10 Research – good, bad and unnecessary

In earlier chapters we emphasized why tests of treatments must be designed properly and addressed questions that matter to patients and the public. When they are, everyone can take pride and satisfaction in the results, even when hoped-for benefits do not materialize, because important insights will have been gained and uncertainty lessened.

Although much health research is good – and it is steadily improving as it conforms with design and reporting standards[1] – bad and unnecessary research continues to be done, and published, for various reasons. And as for the perpetual demand 'more research is needed', a better strategy would be to do less, but to focus the research on the needs of patients, and so help to ensure that it is done for the right reasons. We explore these issues in this chapter.

GOOD RESEARCH

Stroke

Stroke is a leading cause of death and long-term disability. The death rate is between one in six and two in six during a first stroke, rising to four in six for subsequent strokes. One of the underlying causes of stroke is narrowing (stenosis) of the carotid artery, which provides blood to the brain. The fatty material that coats the inside of the carotid artery sometimes breaks away, blocking smaller arterial tributaries, and thus causing a stroke. In the 1950s surgeons began to use an operation known as carotid endarterectomy to remove these fatty deposits. The hope was that

surgery would reduce the risk of stroke. As with any operation, however, there is a risk of complications from the surgical procedure itself.

Although carotid endarterectomy became increasingly popular, it was not until the 1980s that randomized trials were set up to assess the risks and benefits of surgery. Clearly this knowledge would be vitally important for patients and their doctors. Two well-designed trials – one in Europe and the other in North America – were carried out in patients who already had symptoms of carotid artery narrowing (minor stroke or fleeting, stroke-like symptoms) to compare surgery with the best available non-surgical treatment. Several thousand patients took part in these long-term studies. The results, published in the 1990s, showed that surgery can reduce the risk of stroke or death but that benefit depends on the degree of narrowing of the carotid artery. Patients with relatively minor narrowing were, on balance, harmed by surgery, which can itself cause stroke. These important findings had direct implications for clinical practice.[2, 3]

Pre-eclampsia in pregnant women

Another outstanding example of good research concerns pregnant women. Worldwide, about 600,000 women die each year of pregnancy-related complications. Most of these deaths occur in developing countries and many are linked to pregnancy-associated convulsions (fits), a condition known as eclampsia. Eclampsia is a devastating condition that can kill both mother and baby. Women with the predisposing condition – pre-eclampsia (also known as toxaemia) – have high blood pressure and protein in their urine.

In 1995, research showed that injections of magnesium sulphate, a simple and inexpensive drug, could prevent fits *recurring* in women with eclampsia. The same study also showed that magnesium sulphate was better than other anticonvulsant drugs, including a much more expensive one, in stopping convulsions. So, the researchers knew it was important to find out whether magnesium sulphate could prevent convulsions *occurring* in women with pre-eclampsia.

The Magpie trial, designed to answer this question, was a

MY EXPERIENCE OF MAGPIE

'I was really pleased to be part of such an important trial. I developed swelling at 32 weeks which grew progressively more severe until I was finally diagnosed with pre-eclampsia and admitted to hospital at 38 weeks. My baby was delivered by caesarean section and thankfully we both made a complete recovery. Pre-eclampsia is a frightening condition and I really hope the results of the trial will benefit women like me.' Clair Giles, Magpie participant.

MRC News Release. Magnesium sulphate halves risk of eclampsia and can save lives of pregnant women. London: MRC, 31 May 2002.

major achievement, involving more than 10,000 pregnant women with pre-eclampsia in 33 countries around the globe. In addition to normal medical care, half the women received an injection of magnesium sulphate and half a placebo (sham preparation). Magpie gave clear and convincing results. It showed that magnesium sulphate more than halved the chance of convulsions occurring. In addition, although the treatment did not apparently reduce the baby's risk of death, there was evidence that it could reduce the risk of the mother dying. And apart from minor side-effects, magnesium sulphate did not appear to harm the mother or the baby.[4, 5]

HIV infection in children

The results of good research are also making a real difference to children infected with HIV (human immunodeficiency virus), the cause of AIDS. At the end of 2009, figures from UNAIDS (the joint United Nations Programme on HIV/AIDS) show that an estimated 2.5 million children were living with HIV around the world, 2.3 million of them in sub-Saharan Africa. Every hour, around 30 children were dying as a result of AIDS.[6] Bacterial infections, such as pneumonia, which are associated with the children's weakened immune system, are a common cause of death. Co-trimoxazole is a widely available, low-cost antibiotic

that has been used for many years to treat children and adults with chest infections unrelated to AIDS. Studies in adults with HIV additionally showed that the drug reduces other complications from bacterial infections.[7]

When preliminary evidence showed that the infections in children with HIV might also be reduced, a group of British researchers got together with colleagues in Zambia to assess the effects of co-trimoxazole as a possible preventive medicine in a large study. The trial, which started in 2001 and lasted about two years, compared the antibiotic with a placebo in over 500 children. The results became clear sooner than anticipated when it was shown that the drug cut AIDS-related deaths by 43% (74 deaths in the co-trimoxazole group compared with 112 in the placebo group) and also reduced the need for hospital admissions. At this point the independent committee scrutinizing the results recommended that the trial be stopped.

One immediate outcome was that all children in the trial were given co-trimoxazole as part of a Zambian government initiative. A wider consequence was that the World Health Organization and UNICEF promptly altered their advice on medicines for children with HIV.[8, 9]

These organizations continue to recommend co-trimoxazole as an inexpensive, life-saving and safe treatment for such children.[10]

BAD RESEARCH

Psychiatric disorders

Regrettably, research is not always well done or relevant. Take the example of a distressing condition known as tardive dyskinesia. This is a serious side-effect associated with long-term use of drugs called neuroleptics (antipsychotics), which are prescribed for psychiatric disorders, especially schizophrenia. The most prominent features of tardive dyskinesia are repetitive, involuntary movements of the mouth and face – grimacing, lip-smacking, frequent poking out of the tongue, and puckering or blowing out of the cheeks. Sometimes these are accompanied by twitching of the hands and feet. One in five patients taking a neuroleptic for more than three months experiences these side-effects.