



Working on Impact Evaluation

Randomized controlled trials (RCTs) involve assigning individuals, or groups of individuals, to one or other alternative treatments or to a control group. RCTs are an important part of the School's history and will undoubtedly be part of its future. Indeed, Sir Austin Bradford Hill, who is widely acclaimed for introducing to the medical world the technique of the RCT, was a former Dean of LSHTM. School staff are involved in a variety of RCTs, as well as in other types of impact evaluation design.

RANDOMIZED CONTROLLED TRIALS

In the past 12 months two ground-breaking randomized controlled trials were published that illustrate well the potential for randomized controlled trials to evaluate public health interventions and improve public health.

Mobile phone text messaging can help people quit smoking

The *Txt2stop* trial, funded by the MRC, showed that smoking cessation support delivered by mobile phone text messaging doubles biochemically validated quitting at six months. The trial was completed among 5800 smokers in the UK and is the first to evaluate robustly the long-term effects of mobile phone-based smoking cessation support. The text messages worked well across all age groups and all socioeconomic groups. There has already been considerable interest in implementing such a smoking cessation programme in the UK and internationally. It is technically easy to scale-up the intervention for delivery at national or international level. The trial team was led by Cari Free (Lecturer in Epidemiology) based in the School's Clinical Trials Unit, working with

researchers at the University of Sydney and University of Auckland.

The trial's results show that text messaging can be a powerful tool for changing health behaviours which raises the possibility that text messages could alter other important health behaviours. The trial is part of an expanding programme of research based at the Clinical Trials Unit exploring the effects of health communication, much of which focuses on the use of mobile technologies as a delivery system for health communication.

Drug used to treat heavy periods could save the lives of over 100,000 trauma victims per year
Tranexamic acid (TXA) is a potent inhibitor of



Right A video on YouTube (<http://tinyurl.com/67ojtzx>) shows one participant's experience of text message support in ceasing smoking and explores the importance of the trial's result for smoking cessation globally.

fibrinolysis that was first reported in September 1962¹. Since then TXA has been widely used to treat heavy menstrual bleeding and to reduce blood loss in elective surgery where it reduces blood transfusion by about one third. The CRASH-2 (Corticosteroid Randomization After Significant Head Injury) collaborators, led by the researchers in the Clinical Trials Unit, hypothesized that TXA might also reduce bleeding in trauma patients, up to one third of whom die from acute haemorrhage. The CRASH-2 trial was a UK government-funded randomized controlled trial of the effects of the early administration of TXA on death, vascular occlusive events and blood transfusion in bleeding trauma patients.

A total of 20,211 adults with significant traumatic bleeding were randomized to TXA or matching placebo, with 99.6% follow-up. The risk of death due to bleeding was significantly reduced with TXA. Importantly, there was no increase in fatal or non-fatal vascular occlusive events. All-cause mortality was also significantly reduced with TXA. The large numbers of patients studied in a wide range of different health care settings help these results to be generalized widely. Subsequent analyses showed strong evidence that the effect of TXA on death due to bleeding varied according to the time from injury to treatment with early treatment, (within an hour from injury) significantly more effective than late treatment. Cost-effectiveness analysis shows that TXA administration is highly cost-effective in high-, middle- and low-income countries. The estimated incremental cost-per-life-year gained of administering TXA is US\$48, US\$66 and US\$64 in Tanzania, India and the UK respectively. It is estimated that approximately 140,000 lives could be saved each year worldwide if all hospitalized bleeding trauma patients were treated with tranexamic acid.

Large, simple randomized trial using electronic health records

The *Text2stop* and CRASH-2 trials indicate the potential that randomized controlled trials have to improve public health. But could the benefits of large-scale trials be reaped more efficiently and cost-effectively? The increasing use of computers in clinical care offers the potential for large, simple pragmatic trials to be undertaken using electronic health records. Randomization could occur at the point of care, with subsequent data collection and follow-up undertaken electronically. As well as being resource-efficient, high rates of follow-up could be achieved and the results would be capable of wider generality. However, there

are considerable challenges to adopting such an approach, including practical issues and ethical concerns. School researchers are working closely with the General Practice Research Database and a range of other collaborators to implement two feasibility trials. One, funded by the NHS Health Technology Assessment programme, is a trial of antibiotics for mild exacerbations of chronic obstructive pulmonary disease. The other, funded by the Wellcome Trust, is testing two alternative prescribing strategies for cholesterol-lowering drugs (statins).

CLUSTER RANDOMIZED TRIALS

Over the past 25 years, the School has built up expertise in the use of a special type of RCT, cluster randomized trials (CRTs), to evaluate the impact of health interventions. CRTs randomize groups of individuals – e.g. schools, clinics, villages, cities or regions – to two arms: intervention and control. This design is of special value for the evaluation of infectious disease interventions as well as complex, social interventions, since it is able to capture the impact of programmes at both the individual and social level. As well as carrying out methodological work on the design and analysis of such trials, which require special statistical methods, staff across the School have used this design to carry out landmark studies of the impact of a wide range of interventions, including impregnated bednets against malaria, school-based health promotion, vitamin A supplementation to reduce child mortality, and treatment of sexually transmitted infections and behavioural and structural interventions to reduce HIV incidence.

Cluster randomized trial of a population-wide intervention to reduce HIV infection

Building on previous work on HIV prevention, the School has recently secured funding from the HIV Prevention Trials Network (HPTN) of the US National Institutes of Health to carry out a CRT to measure the impact of a combination prevention programme that includes universal voluntary HIV testing and counselling, the offer of male circumcision to men who test negative for HIV and the offer of immediate antiretroviral treatment for all who test HIV-positive, irrespective of CD4 count (which measures immune status). This contrasts with the usual approach where treatment is only commenced when the CD4 count has reached low levels. Mathematical models show that such strategies could lead to steep reductions in HIV incidence even in severely affected populations, and a recent HPTN trial has confirmed that early treatment

¹ Okamoto S, Okamoto U. Amino-methyl-cyclohexane-carboxylic acid: AMCHA. A new potent inhibitor of fibrinolysis. *Keio Journal of Medicine*, 1962, 11:105–115



for HIV reduces the risk of transmission to sexual partners by more than 90% as well as providing clinical benefit for HIV-infected individuals. The proposed CRT will randomize 24 communities in Zambia and South Africa and will measure the impact of the intervention on population-wide HIV incidence over two years, as well as the effects on tuberculosis incidence, sexual behaviour, clinical events, HIV drug-resistance and HIV-related stigma. This five-year trial will be carried out in close partnership with the ZAMBART Programme, Desmond Tutu TB Centre, the Ministries of Health of Zambia and South Africa, and Imperial College London.

Pilot trial of a programme to reduce aggression in UK schools

Staff across the School are conducting a pilot CRT of 'Inclusive', a programme to reduce aggressive behaviour among young people in secondary schools in and around London. This work is timely in the wake of London's riots in the summer of 2011, policy-makers' concerns about gang-related violence and the high rates of bullying in UK schools. The programme takes a holistic approach involving not only classroom education to improve young people's social and emotional skills but also changes to how schools are managed so that young people feel a greater sense of belonging to their school community. The programme is also informed by the principle of 'restorative justice' whereby the focus is on repairing the harm that violence causes to relationships and learning from previous experiences rather than only prevention and retribution. In addition, students will play a much greater role in deciding how the school is run, sitting on an Action Team with staff to plan the work that occurs in each school. Students will also work as mediators aiming to intervene to prevent and resolve conflicts among their peers and will work alongside staff to re-write the school's rules and policies. Each school will benefit from the advice of an external facilitator who has direct experience running a secondary school and will act as a 'critical friend' suggesting how each school might become a safer and more inclusive place. The project, funded by the NIHR Health Technology Assessment Programme, is a collaboration with UCL's Institute of Child Health, the MRC's Social and Public Health Sciences Unit, and the Institute of Education.

Right Conducting a rapid diagnostic test for malaria.

OTHER DESIGNS FOR IMPACT EVALUATION

RCTs are not always possible – or even desirable, e.g. for policies already implemented or where the policy works at the national level, as with mass media

or legislation, for instance. The School is involved in a number of evaluations of impact using a mixture of RCTs and other methods, or other methods only.

Optimizing antimalarials in Africa and Asia

Researchers from across the School are working with colleagues from 20 other research and partner institutions worldwide as part of an international research consortium that aims to optimize artemisinin combination therapy (ACT) antimalarial drug delivery and use in Africa and Asia. The School is leading eleven evaluations in seven countries of interventions that use different approaches to improve the way antimalarial drugs, and malaria tests, are used. Of these, nine are CRTs where health centres, drug shops or catchment areas are randomized to receive different interventions or routine supplies and services. Interventions include new technologies, mostly rapid diagnostic tests (RDTs) for malaria, together with different behaviour change programmes. Two further studies are assessing the impact of the national scale-up of drug subsidies at accredited drug shops; and malaria RDTs at different health providers. All evaluations are assessing the costs and cost-effectiveness of interventions. The School's team draws on medicine, epidemiology, statistics, economics, anthropology and



other disciplines. The findings from ACT Consortium's research will provide evidence for policy and programme makers about what interventions will support better access to effective and safe antimalarial treatment for those who need it.

Evaluating maternal health programmes in China

Work carried out by the Faculty of Epidemiology and Population Health with colleagues at Beijing University has shown how routine data can be used to evaluate the impact of large-scale programmes on health outcomes.

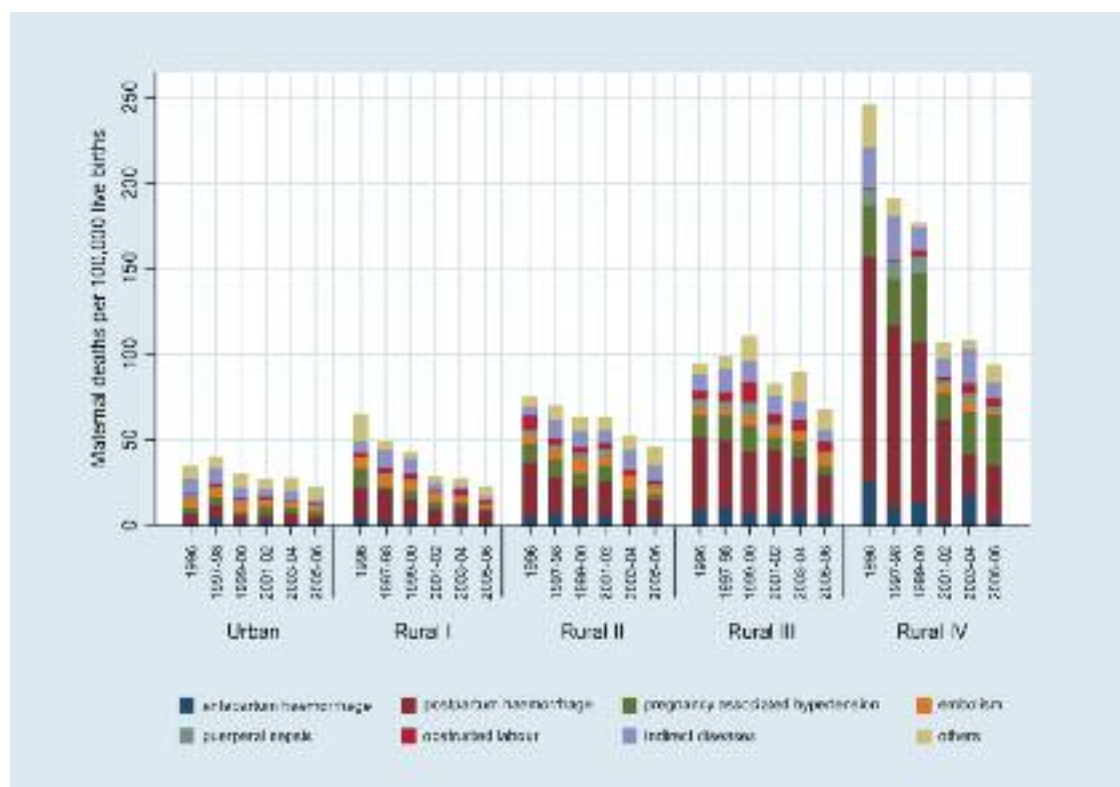


Figure 1. Maternal mortality ratios by socio-economic region, year and cause of death (China 1996-2006).

Using nationally representative data from China's National Maternal and Child Mortality Surveillance System, they quantified the impact of China's Safe Motherhood strategy on maternal and neonatal mortality. Between 1996 and 2006, maternal and neonatal mortality fell by 6% and 5% per year respectively, suggesting that China is achieving the targets set by Millennium Development Goals 4 and 5. Maternal and neonatal mortality fell in all regions, and there is no evidence of widening disparities in maternal mortality across socio-economic regions (see Figure 1). The team also demonstrated that the decline is largely explained by the dramatic rise in institutional births. More than 90% of Chinese women now give birth in hospital, and China's hospital-based birth strategy may have prevented between 49% and 70% of neonatal deaths. As China approaches universal hospital delivery, the quality of care in hospitals becomes the prime concern. Other emerging economies can learn from China's focus on the supply and quality of maternity services along with more strengthening general health systems.

Multi-method evaluation of blindness prevention across the UK

A multidisciplinary team of researchers from across the School is evaluating work by the Royal National Institute of Blind People (RNIB) to stop people losing

their sight unnecessarily, involving local community engagement projects in five sites across the UK. The programme aims to increase the uptake of primary preventive services and enable earlier detection and treatment of eye health conditions; to improve referral to, and uptake of, secondary eye care services; and to improve compliance with treatment. At each site interventions will focus on a particular community. A Bradford-based project, for example, is aimed at the Pakistani community which experiences high rates of diabetes. In Hackney, the condition is glaucoma and the target population the Caribbean community. In each area, RNIB staff are working with local clinicians, community representatives, and other interested agencies and organizations. Formative research has been carried out to explore barriers and enablers to accessing care at key points in the patient pathway. In each intervention site, the evaluation will have three components – outcome, process and economic. Using both primary and secondary data sources, an evaluation of the programme as a whole will also be carried out.

A key feature of all these impact evaluations is their multidisciplinary – the collaboration amongst epidemiologists, statisticians, economists and other social scientists which enables the School's research to be truly cutting-edge.