Portfolio Review Summary

Population and Public Health, 1990–2011

April 2013

wellcome trust

Population and public health

Key
- Scientific advance
- Advance in knowledge
- Funding development
- Policy development

Eighth century BCE
Earliest known reference to smallpox inoculation

Fifth century BCE
Hippocrates establishes foundations of modern medicine

Tenth to 15th century
People with leprosy isolated for disease control

1671
The Midwives Book published in England

1717
Malaria linked to exposure to mosquitoes

1753
Treatise on Scurvy published

1000 | 500 | CE | 500 | 1000 | 1500

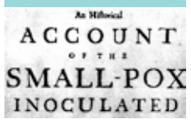
180–160 BCE
Concept of plague developed

1500s
Syphilis spreads through Europe

Mid-1500s
Regulations to prevent bubonic plague introduced in Europe

1700
Diseases of Workers published

1721–22
Inoculation for smallpox introduced in Britain



1796
Immunisation with matter from cowpox pustules is trialled

1840 | 1850 | 1860 | 1870 | 1880 | 1890 | 1900 | 1910 | 1920 | 1930 | 1940 | 1950 | 1960 | 1970

1842
Chadwick's *Report on Sanitary Conditions* published

1845
The Lunacy Act

1848
The Public Health Act

1854
Spread of cholera attributed to contaminated water

1861
Florence Nightingale establishes school of nursing

1870
Pasteurisation process discovered

1882
Cause of tuberculosis identified as *Mycobacterium tuberculosis*

1898
Mosquitoes confirmed as malaria vector

Early 20th century
Germ theory developed

1918–19
Pandemic influenza causes more than 50 million fatalities across the world

1920
First human trials with the attenuated viable vaccine Bacille Calmette-Guérin (BCG)

1920s
Technology to mass produce latex condoms developed

1928
Penicillin discovered

1930
National Birth Control Council formed in the UK

1939–45
World War II prompts global action against malaria

1943
Streptomycin developed

1946
World Health Organization (WHO) founded

1950s
Vaccines for polio prevention developed by American medical researchers

1954
Link between smoking and lung cancer established

1958
The National Child Development Study (1958 Birth Cohort) launched

1960
First oral contraceptive pill approved

1970
Victoria, Australia, becomes first state to legislate compulsory seat belt use

1970s
Asylums to treat mental illness patients gradually replaced by pharmaceutical treatments

1977
Smallpox eradicated worldwide

1921
UK's first family planning clinic founded

1935
Prontosil, the first commercially available antimicrobial, developed

1940s
Large-scale food fortification begins

1945
Penicillin-resistant *Staphylococcus aureus* emerges

1948
Britain's NHS established

Randomised controlled trials (RCTs) introduced

1953
BCG vaccination introduced in secondary schools in the UK

1955
Research on the link between seat belt use and injury prevention in automobiles published

1961
Methicillin-resistant *S. aureus* (MRSA) emerges in the UK

1967
Association for the Study of Obesity (ASO) established

1974
WHO launches Expanded Program of Immunization

1978
Declaration of Alma-Ata

1980 | 1981 | 1982 | 1983 | 1984 | 1985 | 1986 | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011

1981
First documented cases of AIDS reported in the USA

1984
Researchers in France and the USA discover the retrovirus responsible for AIDS

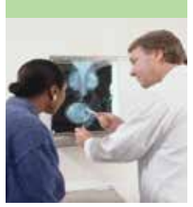
Demographic and Health Surveys project launched

1986
Ottawa Charter frames the 'new public health'

1987
First antiretroviral HIV drug made available

WHO launches Global Programme on AIDS

1988
Widespread breast screening introduced in the UK



1991
A large-scale birth cohort study, the Avon Longitudinal Study of Parents and Children (ALSPAC), begins with the recruitment of more than 14 500 pregnant women in the Avon area of England

1990
The National Surveys of Sexual Attitudes and Lifestyles (NATSAL) launched

Human Genome Project begins

1990s
Decline in sudden infant death syndrome (SIDS) after campaigns in Europe and the USA

1992
Hib vaccine becomes part of the routine childhood immunisation schedule in the UK

1993
WHO declares TB a global emergency

Cochrane Collaboration launched

World Development Report 1993: Investing in health published by the World Bank

1994
The UN holds the International Conference on Population and Development in Cairo, Egypt; the meeting adopts recommendations for improving reproductive health services and the position of women in society

The WHO Region of the Americas (36 countries) is certified polio-free

1995
The Barker Hypothesis developed

Directly observed treatment, short-course (DOTS) strategy for controlling TB launched

1996
World Health Assembly passes resolution on violence as a public health issue

1998
Link between MMR vaccine and risk of autism suggested in the *Lancet*, causing major public health scare and a rise in measles in the UK, despite the later retraction of the findings

WHO launches the Roll Back Malaria Campaign

2000
Millennium Development Goals (MDG) launched

The WHO Western Pacific Region (37 countries and areas, including China) is certified polio-free.

UN establishes the Millennium Development Goals

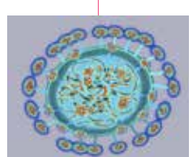
2001
First HIV testing in the Demographic and Health Surveys

UN holds special General Assembly session on HIV/AIDS

2002
Global Fund to Fight HIV/AIDS, Malaria and Tuberculosis launched

UK Biobank project approved

The WHO European Region (51 countries) is certified polio-free



2003
Global outbreak of SARS

2005
Framework Convention on Tobacco Control established

2006
European Commission launches *E-health ERA Project* to help establish a European e-health research agenda

ACTs (artemisinin-based combination therapies) developed and recommended by WHO as first-line malaria treatment

WHO reports evidence of human-to-human transmission of H5N1

2007
Health Act prohibits smoking in most enclosed spaces in the UK

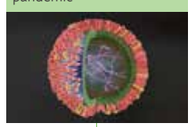
The WHO and UNAIDS announce recommendations on male circumcision for HIV prevention

2008
HPV vaccination for girls aged 12–13 provided in schools in the UK

Commission on the Social Determinants of Health publishes final report

GAIN-UNICEF Universal Salt Iodization Partnership Project established

2009
WHO declares H1N1 pandemic



2011
UN High-Level Meeting on Non-Communicable Diseases

UK Government calls for action on obesity in England

Phase III trial of RTS,S/AS01 malaria vaccine yields first results

UN High-Level Meeting on AIDS

Unless stated, all images are courtesy of the Wellcome Library, London (**images.wellcome.ac.uk**).
Fifth century BCE: Hippocrates. **180–160 BCE:** Galen of Pergamon, who wrote repeatedly about the Antonine Plague. **Tenth to 15th century:** A lepers' retreat (15th century). **1671:** The title page from the third edition of *The Compleat Midwife's Companion*. **1700:** Bernardino Ramazzini. **1717:** A mosquito feeding. **1721–22:** The title page from *An Historical Account of the Small-pox Inoculated in New England*. **1753:** The title page from *A Treatise of the Scurvy*. **1796:** A hand infected with cowpox. **1898:** Sir Ronald Ross. **Early 20th century:** The Germ Theory of Putrefaction, from the papers of Joseph Lister. **1921:** An early birth control clinic. **1928:** Sir Alexander Fleming. **1935:** A tube of Prontosil tablets. *Science Museum, London/Wellcome Images* **1939–45:** A colour lithograph to warn about mosquitoes. **1943:** A Salman Waksman. **1945:** Penicillin-resistant *Staphylococcus aureus*. *Wellcome Images* **1950s:** Polio vaccine is dropped onto a sugar lump for a child. **1954:** A woman smoking. *Anthea Sieveking/Wellcome Images* **1955:** A model of a vintage Porsche. **1960:** Oral contraceptive pills. *Wellcome Images* **1974:** Syringes and needles. *Paul Griggs/Wellcome Images* **1977:** Detail from a Japanese woodcut representing smallpox being repelled. **1978:** Digital artwork on diagnosis and treatment. *Neil Leslie/Wellcome Images* **1984:** Cut-away model of HIV. *John Wildgoose/Wellcome Images* **1987:** AIDS ribbon. *Stevie Taylor/Wellcome Images* **1988:** Mammography consultation. *Wellcome Images* **1990s:** A baby lying on his back (considered by doctors the best sleeping position to avoid SIDS). *Anthea Sieveking/Wellcome Images* **1991:** Schoolchildren. *Fiona Pragoff/Wellcome Images* **1992:** A baby receives the Hib, diphtheria and whooping cough vaccine. *Wellcome Images* **1995:** Tuberculosis seen via X-ray. *Wellcome Images* **1998:** A mosquito on a bednet in contact with skin. *Wellcome Images* **2001:** A travelling HIV testing clinic. *Clive Chilvers/Wellcome Images* **2002:** Test-tubes at the UK Biobank. **2003:** SARS illustration. *Wellcome Images* **2009:** A model of the H1N1 virus ('swine flu'). *Anna Tanczos/Wellcome Images*

The Wellcome Trust portfolio review on population and public health was designed to describe the key breakthroughs in population and public health-related research over the past two decades and to identify the Trust's role within this.

Between 1990 and 2011, the Wellcome Trust awarded 1741 grants (totalling £634 million) to population and public health-focused research, representing nine per cent of total funding commitment over this time period. Funding has been awarded within the UK and internationally, to researchers at different career stages and via project-based grants.

In addition, more than £204m has been allocated during this time for core support and infrastructure at Wellcome Trust Centres and the Major Overseas Programmes in South-east Asia, Kenya and Malawi; much of their research has ultimate implications for population and public health research.

In this field of research, the Trust has actively engaged in several funding partnerships, including one with the Medical Research Council and UK Department of Health for UK Biobank, one with the UK Department for International Development in its Health Research Capacity Strengthening Initiative, and one with the Indian Government to support the Public Health Foundation of India to build capacity to translate research into practice. In this area of research, perhaps more than any other supported by the Trust in recent decades, funding has been international in much of its focus.

This is an edited summary of the Population and Public Health Portfolio Review. The full version can be downloaded at **www.wellcome.ac.uk/populationhealth**.

Over the past two decades, the Wellcome Trust has supported a range of population and public health-based research activities and initiatives (both in the UK and in low- and middle-income countries) that have contributed to key developments in the field, such as new guidelines for HIV and malaria prevention.

A total of 546 population and public health grants, totalling £145m, have been career-based, supporting individual researchers. These include studentships (£15m), early career fellowships (£31m), intermediate fellowships (£35m), Senior and Principal research fellowships (£61m), and the Investigator Awards scheme (£3m).

1195 grants, totalling £489m, were awarded to research and project support. These include strategic awards (£60m), equipment grants (£5m), project grants (£132m) and programme grants (£120m).

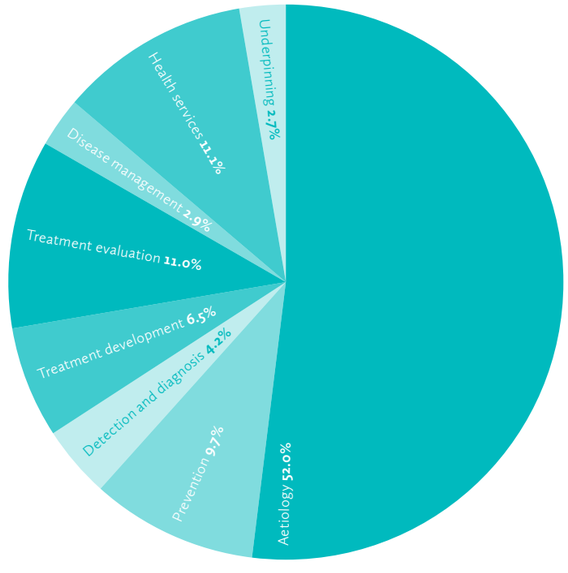
An additional 47 grants, totalling £204m, were allocated for core support and infrastructure at Wellcome Trust Centres and the Major Overseas Programmes in South-east Asia, Kenya and Malawi. These grants were kept separate during analysis because the funds mainly support infrastructure that facilitates population and public health research.

To provide an overview of the subject focus of the population and public health-related grants funded by the Trust over the past two decades, all grants were classified according to the Health Research Classification System (HRCS).[1] The distribution of Trust grants by research activity type is represented in Figure 1. Between 1990 and 2011:

- More than half (52 per cent) of Trust population and public health funding supported aetiology-focused research, which includes the modelling of complex epidemiological data.
- 11.1 per cent of research supported health services research, which includes the evaluation of health and social care interventions, and healthcare policy.
- Treatment development and treatment evaluation accounted for 6.5 per cent and 11 per cent of funding, respectively. Treatment development includes therapeutic discovery, development and testing in model and preclinical systems. Treatment evaluation includes the testing and evaluation of therapeutic interventions.

1 The HRCS, which was developed in 2004/05, categorises research according to area of health or disease and the type of research activity taking place. Full details of the HRCS can be found on the UK Clinical Research Collaboration's website, **www.ukcrc.org/researchcoordination/**.

Figure 1. Proportion of population and public health research spend by research activity, 1990–2011

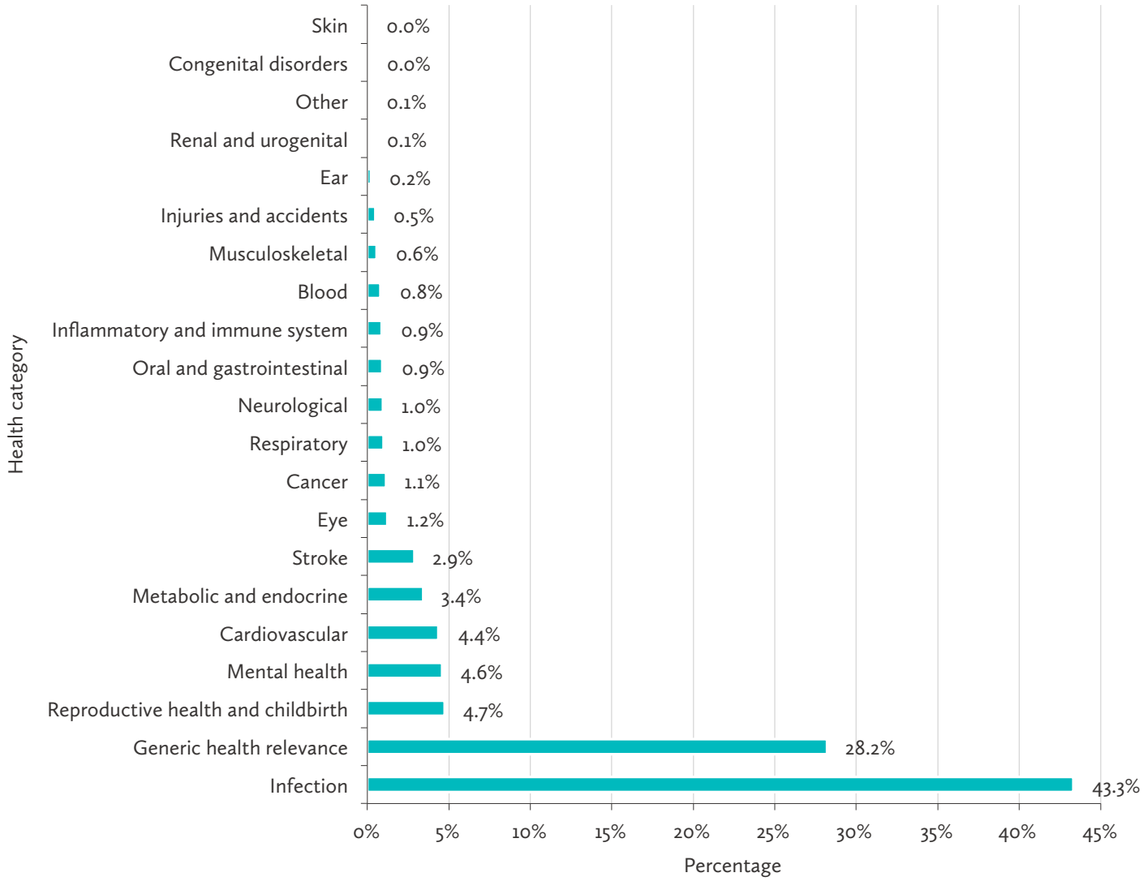


Base: 1765 Wellcome Trust grants associated with population and public health research. Total spend: £837m.
Source: Wellcome Trust AS400 grant system.

The HRCS includes categories for the classification of 'health' (or disease) type; the relative distribution of Wellcome Trust population and public health research funding across these categories is presented in Figure 2.

The highest proportion of funds (43.3 per cent) have been directed at 'infection', which includes pathogenic diseases, HIV/AIDS, sexually transmitted infections and research on infection and infectious agents. In addition, more than a quarter of funds (28.2 per cent) have been allocated to research of 'generic health relevance', which is likely to reflect the Trust's investments in cohort studies and prospective longitudinal research.

Figure 2. Proportion of population and public health research spend on health-specific categories, 1990–2011

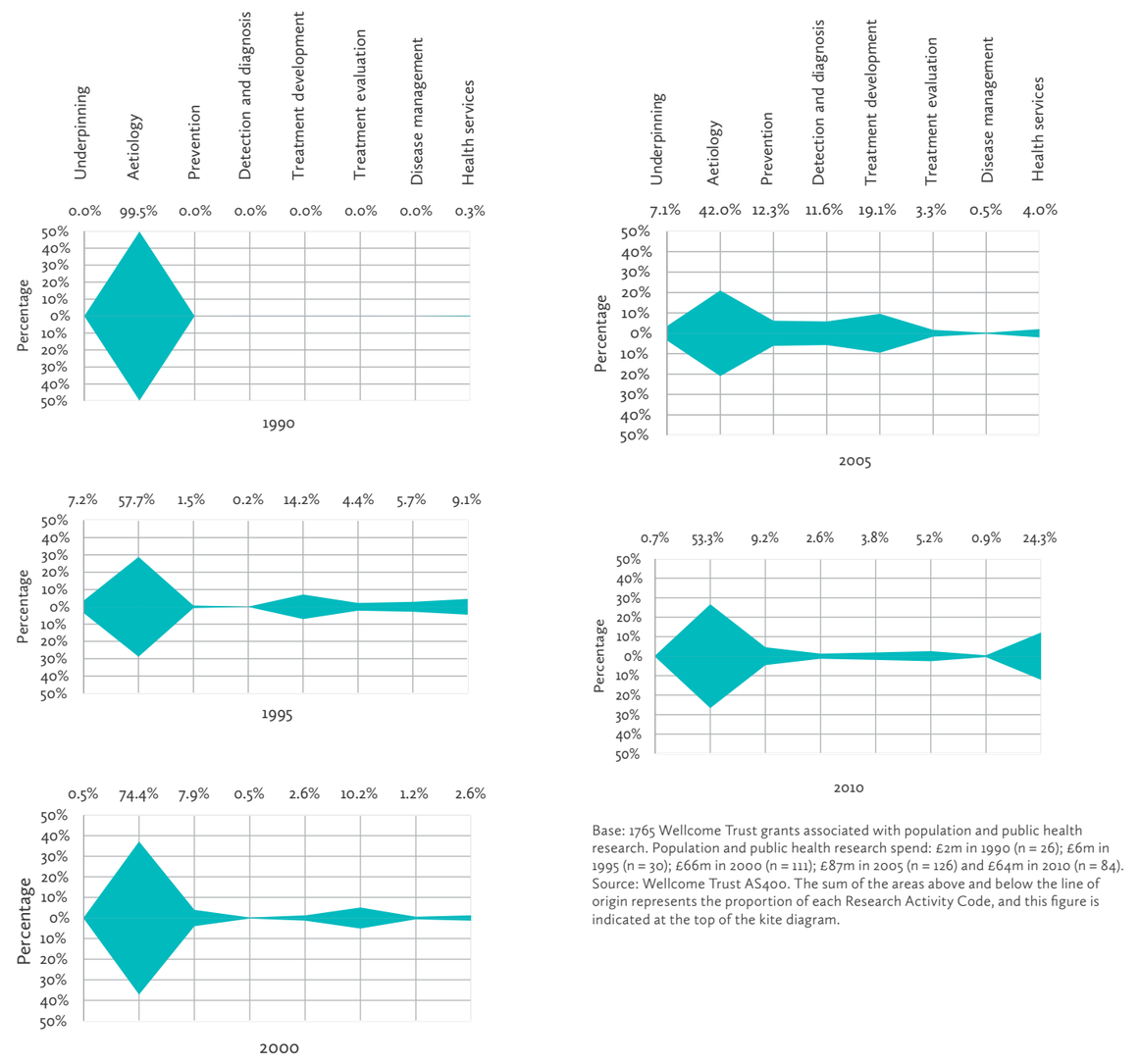


Base: 1765 Wellcome Trust grants associated with population and public health research.
Total spend: £837m.
Source: Wellcome Trust AS400 grant system.

Wellcome Trust and population and public health research
Detailed view

The change in the proportion of Wellcome Trust population and public health research spending can be seen in Figure 3, below. Research funding has diversified from 1990, when it was spent almost entirely on aetiology, to include all the disciplines listed above, albeit at lower levels.

Figure 3. Change in proportion of population and public health research spending between 1990 and 2010



Base: 1765 Wellcome Trust grants associated with population and public health research. Population and public health research spend: £2m in 1990 (n = 26); £6m in 1995 (n = 30); £66m in 2000 (n = 111); £87m in 2005 (n = 126) and £64m in 2010 (n = 84).
Source: Wellcome Trust AS400. The sum of the areas above and below the line of origin represents the proportion of each Research Activity Code, and this figure is indicated at the top of the kite diagram.

In 1996, the Trust established its Population Studies Programme, which was funded for five years before evolving to become the Health Consequences of Population Change Programme in 2000. This five-year, £65m programme was designed to support researchers and projects that addressed the changing pattern of disease in low- and middle-income countries, and the relationship between five key drivers of population change: growth, migration, urbanisation, ageing and lifestyle changes.

In 2004, the population and public health stream was established, with an expanded remit that removed the need for a fixed-term, focused programme. The stream covers research into the determinants of infectious and non-communicable disease and the quality of life in populations, and it aims to provide a sound evidence base to inform decisions in public health. Promoting translation into policy and practice, and fostering disease prevention approaches, are other important aims. The stream also provided for major resources, such as ongoing, large-scale prospective cohort studies in the UK and overseas.

In 2008, the Wellcome Trust and the UK Department for International Development jointly provided £10m over five years to fund the Health Research Capacity Strengthening Initiative.[2] Its aim is to strengthen capacity for the generation of health research knowledge and to improve its use in evidence-based decision making and policy formulation. The Health Research Capacity Strengthening Initiative has led to the establishment of the Consortium for National Health Research in Kenya and the National Commission for Science and Technology in Malawi.

In 2009, the Wellcome Trust introduced the £30m African Institutions Initiative to help African universities and research institutions to effectively manage research projects and train promising scientists.[3] In 2009, the Trust made awards to seven international and pan-African consortia, each led by an African institution. In total, 51 institutions from 18 African countries are involved.

Four awards for initiatives in Africa (totalling £20m) and three awards to programmes in India (totalling £15m) were made in 2008. They included a partnership between the Public Health Foundation of India (PHFI) and a consortium of UK universities to train multidisciplinary researchers who will populate the Indian Institutes of Public Health and strengthen the national public health workforce (see the PHFI case study).[4] The Wellcome Trust/DBT India Alliance, a joint initiative between the Wellcome Trust and the Indian Department of Biotechnology, was also launched in 2008, to support research fellowship programmes that strengthen biomedical sciences in India.

Fellowships in Public Health and Tropical Medicine were introduced in 2006, to provide support for researchers from low- or middle-income countries wishing to carry out work on diseases of importance to local, national and global health. To nurture and build research capacity in public health and tropical medicine, the Wellcome Trust set up the Public Health and Tropical Medicine Interview Committee (PHATIC) to interview fellowship candidates at training, intermediate and senior levels. Between 2006 and 2011, the Trust received 502 applications for Public Health and Tropical Medicine Fellowships, and 109 awards have been made across 27 countries.

Global Health Trials is a joint £36m initiative between the UK Department for International Development, the Medical Research Council and the Wellcome Trust for late-stage clinical trials of interventions that will improve health in low- and middle-income countries.

The Trust's Technology Transfer Division supports a wide range of translational initiatives with relevance to the population and public health arena. These include the R&D for Affordable Healthcare in India initiative and the Health Innovation Challenge Fund.

2 The HRCS was not included in our funding analysis, which covered Wellcome Trust financial years 1989/1990 and 2007/2008.

3 **africaninstitutionsinitiative.org/**

4 **www.phfi.org/**

Scottish Health Informatics Programme (SHIP)

Impact:

- SHIP is a world leader in the management of electronic patient records, working to provide researchers with access to a wealth of anonymised NHS Scotland data.
- SHIP has published several Scottish public health studies, influencing Scottish Government policy, and is proving a model for the use of electronic patient records in England.

123RF.com

The Scottish Health Informatics Programme (SHIP) is a Scotland-wide collaboration between the NHS and Scottish universities that provides a platform for the management, analysis and linkage of electronic patient records (EPRs).

Scotland is substantially more advanced in this area than England and Wales; all Scottish patients registered with a GP since the 1970s have been allocated a unique patient identification number, maintained in the Community Health Index. During patient care, these numbers allow medical staff to quickly identify an individual's treatment history, but they also provide an opportunity for researchers to assess the effectiveness of health interventions and investigate patterns of disease across Scotland.

SHIP was established in 2008, with funding from the Wellcome Trust, the Medical Research Council, the Economic and Social Research Council, and the Engineering and Physical Sciences Research Council. The Principal Investigator for the project is Professor Andrew Morris, co-Director of the Medical Research Institute at the University of Dundee and Chief Scientist for Scotland.

SHIP has four core programmes, which aim to create secure access to EPRs in addition to investigating the ethical, legal and cultural challenges associated with their use. SHIP has already published a good governance framework for the use of EPRs for research and created a national indexing and linkage service within the NHS. The governance plans, formulated by SHIP's legal team, were informed by extensive engagement with public attitudes to the use of medical records for research.

SHIP also has four research aims: determining whether some clinical trials can be virtualised, by comparing real trial outcomes with information drawn from EPRs; undertaking epidemiological research on a national scale; using EPRs to identify adverse reactions to prescription drugs; and linking EPRs to socioeconomic and environmental data.

Although it is currently a developing resource, data linkage has been used in several health studies in Scotland. SHIP researchers used anonymous linked clinical diabetes and cancer data to show that patients using synthetic insulin were at no greater risk of developing cancer than those using traditional insulin. Linked data were also used to define the higher risk of heart disease and stroke in those with diabetes on a national scale.

The ability to collate and analyse large amounts of complex data is central to the advancement of medical research. The UK has a wealth of routinely collected, high-quality patient data, which could be a powerful resource to improve healthcare practices and public health, yet much of it remains underused.

In 2011, the Prime Minister announced plans to make it easier for scientists to access NHS data, proposing that all patient data would automatically be included in research and that patients who qualify for clinical trials could be contacted directly. Scotland, through its use of SHIP, has become a world leader in the use of EPRs. Although national health systems are devolved, SHIP, along with the Welsh Secure Anonymised Information Linkage (SAIL) system, are providing model systems that NHS England can learn from as it develops its own linked EPR system.

The Avon Longitudinal Study of Parents and Children (ALSPAC)

Impact:

- Research using data from the ALSPAC study has produced findings of public health and policy importance.
- The study has developed an internationally recognised open-access biomedical data resource used by researchers from around the world working in a variety of disciplines.

Avon Longitudinal Study of Parents and Children

The Avon Longitudinal Study of Parents and Children (ALSPAC), based at the University of Bristol, is one of the most detailed and comprehensive prospective birth cohort studies ever undertaken in the UK. It was the first to have a genetic component, including appropriate consent for DNA analysis, built into the design from the outset. Research arising from the study provides key insights into how genetic and environmental factors influence development, health and disease.

ALSPAC began in 1991 with the recruitment of more than 14 500 pregnant women in the Avon area of England. The study has followed the children of these women, born between April 1991 and December 1992, and will continue to do so for the duration of their lives. ALSPAC was launched to investigate the genetic and environmental determinants of childhood disorders, with later work researching chronic diseases and health-related behaviour. ALSPAC's value is in its large amounts of detailed, routinely collected social and biological data and its evolution as a world-class open-access data resource. The study was founded by Professor Jean Golding, who received an OBE for her work on the study in 2012. In 2006, Professor Golding retired from leading the ALSPAC project and Professor George Davey Smith took over as Scientific Director.

From birth to the age of six, data on the participating children were collected mainly by questionnaire, although a 10 per cent subset – the 'Children in Focus' – had six-monthly examinations. From the age of seven, all children and their parents were asked to participate in more detailed assessments every one to two years. These involved physical examinations (including the collection of urine and blood samples), in-depth questionnaires, and interviews about diet, lifestyle, their thoughts and feelings, family relationships and socioeconomic status.

The Wellcome Trust, the Medical Research Council and the University of Bristol provided core support to ALSPAC in 2001 and again in 2006. The Trust and MRC support was renewed in 2011 for a period of three years.

The large amount of data collected by ALSPAC has generated key findings that have influenced several areas of public health policy. For example, the data verified the safety of the Back to Sleep campaign, which promoted placing babies on their backs to sleep. As a consequence of this campaign, levels of sudden infant death syndrome (SIDS), also known as cot death, have fallen dramatically. Other work has shown that using eczema cream containing peanut oil is associated with children developing peanut allergies later in life. The study has also demonstrated that women who eat oily fish regularly during pregnancy have children with higher IQs and better neurological function.

DNA samples have been taken from more than 10 000 children and their mothers, allowing many genome-wide assessment studies to be undertaken. ALSPAC played a substantial part in the discovery of the first gene linked to obesity, the *FTO* gene. The availability of maternal DNA also allows researchers to investigate how a mother's genetic makeup affects fetal development; for example, mothers with mutations in the gene *TCF7L2* had babies with increased birth weight.

ALSPAC is a world-famous research project and biomedical resource, which has received more than 1300 proposals from scientists worldwide to use its varied dataset. It continues to collect data from the original cohort of mothers and young adults, and the project is currently expanding to include fathers, siblings and the third generation – children of the original cohort.

Case studies

UK Biobank

Impact:

- UK Biobank has collected samples and health data from 500 000 participants to help understand the causes of diseases that occur in mid- and later life.
- The resource is one of the most detailed collections of health data in the world.


Test tubes at UK Biobank. *Wellcome Library, London*

In 2002, the Wellcome Trust, the Medical Research Council, the Department of Health and the Scottish Government collaborated to create UK Biobank, a resource for researchers investigating how lifestyle, the environment and genetic factors influence the risk of a wide range of diseases that affect people in mid- to later life. The Trust and the MRC provided initial investments of £28 million each, and the other funders committed an extra £5.5 million.

In total, 500 000 men and women aged between 40 and 69 participated in the study. Recruitment took place between 2006 and 2010 in 22 assessment centres across the UK. The age range 40–69 was chosen because, within a reasonable timeframe, many participants will go on to develop diseases such as cancer, heart disease, diabetes and depression. Volunteers completed detailed health and lifestyle questionnaires, had physical measurements, and provided samples of blood and urine. An additional £6 million was provided by the Trust, the MRC, the Department of Health and British Heart Foundation to enable a more detailed study of a subset of participants, including eye measurements from more than 100 000 people in the UK. When recruitment was completed, around one in 50 of the eligible UK population had participated.

The UK Biobank coordinating centre is located in Stockport, where its state-of-the-art automated freezer facility ensures the accurate processing and storage of millions of samples. Its Chief Executive and Principal Investigator is Rory Collins, BHF Professor of Medicine and Epidemiology at the University of Oxford, who received a knighthood in 2011 for his services to science.

After a public consultation in 2011, the procedures that researchers must follow to access UK Biobank were finalised. The resource was launched in March 2012, and its data and samples are available to approved academic and commercial scientists internationally for all areas of health research that are in the public interest. Information provided to researchers will not identify participants, whose data are anonymised – one of the key components of the study. UK Biobank works within an ethics and governance framework, which describes the ethical, legal and sociological standards that the resource must adhere to, monitored by the independent UK Biobank Ethics and Governance Council.

In 2010, a further £25 million of funding was awarded over a period of five years, split between the MRC and the Wellcome Trust. This award was given to maintain the resource, repeat measurements in some of the volunteers and to establish links to participants' medical and other health-related records.

Typically, big cohort studies like UK Biobank collect either a large amount of data on a small number of people (data 'depth') or a small amount of data on a large number of people (data 'breadth'). UK Biobank has achieved both, making it one of the world's most detailed collections of health data.

The Consortium of Health-Orientated Research in Transitioning Societies (COHORTS)

Impact:

- A long-standing collaboration between five large cohort studies in low- or middle-income countries has shown how early life nutrition affects adult health and economic productivity.
- The Wellcome Trust has supported this collaboration from its inception.

A grandmother feeding a child in rural India. *John and Penny Hubley/Wellcome Images*

Birth cohort studies follow large numbers of participants from birth, collecting information on the part that health, environmental and socioeconomic factors play in their long-term health outcomes and human capital achievements. Many such studies have been undertaken in high-income areas, particularly in northern Europe, but their results cannot necessarily be extrapolated to populations in low- or middle-income nations, where few long-term studies have taken place.

In 2005, the *Lancet* commissioned a series of research papers investigating the impact of maternal and infant nutrition in human health. The second of the papers was to be written by Cesar Victora, Professor of Epidemiology at the Federal University of Pelotas, Brazil, who received funding from the Wellcome Trust to pool the data from five long-term cohort studies in low- or middle-income countries, collaborating with their principal investigators.

The studies in Professor Victora's review all began at – or before – birth and had a follow-up period of at least 15 years. These were the 1982 Pelotas Birth Cohort Study (Brazil), the Institute of Central America and Panama Nutrition Trial (Guatemala), the New Delhi Birth Cohort (India), the Cebu Longitudinal Health and Nutrition Survey (the Philippines) and the Birth to Twenty study (South Africa). In total, more than 10 000 people were enrolled, and the Trust provided funds for both the Brazilian and South African studies. This collaboration allowed researchers to verify whether their results were prevalent across a range of countries, socioeconomic circumstances and cultural backgrounds. For most outcomes, there was remarkably similarity between the five studies: maternal and child undernutrition is strongly associated with less schooling, shorter adult height, lower offspring birth weight and reduced economic productivity.

As a result of this work, Professor Victora applied for renewed funding to strengthen the collaborative network between the studies, which became the Consortium of Health-Orientated Research in Transitioning Societies (COHORTS). This second project, which began in 2007, focused on the effects that rapid growth and breastfeeding during childhood have on adolescent and adult health.

Results showed that infants who began eating solid foods in their first six months of life were more likely to become overweight adults. Having a high birth weight or gaining weight rapidly during the first two years of life was associated with increased height and school performance. Rapid weight gain after two years was not associated with increased performance but was strongly associated with an increased risk of several non-communicable diseases. The third phase of the COHORTS project began in 2009 with a Trust project grant awarded to Professor Linda Richter, from the Human Sciences Research Council, South Africa. Whereas the previous two studies primarily investigated the role of nutrition in child development, this series of analyses looked at how environmental and socioeconomic factors in early life affect growth and adult health.

The unique nature of this collaboration between five large cohort studies from different low- and middle-income countries has enabled large quantities of epidemiological data to be pooled, improving the quality of the results gained. COHORTS has already made substantial contributions to public health knowledge by showing the lasting effects of poor nutrition in early life and that rapid weight gain after two years of life increases the risk of chronic disease. This work will inform national programs to emphasise the importance of appropriate nutrition throughout childhood.

Case studies

HIV and breastfeeding

Impact:

- Professor Coovadia's work in South Africa has shown that exclusive breastfeeding reduces the risk of transmitting HIV from mother to child.
- As a result of this work, international guidelines on best feeding practices have been changed.

Cut-away model of the human immunodeficiency virus. *John Wildgoose/ Wellcome Images*

HIV can be passed from mother to child during pregnancy, delivery or breastfeeding. Although much research had been carried out on HIV transmission during pregnancy and delivery, scientists and policy makers were divided regarding the risks of transmission while breastfeeding.

A study at a Wellcome Trust major overseas programme, the Africa Centre for Health and Population Studies, South Africa, was led by Professor Hoosen "Jerry" Coovadia. The work revealed that exclusive breastfeeding can significantly reduce the risk of HIV transmission from mother to child in infants under six months.

A six-year Wellcome Trust-funded study, which ended in 2007, enrolled 2722 HIV-infected and uninfected pregnant women attending clinics in KwaZulu-Natal. More than 2800 babies were born during the trial and were divided into two groups depending on how their mothers fed them: using breastfeeding exclusively or using a mixture of breast milk and replacement food (formula milk or solids).

The results showed that when the children were fed on breast milk only between the ages of six weeks and six months, there was a 4 per cent risk of postnatal HIV transmission from mother to child. Infants fed on a mixture of formula and breast milk were nearly twice as likely to be infected, and those who also received solid food were almost 11 times as likely to become infected.

The mucous membrane within the intestine is thought to act as a barrier to HIV infection. Breastfeeding strengthens this lining, whereas solid foods might damage it and allow the virus to pass through the intestinal wall. Frequent breastfeeding was also associated with fewer maternal health problems, such as breast abscesses, which can increase the amount of virus in the mother's milk.

In high-income countries, it is recommended that HIV-infected mothers feed their babies exclusively with formula. However, this is not practical in many low-income countries because of the lack of access to clean water, sanitation and sterilising equipment. In addition to increasing HIV risk, diarrhoeal infections from unclean water account for high levels of morbidity and mortality in infants throughout the world. Breastfeeding protects against diarrhoea and other potentially fatal conditions and is thus suggested as the best option.

Professor Coovadia's work has impacted WHO policy, which now states that: "Every effort should be made to accelerate access to antiretrovirals for both maternal health and also prevention of HIV transmission to infants…Even when ARVs are not available mothers should be counseled to exclusively breastfeed in the first six months of life and continue breastfeeding thereafter unless environmental and social circumstances are safe for, and supportive of, replacement feeding."

Kenya major overseas programme

Impact:

- Work from researchers at the KEMRI–Wellcome Trust Research Programme has led to evidence-based policies and practice that can be used to improve public health in Kenya.
- The resulting improvements in clinical practice and epidemiology are applicable to many other African countries.

A mosquito, the vector for malaria, full of blood. *Hugh Sturrock/Wellcome Images*

The KEMRI–Wellcome Trust Research Programme is known internationally for its work tackling malaria and other infectious diseases, particularly bacterial and viral childhood infections. The Programme was formally established in 1989, in partnership with the Kenya Medical Research Institute (KEMRI). It conducts basic and clinical research, and its results feed into local and international health policy. Its aim is to expand the country's capacity to conduct multidisciplinary research that is strong, sustainable and internationally competitive.

Mike English

Professor Mike English is a Wellcome Trust Senior Clinical Fellow who works to improve the delivery of evidence-based care of severely ill children in Kenya. He began working for the KEMRI-Wellcome Trust Research Programme in the Kilifi District of Kenya in 1992 before moving to Nairobi in 2004, where he leads the Child and Newborn Health Group.

In Kenya, 74 in every 1000 children die before their fifth birthday. Diseases such as pneumonia, malaria and diarrhoea are major causes of infant and child mortality. After establishing that rural hospitals were not providing effective care to these populations, Professor English's research has focused on long-term studies initiating and establishing best practices within rural government hospitals. In a 2011 paper, Professor English and colleagues showed that comprehensive implementation strategies are required to improve hospital care for Kenyan children. During this three-year project, eight Kenyan hospitals were assigned to either 'full' or 'control' intervention groups. Those in the full intervention group received clinical guidelines, training, job aides, performance feedback and face-to-face supportive supervision, whereas those in the control group received guidelines, short training, job aides and written performance feedback. Hospitals in the full intervention group completed more admission assessment tasks and incorporated more good clinical practices into their treatments. In addition, a lower proportion of children in these hospitals received inappropriate doses of drugs and managers were more likely to tackle resource and organisational shortcomings.

In 2005 and 2010, work from the Child and Newborn Health Group was used in the development of national treatment guidelines for Kenya, based on locally conducted systematic reviews. These guidelines and the training they are linked to are now widely disseminated in Kenya and have been adopted in Uganda and Rwanda. Professor English continues to work closely with the Kenyan Ministries of Health, the University of Nairobi and the WHO (for whom he acts as a technical advisor and contributes to the *Pocket Book of Hospital Care for Children*).

Bob Snow

Professor Bob Snow is a Wellcome Trust Principal Research Fellow and head of the Malaria Public Health and Epidemiology Group at the KEMRI-Wellcome Trust Research Programme. He is in the top five authors of highly cited malaria research papers worldwide, 1989–2008, and has written over 300 papers on the subject. He is also an advisor to the Kenyan Government and other international panels.

Professor Snow's work mapping malaria transmission and its impact on health evolved into a global initiative known as the Malaria Atlas Project, which began in 2005. Under his directorship, the project has assembled a spatial database containing medical information and satellite-derived climate data to map the burden of two of the most deadly strains of malaria: *Plasmodium falciparum* and *Plasmodium vivax*. This work, provided free to researchers and public health officers, is the first evidence-based map of malaria prevalence and risk and has already begun to provide international agencies with a framework to prioritise investment worldwide.

Case studies

Professor Snow's group has used a combination of operational research and detailed statistical models to guide the Kenyan Government's malaria strategies on delivering insecticide-treated bednets and where to target donor-assisted malaria funding. The team is also working with neighbouring countries to provide research evidence to support the best use of limited financial resources in the treatment, control and elimination of malaria in Somalia, Djibouti, Sudan, Uganda, Malawi and Namibia.

Anthony Scott

Professor Anthony Scott, a Wellcome Trust Senior Clinical Fellow, is Head of the Invasive Bacterial Diseases Group at the KEMRI–Wellcome Trust Research Programme. His work focuses on the evaluation of vaccines in children, particularly those that protect against bacterial pneumococcal disease – a leading cause of infant death in Africa. He also studies the epidemiology of the disease, investigating how its prevalence is linked with that of malaria.

In 2011, work by Professor Scott and colleagues showed that immunising babies against pneumococcus within the first three days of life is both safe and effective. The vaccine given at birth, ten weeks and 14 weeks was shown to be as safe as when given at six, ten and 14 weeks, one of the schedules recommended by WHO. Because many deaths occur before babies receive their first dose of vaccine, early immunisation might have a considerable impact on the health of African children. Professor Scott's work on the epidemiology of pneumococcal disease in Kenya was instrumental in developing a successful application to the Global Alliance for Vaccines and Immunization that meant Kenya became the first African country to provide the vaccine as part of its routine immunisation programme.

His research on *Haemophilus influenzae* type b (Hib) has led to a direct policy change in Kenya. Infection by Hib can cause pneumonia or meningitis, but infection is difficult to diagnose and expensive to treat. Despite these difficulties, the Ministry of Health in Kenya introduced Hib vaccine into the routine childhood immunisation programme in 2001. Professor Scott's work showed that this reduced the incidence of Hib by 88 per cent among children under five. As a result, the Kenyan government has decided to sustain the vaccination programme, which was originally funded by the Global Alliance for Vaccines and Immunization.

Public Health Foundation of India (PHFI)

Impact:

- The PHFI was established to address the shortage of highly qualified public health professionals in India.
- Wellcome Trust funding is supporting initiatives to improve public health capacity in India.

Women carrying water pots. *The Leprosy Mission International/Wellcome Images*

With approximately 30 per cent of its population of 1.2 billion people still living below the poverty line, India faces substantial public health challenges. To address these issues, the Prime Minister of India, Dr Manmohan Singh, founded the Public Health Foundation of India (PHFI) in 2006. India has a weak research base for public health, with few specialists trained to further degree level. The PHFI aims to improve health outcomes in Indians by training a new generation of public health workers.

The PHFI is a public–private partnership comprising government agencies, academic institutions and charitable foundations, including the Wellcome Trust. Professor K Srinath Reddy has been President since its inception. The Foundation has established four Indian Institutes of Public Health (IIPH), located in Gujarat, Andhra Pradesh, Orissa and Delhi. Each IIPH offers teaching and research programmes and is developing its faculty. A PHFI Centre of Excellence in chronic diseases has been established, along with three other centres focusing on cardiometabolic risk reduction, disability-inclusive development and social determinants of health.

In 2008, the Trust awarded a £5 million strategic award to fund Master's degrees, PhD studentships and research grants. This grant was split between India and the UK; the London School of Hygiene and Tropical Medicine was placed in charge of managing the UK consortium. Students undertaking these courses split their time between India and one of 16 UK institutions, and the fieldwork aspect of the study occurs in India. After completing their courses, students are expected to stay in India, working in one of the IIPHs. Currently, 19 PhD studentships are being undertaken and 15 Master's projects have been completed or are in progress as part of the capacity building programme.

In addition to further degrees, the PHFI offers seven postgraduate diplomas – four on campus and three via distance learning – and runs several short training courses on crucial public health issues such as health communication and quantitative analysis. Since they began in 2008, more than 5000 people have completed these short courses, including many government employees – some states are making them mandatory for their staff. Although government-run public health institutes exist in India, they generally do not operate to a standardised qualification level. The PHFI is working to establish an independent accreditation body for degrees in public health.

Research is central to the work of the PHFI. The Trust funding provides India- and UK-based research fellowships and includes grants for Indian research staff to undertake collaborative projects with UK partner institutions. Currently, 11 research grants have been awarded, and 11 fellowships are being undertaken.

India has the highest number of people with diabetes in the world – an estimated 50 million people. A Wellcome Trust Strategic Award made to Professor Shah Ebrahim from the London School of Hygiene and Tropical Medicine led to the establishment of the South Asia Network for Chronic Diseases, a collaboration between the PHFI and the Wellcome Trust Bloomsbury Centre for Clinical Tropical Medicine that aims to strengthen chronic disease research capacity. In other work, a translational award has been made to PHFI researchers to investigate the effectiveness of 'mWELLCARE', mobile phone software for community health centres that will be used to assess a patient's health profile and help inform health workers of best treatment practices. In 2012, a $38 million dollar grant from USAID was awarded to the PHFI to help strengthen the national HIV/AIDS control programme. This is the first time that a consortium led by an Indian NGO has been selected for such a grant.

In February 2012, the Indian Prime Minister announced that India should look to increase its healthcare spending from 1.4 per cent to 2.5 per cent of GDP, at a cost of over $40 billion at today's prices. The Trust is working closely with the India–UK CEO Forum, founded by the Indian and UK Prime Ministers, to investigate how India might develop healthcare provision.

The Wellcome Trust's key influences on the population and public health landscape

We conclude that there are four broad areas where the Wellcome Trust is thought to have made a significant impact on the field:

- its long-term funding of projects and researchers, which has helped to nurture some of the current leaders in the field
- its investment in research capacity building and infrastructure in low- and middle-income countries, which has helped to bring about several major discoveries of relevance to endemic health issues
- its committed support to longitudinal studies, both in the UK and in low- and middle-income countries
- its leading role in the open access and data sharing agenda, which is starting to have a significant impact upon research and associated research management, and policy in the field of population and public health.

Current and future challenges for population and public health research

With the help of experts in the field, through a consultation survey and an in-person group, several current challenges were discussed. In addition to perceived limited funding for population and public health research, the importance of building capacity was a key focus for experts. There was a view that 'population and public health research', as an inherently multidisciplinary field, lacks the cohesiveness and profile (and funding sources) of other scientific and emerging scientific fields and is failing to attract appropriately qualified practitioners.

There was a sense that undergraduates in many biomedical disciplines are not receiving the quantitative and statistical training that is a prerequisite to working in population and public health-related research. Those researchers with appropriate skills are increasingly attracted to other, more fruitful, fields or potentially lucrative professions. Furthermore, there was a view that traditional research funding mechanisms are not ideally structured to support the multidisciplinary nature of most population and public health projects; focus on a Principal Investigator can obscure the importance of other contributors in a population and public health-related project.

As a result, the field is experiencing talent drain, which is not easily addressed without increases in funding. This was seen to be an issue in low-, middle- and high-income countries alike.

> "Attracting high-quality people into our discipline is difficult for a number of reasons: there isn't much of a career trajectory, and the smart folks are often attracted to other disciplines rather than public health, which is seen as low priority."
>
> Wellcome Trust Expert Group on Population and Public Health, June 2012

A third major challenge for the field was the often-cited need for research to be effectively translated into policy. This is something that was especially pertinent for research that focused on population and public health where there might be the opportunity to rapidly translate findings into practice.

The importance of involving public health practitioners and policy makers in research to ensure effective and more rapid translation in practice is well cited (e.g. in the UK House of Lords Science and Technology Committee report from 2011, *Behaviour Change*); however, this engagement is not always done sufficiently or effectively.[5] There was a general consensus that fostering dialogue and the exchange of research between policy makers, researchers and public health practitioners would assist the uptake of research data into the policy decision-making process.

> "We've got the skills to perform research. What we really don't know is how to translate that into practice, with all the political and social factors that influence policy decisions. It seems to me that what's missing is a cadre of people who can actually study how to get research into practice."
>
> Wellcome Trust Expert Group on Population and Public Health, June 2012

In the consultation survey, experts were asked to describe the key factors that could assist in the translation of population and public health research into policy and practice. It was suggested that research funders could play an important part in this and do more to support interaction between researchers and those involved in policy making and implementation; innovative strategies that value dialogue and collaboration are required.

5 www.publications.parliament.uk/pa/ld201012/ldselect/ldsctech/179/179.pdf

Current and future challenges for population and public health research

In terms of future research priorities for the population and public health field, the consultation survey experts highlighted what they perceived as the most important issues that population and public health researchers will face in the future. The responses were endorsed by the Expert Group, who described non-communicable diseases, climate change, and ageing and its associated mental health issues as priorities. Together, these further underpin the need for the structural issues surrounding funding and capacity to be addressed.

> “A key challenge is the obesity epidemic: it’s both local and global, and we have an answer to virtually none of the appropriate questions on how to deal with it.”
>
> Wellcome Trust Expert Group on Population and Public Health, June 2012

It can, however, be difficult to predict what future public health issues might be; the Expert Group discussed how the morbidity and mortality associated with the increased prevalence of smoking and motor vehicle use in the mid-20th century was not predicted. In this light, the Group highlighted the importance of research to explore the potential health impact of the massive increase in the use of communication and mobile technologies among populations – impacts that could be both positive and negative.

In addition, the Expert Group discussed the need for significant development in the tools and techniques used by population and public health-related researchers. While the randomised controlled trial has been used as the mainstay of investigations to understand the efficacy of an intervention, they are not always feasible or the most appropriate study design to assess population-based issues and behavioural traits for which there is an absence of ‘norms’. The expert group argued that considerable investment in research methods is needed to support the rigorous evaluation of public health interventions and programmes, and this rigour will help to build the profile and credibility of the field and potentially speed up the translation and implementation of findings.

> “For the next 20 years – and [this] has been mentioned by several people – there is a need for robust science designs that may not be a randomised controlled trial, which can address new interventions for diseases, issues for the social determinants, issues for how you measure policy. And it seems like that is something that the Wellcome Trust could play a lead role in driving.”
>
> Wellcome Trust Expert Group on Population and Public Health, June 2012

In summary, this review provides several suggestions for the future of population and public health research that funders could work together to help resolve:

- There is a need to consider whether existing funding mechanisms are appropriately structured to support the inherent and valuable multidisciplinarily nature of population and public health research, both in the UK and beyond.
- Population and public health research needs to attract high-quality researchers from a range of different backgrounds to build and sustain capacity. The current profile, relative to other disciplines and professions, may be deterring retention of appropriately trained researchers; could the Wellcome Trust do more?
- One of the key factors that could enhance the profile and impact of population and public health as a field would be an enhanced ability to rigorously assess and evaluate public and population-based interventions and programmes – beyond the randomised controlled trial. Investment in the development of new and novel methodologies is required.
- More could be done to support the translation of research into practice. Can we now develop innovative solutions to speed the translation of research findings into policy and practice?

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