

A photograph showing a group of people in a meeting or workshop. A woman in a green patterned shirt is leaning over a table, looking at something on it. Other people are seated around the table, some looking at the same point of interest. The setting appears to be a bright, indoor space with large windows in the background.

Longitudinal Population Studies Strategy

**Wellcome's Longitudinal
Population Studies Working Group**

July 2017

Executive summary

Opportunity

Longitudinal population studies (LPS), which include cohorts, panel surveys and biobanks, are valuable resources for the scientific community as there is no other way of understanding how biological, social and environmental factors interact over time in a population to produce health outcomes. LPS become more valuable with time, and often develop in unexpected ways, yielding outcomes that could not have been predicted at the outset. However, they are expensive and require long-term commitment. Wellcome has therefore agreed a strategy and funding mechanism to support LPS and related activities, and to maximise their value. We will maintain a flat budget for LPS and related activities over the next five years, but our strategy will enable us to make more co-ordinated and strategic investments.

Overview of strategy

Our strategy brings all LPS investments under one advisory mechanism. It has three aims:

Aim 1 | To fund LPS that contribute to improving human health

We will evaluate existing and new LPS against six criteria, to help us decide which to invest in and which to stop. This will allow us to provide longer term sustainable funding to LPS with the greatest value.

Aim 2 | To encourage the integration of LPS data from a variety of sources

We want to increase the value of LPS by combining cohort data with routine data such as clinical and social care records, and other 'big data' such as environmental measures and social media data. This integration will enable new research questions to be answered. We will support the research community by helping address any ethical, technical or regulatory challenges that might arise.

Aim 3 | To work in partnership with other funders when appropriate

LPS frequently require coordinated funding, and it will be important to work with our funding partners, both in the UK and in low and middle income countries (LMICs), to minimise duplication and maximise the scientific value of our LPS investments.

Funding process

No additional funds are being made available for funding LPS. Rather, we are coordinating under one strategy how we invest in LPS. We will assess funding applications once a year. Preliminary applications will be due in January, with full applications due in April, and interviews and final decisions in July. Applications can be for up to £5 million for a duration of up to 5 years and we will continue to accept applications that make use of co-funding.

Background

The value of longitudinal population studies

The UK hosts a large number of longitudinal population studies (LPS), and is a leader in research across the life course. Hypotheses derived from LPS can be tested through directed research; such hypotheses have included the link between smoking and lung cancer, the influence of early life experience on later life, and the impact of socio-economic position on health and wellbeing.

LPS included in our strategy

LPS follow a group linked by a shared characteristic, such as week of birth, over time. They include cohorts, which follow the same individuals, Health and Demographic Surveillance Systems (HDSS), which repeatedly sample the same population, and biobanks, which collect samples over time.

Our strategy includes LPS that fulfil all the following criteria:

1. they are designed to answer a wide range of scientific questions in the UK or low and middle income countries (LMICs);
2. they usually have more than 1,000 baseline participants;
3. they require long-term funding (>5 years), even if this is not all Wellcome funding.

Our strategy excludes small and time-limited LPS aimed at answering specific research questions within the duration of a research grant, and applications which simply make use of LPS data. Such studies are frequently funded through investigator-initiated schemes, and this will continue.

Recognising that maximising the value of LPS requires many supporting activities and structures, our strategy also includes:

1. networks which harmonise data across LPS;
2. initiatives to link LPS data to other types of data;
3. efforts to improve the accessibility and use of LPS data.

Wellcome's investment in LPS

Wellcome has invested extensively in core support for LPS in the UK and in LMICs.

Most UK investment has been in partnership, but co-funding in LMICs has been considerably smaller. Since 1990 we have provided core funding to nine of the 34 LPS in the UK and have invested in 24 LPS overall. We no longer fund nine of these 24 studies, which were smaller and more geographically-focussed.

Our funding in the UK has focussed on larger, more biomedical studies, and it includes highly regarded resources such as UK Biobank and ALSPAC. Our investments in LMICs are more in HDSS and in networks of LPS, such as the ALPHA and INDEPTH networks.

Overview of strategy

Our strategy brings all investments in LPS and related activities under one advisory mechanism to ensure that:

- we make transparent decisions as to what to support and what to stop;
- we coordinate investments across Wellcome and with other funders where necessary;
- we invest in supportive structures to maximise the value and impact of LPS.

Our strategy has three aims, informed by a review of LPS, discussions with other major funders of LPS, and consultations with the research community.

Aim 1 | To fund longitudinal population studies that contribute to improving human health

We will assess applications from the research community once a year. Six criteria will be used to make funding decisions, and to conduct mid-term reviews of funded LPS as necessary:

1 A clear vision with scientific impact and potential

We need to minimise duplication between LPS to ensure that each resource addresses a unique scientific need. Each LPS should offer a resource that enables important questions to be answered, questions that could not be easily answered through other means. Thus it is critical that every LPS is able to describe its vision, potential scientific impact, and strategic need, including how it fits in the research landscape. A project plan to achieve the vision should be presented from the outset, and should include clear milestones. Resources will be assessed in the context of existing studies, using the MRC Cohort Directory which currently lists all UK LPS. With the MRC and ESRC, we have commissioned the expansion of this database to include LMIC LPS.

2 Robust leadership, management, training and governance structures

Strong leadership and governance are vital to the success of LPS. Resources should have appropriate leadership and governance structures to set strategy and manage risks. This includes a scientific advisory board, which should be actively utilised for scientific advice and horizon scanning. It also includes capacity building structures to develop relevant skills such as data management and biobanking, to ensure the core team has the skills to sustainably maintain the LPS.

3 Effective recruitment, and rigorous data and sample quality and data governance

It is essential that the highest standards of recruitment, data and sample quality, and data governance are aspired to in all aspects of the LPS to maximise the long term potential of the data generated. This includes robust ethical oversight, monitoring of recruitment and attrition rates, adhering to International Organization for Standardization (ISO) and ISBER biobanking standards, transparency and accountability over participant data governance, and obtaining and managing data using defined ethical, clinical and industry standards where available.

There is an opportunity for LPS to lead in the establishment of standards around the collection of biological samples and clinical data in order to maximise opportunities for cross-resource investigations. Much of the work that is being done in other research areas, including genomics and pandemics, is directly applicable to LPS, and the funders have an opportunity to encourage early adoption to maximise data sharing.

4 LPS must be as accessible as possible to researchers

The basic tenet of this strategy is to create resources that will be used by researchers to answer questions that cannot be easily answered through other routes. Thus it is essential that these resources should be made appropriately accessible. Each LPS is expected to actively engage with researchers outside their existing networks to share knowledge, foster new collaborations, and enable data to be used by non-collaborators. Our ongoing work to add LMIC LPS to the MRC Cohort Directory will significantly improve discoverability.

Wellcome is committed to supporting good practice in data management, which will enhance the value and accessibility of LPS data and associated biological samples. We provide the Secretariat for the Expert Advisory Group on Data Access (EAGDA), which is seeking to broaden its scope to include strategic issues in data management and use. This could enable the funders to collaborate further on ensuring that we jointly maximise the value of the data generated by our LPS resources. In 2015, EAGDA published recommendations in relation to data access for LPS. In line with the Funders' Response, to which Wellcome contributed, we have adopted these as the metrics to evaluate this criterion.

5 Value must be maximised through linkage with other data sources

Research would be more effective if data from LPS were integrated with other existing datasets, within appropriate ethical and regulatory frameworks. Such linkage is essential if we are to move towards the integrated data resources outlined in Aim 2. Such datasets include those held by the NHS, government departments, non-governmental organisations, researchers and the private sector. Together, such rapidly increasing volumes of data offer profound research opportunities, and combining the breadth of these data sources with the depth and quality of data collected through LPS would provide exceptional power to understand how complex factors interact to drive individual and

population health. Individual resources will be expected to make positive efforts towards linking with other datasets to increase the range of research questions that can be answered with that resource.

6 Meaningful engagement with participants, the wider public, industry, policy makers and practitioners

There is much to be gained from involving participants and end-users in the research process. A bidirectional dialogue with participants, their families and the wider community not only enhances retention but also improves research design and enhances impact. Each LPS should therefore present an appropriately costed programme for engagement with stakeholders, including a policy for returning findings to participants.

Applications for new LPS will be discussed with Wellcome prior to submission to ensure that only the best applications are considered, and that they are funded in partnership where possible. At the end of their funding cycle, all LPS will go through a competitive renewal process where they are assessed against the criteria above. If the investment is discontinued, efforts will be made to ensure that the data are appropriately curated and that the resource remains accessible.

The associated metrics (essential/discriminatory/not applicable) will be finalised before the scheme is launched in autumn 2017. While these criteria are universal, we recognise that LPS in LMICs operate in a different context to those in the UK, which affects their ability to meet the standards for Wellcome funding. This includes different political, funding and regulatory contexts to the UK. Our strategy will therefore seek to fund LMIC LPS that represent unique research resources and which meet the highest achievable quality standards for the context in which they operate.

We appreciate that additional work may be required by LPS directors, researchers and other stakeholders in order to support existing LPS to meet these criteria, and that this may have resource implications which will be covered by the core grant to the resource.

Aim 2 | To encourage the integration of longitudinal population study data from a variety of sources

Our strategy encourages LPS to integrate data from a variety of sources to allow researchers to answer and pose new questions. Such data might include health, social care and education records; disease registries; ‘wearable’ technology; geocoding; climate data; social media feeds; and commercial data on shopping habits.

This move towards shared resources will exploit ‘big data’, including initiatives in which Wellcome is already involved, like Health Data Research UK. The scientific vision is to establish discoverable, accessible and usable data at a population level to address pressing new questions. In collaboration, we will promote the following areas:

1 Understanding the acceptability and feasibility of creating integrated data resources for researchers, policy makers, participants and citizens

To ensure that integrated data resources are viable, we will need social science and engagement work to understand participants’, researchers’, policy makers’ and the general public’s aspirations and concerns related to the concept of these resources. We will also need to examine the risk of losing LPS participants if re-consenting is required for their wider data to be linked to a platform. These views may differ depending on the type of data source (e.g. centrally collected administrative data versus social media feeds) and the degree of control an individual already has over how that data is collected and used. In some cases, seeking to link additional data sources would be of questionable value and may harm participant trust.

2 Defining new ethical and consent frameworks to enable data from multiple sources to be linked for research

The possibility of linking data across multiple sources adds complexity to consent procedures and can introduce additional risks for identity disclosure. If it is not possible to fully inform participants about how their data could be used, it is essential that robust governance is in place, for example, ensuring there is an independent, accountable decision-making body that can provide assurances that data are being used and linked appropriately and responsibly.

Wellcome has supported initiatives developing best practice for data governance for LPS, such as METADAC, that could be scaled to demonstrate transparency and accountability. These activities will integrate with the system to be set up by the National Data Guardian and the Caldicott Review, which will create an opt-out model for the use of personally identifiable data collected through the health and social care system.

3 Exploiting and extending existing governance frameworks for population-level datasets to allow LPS to gain access to additional sources

Realising this opportunity will require partners such as Health Data Research UK (‘Farr 2’) and NHS digital, as well as more extensive collaboration between researchers. We will work with our community and enhance existing activities to enable the ongoing development of standards, and also to improve transparency and discoverability of data and access arrangements. Ongoing efforts in this area include Health Data Research UK, the Centre for Longitudinal Studies Enhancement Resource (CLOSER), Administrative Data Research Network, the NIHR Health Data Finder, and the work of the Research Advisory Group for NHS Digital and the Office for Strategic Coordination of Health Research.

Driving approaches to allow data interoperability, accessibility and analysis

It is widely recognised that increased capacity in technology and methodology-based skills (including health informatics and bio-statistics) is needed to drive forward a new research agenda towards integrated data resources. The following methodological developments are needed in order to enable a shift to integrated data resources, which could be funded as cross-cutting investments:

- Methods to inform regulatory or organisational changes to improve access to data. Research is needed to improve understanding of how decisions are made about access to linked data. This could inform more timely, evidence-based and ethically acceptable processes for access.
- Methods to improve data linkage and analysis of complex data. Research methods are needed to underpin efficient linkage of multiple datasets, to quantify potential biases resulting from linkage and how this impacts on results, and to handle linkage error in data analyses. A study to investigate linkage procedures and management in different countries would be very informative.

Internal activities we will undertake to support Aim 2 include:

- Work to understand which types of data are most important to be linked to LPS data, the feasibility of making these links, and which of our current LPS investments would be most suitable for developing into integrated data resources.
- Funds to support social science and engagement work with participants and citizens around the integrated data resources concept, to ensure that such a model could successfully recruit participants and to develop appropriate ethical frameworks and consent models.

Aim 3 | To work in partnership with other funders when appropriate

Working in partnership is essential to achieve Aims 1 and 2 and to provide more sustainable funding to valuable resources. It will continue to be Wellcome's preferred mode of funding for large LPS, especially in the UK.

Implementation

Application process

Applications will be considered once a year, with the first call launching in autumn 2017. Preliminary applications will be due in January 2018, with invited full applications due in April 2018. Shortlisted applications will be sent for peer review, followed by interviews and funding decisions in July 2018.

We strongly encourage all studies applying for support for the core costs of maintaining LPS resources under Aim 1 of our strategy to speak to us before submitting an application. Grants can include some level of answering scientific questions, but the balance of the application should be on core costs. Applications for LPS we have not previously funded will only be considered after an initial conversation with us, prior to submitting a preliminary application.

We will continue to welcome applications to use data from LPS to answer important scientific questions, but will consider these through our other funding schemes, for example Investigator Awards, Collaborative Awards and Fellowships.

Level of funding

We will continue a flat investment in LPS, with no additional funds being made available. Applications to support the core costs of LPS can be for up to £5 million for a duration of up to 5 years, and we will continue to accept applications that make use of co-funding. Applications will additionally be eligible to apply for public engagement funding as part of their grant to support their work.

Wellcome exists to improve health for everyone by helping great ideas to thrive.

We're a global charitable foundation, both politically and financially independent.

We support scientists and researchers, take on big problems, fuel imaginations and spark debate.

**Wellcome Trust, 215 Euston Road, London NW1 2BE, United Kingdom
T +44 (0)20 7611 8888, E contact@wellcome.ac.uk, wellcome.ac.uk**

The Wellcome Trust is a charity registered in England and Wales, no. 210183.
Its sole trustee is The Wellcome Trust Limited, a company registered in England and Wales, no. 2711000
(whose registered office is at 215 Euston Road, London NW1 2BE, UK). SI-6768/06-2017/LP