection continue to develop. In the next 5 years of the study, the G2 (second generation children) of the study will substantially increase in number. Consequently, the opportunity to undertake extremely detailed examination of biosamples from the same event (pregnancy), but years apart in related participants with extensive contextual data (e.g. two generations of related cord blood samples in relation to foetal health outcomes) becomes real. These are exceptional conditions and not only will they be unique to ALSPAC, but if not done they remain unlikely to happen at all.
Neuroscience and mental health	MRC	MRC - Research that delivers – Resilience & repair (mental health & well-being) MRC - Research that delivers – Lifestyles affecting health Wellcome - Mental health	ALSPAC is uniquely placed to examine mental health in exceptional circumstances, but also across life events which may have a precipitating effect <sup>19,20</sup> . Work is underway to examine the causes of and impact of mental health in differing scenarios across the life course and to tie together a broad range of potentially related measures and health outcomes (attention deficit, cognitive function, psychosis, autism (spectrum), depression). ALSPAC has also been an important contributor to studies concentrated on the molecular breakdown of these complex health outcomes <sup>21-23</sup> .	Record linkage, detailed individual participant data collection, omic data sets and a multigeneration data set where one can track similar life course events, but in differing environmental conditions are all assets that ALSPAC makes available for the analysis of neuroscience and mental health. This combined with the increased sampling of a new generation and the radical differences in socio-demographic/communication/economic conditions between generations (over which shared measures are available) makes for a uniquely placed study resource which can generate new insights in this area.
International and global health	MRC	MRC - Going global – International partnerships and shaping the agenda	Recently ALSPAC has been used as a backbone resource for the planning and maturation of cohort and bioresources elsewhere in the world. An excellent example of this is the MRC GCRF supported work ALSPAC is doing with MRC Gambia to enhance and develop the bioresource which accompanies that work. The placement of best practice approaches to bioresource design and research is a critical step and one which ALSPAC can help to facilitate through learning as a result of shared knowledge.	We will continue to offer support to international developments (including helping to support resource construction elsewhere) and studies elsewhere. In addition to this, we will pursue specific research opportunities which are more general than any one scientific question, but which note the utility of ALSPAC and similar resources. CoI Tilling is excellently placed to help guide this and to ensure that the science of the study use and its maximal gain is realised by researchers looking to work with ALSPAC and other collections.

-	-	Wellcome - Diversity and inclusion	Current practice within ALSAPC for researchers, staff and participants is such to ensure equity where at all possible. ALSAPC is committed to promoting equality and diversity for researchers, staff and participants. Minimising attrition and ensuring that equity in access and the opportunity for participants to take part is a key effort and reflected in the effort and systems in place to recruit for all ALSAPC activity. Staff are supported by a robust University policy on equality and diversity ( <a href="http://www.bristol.ac.uk/inclusion">www.bristol.ac.uk/inclusion</a> ) and ALSAPC management looks to uphold the principles of equality and diversity across the study and team.	The formal inclusion of policy for diversity, inclusion and equity is increasingly important for ALSAPC and we will recognise specific stake holders in the pursuit of balance in the way that research is undertaken and that opportunities from it are made available. Stake holders include the participants of ALSAPC, the researchers working on data and the staff and connected personnel to the study. Working with our own Board and the Elizabeth Blackwell Institute at the University of Bristol, we will look to ensure that this is an active area and one which follows the explicit steer of our funders. The recent appointment of a champion for this area within the Elizabeth Blackwell Institute provides an excellent point of referral for this as it progresses ( <a href="http://www.bristol.ac.uk/blackwell/about/edi/">www.bristol.ac.uk/blackwell/about/edi/</a> ).
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\*This table does not represent all focus areas – just those pertinent to ALSAPC activity Strategy/priority areas– main ALSAPC overlap

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