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Conducting Clinical Cancer Research in the NHS Benefits Everyone?

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Report by Jennifer Trueland

More than one in five cancer patients in the UK will now be recruited to a clinical trial, a vast increase in the last decade. In a persuasive and fascinating lecture, Professor David Cameron argued that while clinical trials might benefit some of those who take part, a research-active environment is certainly good for the overall health service and for the patient population as a whole.

People diagnosed with cancer in Scotland today will have a much better outcome than would have been the case just 30 years ago; this is good news, but what is making the difference? Earlier diagnosis and better diagnosis techniques, better local treatments (such as surgery and radiotherapy) and new drug therapies are all influencing survival for the better; even in cases where cancer isn't 'cured', there are therapies which mean people can be supported to live longer with the disease.

But research plays a part too: over that time the research base has been growing so that we have more evidence about what works, or, as Professor Cameron puts it, that tells us "we should do this, and not that". And much of that research has been going on in Scotland and the rest of the UK.

Indeed, the UK has the highest recruitment to clinical trials in the world, with one in every five people newly diagnosed with cancer being placed in a study. This is a huge increase over just a decade; before the National Cancer Research Network (NCRN) started in 2001, just 3.75 % of patients would have been recruited to a trial in the UK, compared to 22.8 % in 2011/12.

There are various types of study: academic, including randomised and non-randomised trials; commercial, that is, testing new drugs before approval (and meeting the ever-more stringent demands of regulators); observational; and models of care, for example, seeing how the treatment works in 'real life' outside a trial setting when the drug is in actual use.

Professor Cameron said that although there was some public disquiet about pharmaceutical companies and their research activities, in his experience, they were very well regulated and, in the vast majority of cases, people taking part in trials will be testing a drug that has

already been shown to be safe. Even phase-one trials (which test the safety of a drug) involve treatments that have been tested and found to be safe in animals. In any case, trials are very well regulated by the Medicine and Healthcare Regulatory Agency and others (including ethics committees) which have strong lay membership.

Especially in these financially-austere times, however, there are those who question whether the NHS should be doing clinical trials: arguments include the potential saving of money by getting rid of research nurses, for example. But Professor Cameron argued strongly that clinical trials are of benefit, possibly to the patients taking part, but certainly to the wider patient population of all patients treated in the hospitals conducting research.

Professor Cameron examined the evidence of the impact of clinical trials, both on those taking part, and on the sites undertaking the research. Why should patients do better in trials? It could be that the actual treatment being tried is better than they would have been receiving otherwise; the placebo effect might mean they do better; taking part in trials – the participation effect – can mean doing better, possibly because there's more attention from staff, possibly because of inclusion criteria – fitter patients tend to take part in trials, so possibly they'd do better in any case. But trial participants might not be the main beneficiaries. He quoted several studies which showed no consistent evidence of benefit for individuals who took part in trials; undoubtedly some would benefit from specific treatments, but with small numbers, this wouldn't alter the population statistics.

There is, however, more convincing evidence that research-active healthcare systems (i.e., hospitals which do clinical trials) deliver better healthcare. He cited several European and US studies which show that patients do better in hospitals where trials are taking place. This effect isn't limited to cancer – similar results have been seen for cardiology research.

So why should this be? Centres taking part in trials are more likely to adhere strictly to guidance, which means that care will be more consistent; this covers all stages of care, from the treatment patients receive in hospital to the discharge medication and lifestyle advice they are given. Healthcare staff are also affected by being in a research-active environment – if people are aware that they are being evaluated, it's human nature to conform to standards of treatment and quality. Professor Cameron cited one research trial where patients could only take part in the drugs element if their surgery had been performed well – so the surgeons were being influenced to do their best! Similarly, staff in research-active settings – who feel they are really making a difference to care now and in the future – are motivated and encouraged, which in turn helps recruitment and retention.

Professor Cameron's strong – and evidence-based – conviction is that research benefits patients, not often at an individual level, although there are obvious exceptions if the trial treatment works, but that certainly there is evidence that *the quality and efficacy of therapy in an institution is improved by being involved in research activity*. We don't know yet whether there is a dose response, that is, the more you do, the better you are.

There is currently work taking place to evaluate what the first ten years of the NCRN have delivered. What we do know is that in the UK, every hospital which treats cancer patients with drugs and/or radiotherapy recruits to trials, as does almost every clinical oncologist.

Radiotherapy trials can be more difficult – and the UK is behind many EU countries in its take-up of new techniques – because of the cost of equipment. In England, however, the

implementation of the new radiotherapy techniques needed for the trials is nationally co-ordinated, which, of a necessity, ensures standardised implementation of new techniques. There is no such national co-ordination in Scotland yet.

Professor Cameron touched on the economic benefit of clinical research, saying that the pharmaceutical sector is a big player in the economy and an important contributor to GDP. This is the case in traditionally 'low value' research areas such as mental health, as well as in higher value areas such as cardiovascular disease.

There is much less evidence, however, for how we actually spend money on cancer – what's the rationale behind why we spend as we do? Although the cancer drugs bill is high profile and gets a lot of media attention, the UK actually spends less on this than do other countries, such as France. Indeed, the drugs bill, accounting for around 12 % of spend, pales next to expenditure on salaries and on the actual systems or health services. Conversely, around
80 % of research spend goes on drugs trials, with much less going to research in radiotherapy, surgery, observational and qualitative research. There is very little research into models of health service care – yet this is what we actually spend most money on.

But there is actually evidence that changing the way we deliver care can improve outcomes. Multi-disciplinary team (MDT) meetings were introduced (ahead of evidence) into cancer care in the last two decades and 95 % of cases are now discussed in this way. Professor Cameron is sure they make a difference – and this view is backed by a *British Medical Journal* paper in 2012, which shows MDTs mean better outcomes for breast cancer patients – even in the oldest patients, and the poorest patients, who would be expected to do less well generally.

Although the MDT approach has now been validated by research, Professor Cameron cautioned against making wholesale changes to healthcare delivery models without the benefit of research. For example, he said there were no data to show that the current health reforms planned in England were the right thing to do; likewise, on changes to junior doctor training, and actual decisions on who should deliver care – should it be consultants, nurse specialists, GPs? The biggest area of healthcare spend is least served by research, and decisions, or practice 'drift', tend to be made in crisis mode, rather than underpinned by evidence.

The benefits of taking part in research are not just confined to the developed world, he said, citing screening trials in India, for example, which have shown positive outcomes. Nor, he argues, should the quest for evidence be confined to health and healthcare. Education, for example, is the subject of much debate, but how many schools, teachers and pupils are involved in research to improve the way we educate people? Could a systematic, evidence-based approach be more effective than the current way we do things?

Professor Cameron concluded that clinical trials improve the overall health service, that they are sometimes good for individual patients, and that they are good for the wider patient population. The challenge for the future is to embed research even further into the health service – and to look purposefully at its possible application to other disciplines such as education.

Questions

RSE President Sir John Arbuthnott kicked off the questions (Chair's prerogative) by asking whether targets and ministerial pressure for faster referral for cancer treatment help drive improvements. Professor Cameron said that speedy referral helps, but that other things were important too, such as patient and family awareness (so that people go to see GPs earlier) and also greater awareness among GPs so that they are more likely to suspect cancer.

Asked who should be funding research, Professor Cameron said it is important to have a plurality of funders – including charities, and commercial bodies – but that it is important to have arms-length government funding. "The state benefits, so has a clear role," he added.

Dundee University nutrition and food choice expert Professor Annie Anderson asked about lifestyle advice and whether we are too reliant on trials – should clinicians wait for research evidence before, for example, recommending physical activity for patients with breast cancer? Professor Cameron said his approach is "first do no harm" – there could be merit in advising an approach that would probably benefit, and almost certainly not harm a patient, while trial results are awaited, but he wouldn't like to see that culture shift into drug treatments.

Asked about why evidence-based approaches aren't common in other disciplines, Professor Cameron said he thought it starts with education: medical students start with science, so learn the importance of evidence – other academic areas (such as English literature) might apply critical thinking but it doesn't necessarily spill over into the culture of different fields of employment, such as teaching.

A Vote of Thanks was delivered by Professor Robert Steele, who said that Professor Cameron's "superb lecture" emphasised the importance of research as the "life blood" of medicine, and that the health service in Scotland is ideally set up for clinical research.