

The Wellcome Trust population initiative

B.M.Ogilvie and I.G.Scott¹

The Wellcome Trust, 183 Euston Road, London NW1 2BE, UK

¹To whom correspondence should be addressed

This paper describes what the Wellcome Trust has done and aims to do through its population initiative. The Trust is required to spend its funds to improve the physical welfare of mankind, and in this context there can be no more important issue than the rapid changes that are occurring in the human population. The Trust's first involvement was to help fund the New Delhi population summit covered by the world's scientific academics in 1993 and, following discussions with authorities in the field, initiated its funding programme in 1995. Through this programme, the Trust hopes to bring about improved understanding of the relationship between reproductive health, population growth, and sustainable development and create cadres of high quality research scientists in relevant disciplines. Uniquely, funding is available under this programme to suitably qualified applicants from any country other than the USA.

Key words: population studies/reproductive health/research training/sustainable development

Background

In mid-1996 the world population totalled 5.8 billion, and it is increasing more rapidly now than at any period in history; -88 million people are added to the population each year (Population Reference Bureau, 1996). Demographers believe that population will continue to increase rapidly well into the next century before it begins to level off. Is this a problem? If so, how should governments, societies and individuals respond? The first World Population Conference was held in 1974, in Bucharest. Since then a number of high-profile international meetings have focused the attention of scientists and scholars, business and political leaders on perhaps the single most complex question for the future of life on earth: what does the human race need to do now to ensure its survival, and the preservation of the global and local ecosystems on which all life on this planet is dependent, into the next century and beyond?

In 1993 the world's scientific academies convened for a population summit in New Delhi, with financial support from the Wellcome Trust and other donors. The joint statement of the 60 academies that participated in the summit called upon governments and international decision-makers, especially

those at the 1994 United Nations International Conference on Population and Development, to take immediate incisive action, and to adopt an integrated policy on population and sustainable development on a global scale (Smith, 1994). The statement counselled that the social, economic and environmental problems caused by an unprecedented expansion in human numbers, required that zero population growth should be achieved within the lifetime of our children. Common to this goal should be improvements in the quality of life for all, both now and for succeeding generations. The statement stressed the essential role of natural and social scientists, engineers and health professionals in developing better understanding of the problems, options, and solutions.

The statement from the New Delhi population summit provided a framework for discussion at the latest United Nations International Conference on Population and Development (Cairo, 1994), which produced a consensus in favour of a fundamental shift in population policies worldwide, away from a focus on fertility control to the promotion of reproductive health, women's empowerment and human rights.

The New Delhi and Cairo meetings provided the Trust with a stimulus to determine whether it might play a role, through provision of research and research training support of relevance to the population issue. David Seemungal of the Trust's unit for policy research in science and medicine (PRISM) undertook a review of expenditure in population-related aid and research available from UK and other sources worldwide. The main findings of his review (Wellcome Trust, 1995) were as follows:

Worldwide expenditure on population-related aid and research in 1994 was estimated to be in the region of US\$4.5 billion. In 1991 the total amount committed in this field was US\$1.3 billion. However, only US\$0.73 billion was actually spent. The report emphasises the important distinction between committed and expenditure figures and discusses the reasons why these figures are different.

Annual global contraceptive sales are estimated to be in the region of US\$2.6 billion to US\$2.9 billion.

It has been estimated that current worldwide expenditure on contraceptive research and development stands at ~US\$60 million. The pharmaceutical industry accounts for ~42% of this amount (US\$25 million).

The pharmaceutical industry research and development (R&D) expenditure on contraceptive research is small (<3%), when compared to the industry average (16-19%) for R&D expenditure as a percentage of sales.

The UK spent >£35 million on population aid and research in 1993.

As far as can be determined, the UK percentage of worldwide publications in population-related research is <10% (comparable to its share in other areas of biomedical research).

The largest UK centre for research in this field is the Centre for Reproductive Biology in Edinburgh.

Estimates submitted at the 1994 International Conference on Population and Development, in Cairo, set the cost of achieving fairly broad reproductive health goals (including population targets) in the year 2000 at ~US\$17 billion and US\$22 billion in the year 2015 (at 1994 prices).

The review was carried out to inform a workshop convened by the Wellcome Trust in January 1995 which brought together 25 distinguished international authorities on population issues. It was chaired by one of the Trust's scientific governors, Professor Roy Anderson FRS, with an opening presentation given by Sir Crispin Tickell, Warden of Green College Oxford, and former British Ambassador to the United Nations. The objective of the workshop was in accord with the Plan of Action agreed at the International Conference on Population and Development (Cairo 1994), in seeking to identify research priorities relating to global population growth, within the broad areas of reproductive health and fertility of women, adolescent sexual health and education, health care delivery and demographic change. Following the analysis of the international funding situation carried out by PRISM and the workshop, the Trust decided to commit up to £50 million over a period of 5 years to a new funding initiative, the Population Studies Programme. The advisory committee for the new programme, the Population Studies Panel, met for the first time in June 1995, when it decided to support research through project and programme grants, and research training through personal fellowships; the funding to be made available on a global basis, except to scientists based in the US. Calls for research proposals, and the advertisement of Research Training Fellowships in Population Studies and Reproductive Health, and in Reproductive Biology, were published in the winter of 1995/1996. Additionally, a competition was announced, for the establishment of an International Centre for Population Studies and Reproductive Health in the African region.

The Trust's overarching intentions for its new programme are that it should bring about improved understanding of the relationship between reproductive health, population growth and sustainable development, and create cadres of high quality researchers in relevant disciplines.

Current funding activities of the Trust's population studies panel

Research training fellowships in reproductive biology

Post-Cairo, the issue of sexual and reproductive health has assumed prominence in terms of research and development aid policy. However, part of the global reproductive health agenda is informed by the need to address the unmet need for contraception. New forms of fertility control, both male- and female-controlled methods are required, particularly in developing countries (and increasingly in the former Soviet Union), where the issues of sexually-transmitted diseases (STD)/human immunodeficiency virus (HIV) prevention and contraception are even more acutely intertwined than they are in Western Europe and North America. The PRISM report

highlighted the relatively poor R&D spending commitment of pharmaceutical companies on contraception (<20% of the average for the drugs/health care sector). A recent meeting on academic-industrial collaboration in contraceptive research (Family Health International/Consortium for Collaboration in Contraceptive Research, 1996) recognized that industry was not active in addressing the contraceptive needs of people in poor countries because it could only commit R&D resources to products which held the promise of profits in wealthy industrialized countries.

The Trust's research training fellowships in the area of reproductive biology address the need for more basic studies of potential utility in the development of new and improved forms of contraception. The awards are tenable for a maximum of 4 years in a medical school or university setting, are for research of relevance to the potential development of novel, safe and effective contraceptive methods. They are intended to provide a period of research training for post-doctoral basic scientists or medical graduates, in an internationally recognized centre of excellence, followed by up to 2 years at the fellow's home institution. They can also be held at one institution only for a maximum period of 3 years, e.g. where a fellow does not need to travel overseas to a centre of research excellence in order to gain the requisite research training. By February 1997, six awards had been made. The recipients were Australian, British, Chinese, and German. Their studies, to be undertaken at universities in Australia, Canada, China and the UK, will provide them with an opportunity to become independent research scientists through high quality fundamental or applied research in reproductive biology as it relates to contraceptive research and development.

Dr Eileen McLaughlin will study the heterodimeric sperm surface membrane glycoprotein fertilin, a potential immuno-contraceptive, at the University of Bristol. In research starting at Nottingham University and continuing at the State Key Laboratory of Reproductive Biology, Beijing, Dr Feng Qiang will study the molecular and cellular mechanisms of involvement of extracellular matrix degradation in the processes of implantation and parturition in primates. Dr Paul Riley will investigate the role of helix-loop-helix transcription factors in trophoblast development, at the Mount Sinai Hospital, Toronto, Canada. Dr Xiao Li Feng will take forward a study of early molecular events in human endometrial decidualization, initially at the Royal Postgraduate Medical School, and subsequently at the Zhejiang Institute of Family Planning Research in Hangzhou, People's Republic of China. At Monash University in Australia, Dr Liza O'Donnell will investigate the hormonal regulation of the mechanisms involved in the attachment of round spermatids to Sertoli cells *in vitro*, at Prince Henry's Institute of Medical Research; and Dr Stefan Schlatt will evaluate testicular stem cells as a target for the development of a male contraceptive at the Institute of Reproduction and Development.

Research training fellowships in population studies and reproductive health

These awards, like those for Reproductive Biology, are available on a 4 year, two-site basis. They are for studies in

the social and health science fields, addressing issues in demography, health education (particularly in early adolescence), sexual and reproductive health, population and development. Ideally, candidates should be educated to PhD level in an appropriate subject. Applications from individuals without doctoral degrees may also be considered if they hold a university or equivalent academic post in a developing country.

The first recipient of this type of award will be Dr Bea Vuylsteke, of the STD/HIV Research and Intervention Unit at the Institute for Tropical Medicine in Antwerp. Her research, directed at the creation of a package of comprehensive sexual health services for female sex workers, will involve collaboration between her institute in Antwerp, and the Ministry of Health in Cote d'Ivoire.

Project and programme grant support in the fields of population studies and reproductive health

Proposals may address any relevant question, but applications are particularly encouraged in the following areas: (i) research directed at the improvement of reproductive health in adolescents and adults. This may include quantitative measurement of the outcomes of innovative behavioural interventions addressing sexual disease transmission and/or contraception, and measures to effect the early diagnosis and treatment of STDs; (ii) research on the socio-economic and environmental consequences of long-term demographic change. Interdisciplinary collaborations between demographers, social and environmental scientists, economists and biologists are encouraged. Collaborations between researchers at institutions in developing countries, and those based in centres of research excellence (which might be in the same country, not necessarily overseas), are encouraged.

The first project grants awarded by the Trust's Population Studies Panel were to Dr Gillian Walt and Professor J.G.Cleland of the London School of Hygiene and Tropical Medicine, for studies using policy analyses to assess the integration of family planning and HIV/STD services; and to Dr Louise Ackers of the University of Leeds for a study of citizenship and retirement migration in the European Union.

The first programme grant made by the Panel will be to Dr Helen Lee of the Department of Haematology, University of Cambridge, for studies directed at the development of a rapid DNA dipstick for detection of *Chlamydia trachomatis*. The award, for a grant of ~£1.7 million over 60 months, is designed to enable Dr Lee and her team to complete their work on the creation of a prototype *Chlamydia* diagnostic dipstick, and to facilitate the relocation from the USA and establishment at Cambridge of Dr Lee's senior co-workers, who will form the nucleus for the development of the *Chlamydia* test and other inexpensive STD diagnostic tests for use in resource poor settings. Currently the only means by which an accurate diagnosis of a sexually-transmitted infection can be achieved are by culture of the infective organism, or through the use of nucleic acid amplification technology - methods that, while specific and sensitive, are, slow, expensive and necessitate highly skilled operatives - features that militate against their usefulness in poor developing countries. The dipstick that Dr Lee is developing should enable health care workers

to prescribe antibiotics more effectively, in respect of both symptomatic and asymptomatic infection, reducing the traditional dependency on syndromic management for treatment of STDs. The broader significance of this development is that it holds the promise of a powerful new tool in the battle against the epidemic of STDs and the related tragedy of the HIV/AIDS pandemic in sub-Saharan Africa and elsewhere in the developing world, which is truncating the lives of millions of men, women and children, destroying formerly stable communities, and destabilizing fragile economies.

Development of an international research centre in Africa

In January 1996 the Trust launched a competition for the establishment of a centre of excellence in population and reproductive health in the African region. In all, 15 preliminary proposals were received from five African countries. Formal applications were invited from four groups of scientists, all in southern Africa. These were considered at the Population Studies Panel's 6th February 1997 meeting. The bid from a consortium of Durban-based researchers at the Universities of Natal and Durban-Westville, and the South African Medical Research Council's Centre for Epidemiological Research, represented, in the view of the Panel, the most persuasive case for the establishment of an African centre. The Durban group subsequently hosted a site visit by members of the Panel in late February 1997, providing valuable opportunities for Trust staff and Panel members to see the proposed demographic surveillance platform at Hlabisa in rural north eastern KwaZulu Natal, to engage in thorough-going scientific and managerial discussions with the principal investigators, and to meet with senior academic figures, government officials and the Minister of Health for KwaZulu Natal. It is anticipated that a formal announcement concerning the award of the Africa centre to the Durban consortium will be made by the Autumn of 1997. The Trust intends that the centre should act as a focus for research and research training, not only locally in southern Africa, but also throughout sub-Saharan Africa.

Other awards and activities

WHO consultation on pre-clinical and clinical requirements for non-latex male condoms

The Trust made a contribution to the costs of a meeting on this topic, held in Geneva in May 1996. The meeting was a considerable success, with agreements removing major regulatory hurdles to progress in the development and marketing of plastic condoms. The World Health Organization (WHO) will now be able to produce its own guidelines for the introduction of non-latex condoms into developing and developed countries around the world. A formal report is expected to be published by WHO in 1997.

Consultation on the toxicology of intrauterine quinacrine

Since its first use in Chile in the early 1970s, the quinacrine pellet method of non-surgical female sterilization has been used in a number of developing countries, most notably in Vietnam, where >30 000 women were sterilized by this technique in the late 1980s. The opinion of WHO is that the quinacrine method should not continue to be used in the

absence of adequate data on its safety. On the 7 December 1995 the Trust convened a meeting of a small group of independent experts who had reviewed the existing clinical and toxicological data on quinacrine. The group discussed the nature of the toxicological evaluations that would be needed* for an adequate risk-benefit analysis of its clinical use. After considering a report on the group's deliberations the Population Studies Panel indicated its willingness to receive research proposals-addressing the safety of the method, noting that pre-hysterectomy studies of quinacrine pharmacodynamics would be constructive, and that they could be taken forward without additional data from animal studies. The consensus of the Panel was that the Trust should not actively promote long-term animal studies.

Future developments

Research training

During the Panel's first full year (1996) it became even more strongly apparent than it was at the inception of the Trust's population initiative, that there was a very great need for a considerable increase in the numbers of individuals competent to address population and reproductive health research issues. Population-directed assistance from international aid agencies and national governments is unlikely to produce long-term sustainable results without people on the ground capable of rigorously analysing the outcome of existing and previous interventions, and reporting their findings through the international peer-reviewed literature. Beyond the establishment of a research and research training centre in Africa, the Panel is looking at ways to improve its support for research training in reproductive health, demography and population, e.g. through enhancement of the capacity of existing centres of research excellence in these disciplines to provide MSc level research training through a combination of didactic and research activities. Research training provided through this mechanism should be of practical relevance to the reproductive health, environmental and socio-economic conditions of people in developing countries.

Reproductive health-related research

Since launching its Population Studies Programme, the Trust has found that the greatest demand for funds is in respect of reproductive health and reproductive biology. It is hardly surprising, perhaps, that Research Training Fellowships in Reproductive Biology form the most prominent set of awards to date; the laboratory-based biomedical sciences are already strong in countries like the UK or Australia. It is gratifying to note, however, that the Trust's initiative to stimulate basic studies of relevance to the development of new forms of contraception, through research training, has made an auspicious start.

There is also a great need for increased efforts in the field of STD diagnosis and in the development of contraceptive

methods of relevance to the needs of people in developing countries. Recent meetings of university- and industry-based scientists have highlighted the particular challenge of creating new forms of contraception and microbiocidal protection, for populations in both the rich and poor countries of the world, and the difficulties that the private sector has in committing itself to such products, which have high R&D costs, and perceived disincentives in terms of product liability. A particular challenge is the creation of a non-contraceptive technology that permits sperm survival and conception and at the same time eliminates the risk of infection by the full gamut of pathogen that are transmitted sexually (Harrison and Rosenfield, 1996).

Research priorities in population and development

The Trust's population initiative has taken a clear path with regard to stimulating and funding science in the areas of reproductive health and biology. The Population Studies Panel has recognized, however, the urgent need for a clearer definition of what the Trust's priorities should be in addressing the 'population' side of the coin. With this in mind a Workshop on the Consequences of Population Change will be held in September 1997. It will address such issues as the future of work; migration and urbanization; food, environment and water, methods of enquiry (into these issues), and the challenges in terms of effecting local and global implementation of research findings.

Final comment

The Wellcome Trust recognizes that there are enormous challenges for researchers in the field of reproductive health, population and development. It is determined to meet those challenges in the spirit of Sir Henry Wellcome's will, which commits the Trust to supporting research that is conducive to improvements in the physical condition of humankind.

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