Clinical research in the UK: the beginning of a new era

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The lack of high quality evidence for some of the treatments of lymphoedema and other chronic oedemas is well recognised (Lymphoedema Framework, 2006). Where there has been research, the studies have often only included small numbers of patients or, effectively, have been case reports. A randomised controlled trial (RCT) is often seen as a gold standard of research to determine best practice, but there have been few of these in lymphoedema, and, where they have taken place, the numbers involved have generally been small. A Cochrane review (Preston et al, 2008) of the physical therapies for lymphoedema of the limbs, found only three studies involving a total of 150 randomised patients that met the review criteria. The reviewers concluded that all three trials had limitations and that the results should be reviewed with caution. They called for further well-designed randomised trials of the range of physical therapies to determine the best approach to managing lymphoedema.

National clinical research initiatives

There is, therefore, a clear need for large multi-centre studies to answer important questions in the management of chronic oedema. Such challenges are not confined to lymphoedema research alone. In recent years there have been a number of national initiatives to facilitate recruitment of patients into high quality clinical trials across the NHS. The first one was the National Cancer Research Network (NCRN) which was established in 2001 and aimed to provide an infrastructure to support high quality clinical studies in cancer and to improve the speed, quality and integration of research resulting in improved patient care (www.ncrn.org.uk). The success of the NCRN was followed by the development of other 'topic specific research networks' and the subsequent development of the National Institute for Health Research (NIHR) and its clinical research network in 2006 (www.crncc.nihr.ac.uk). Like the NCRN, these research networks aim to provide an infrastructure to facilitate the development of high quality, multi-centre clinical trials (often RCTs), and enable patients to have access to these across the country. This means that even in smaller district general hospitals outside major academic centres, clinical research can take place and patients can have access to new treatments in a trial setting.

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Central to this process is the NIHR portfolio. This is a national collection of high quality clinical studies that can benefit from the infrastructure provided by the NIHR clinical research network and have the 'stamp of approval' of the NIHR. To be included in the portfolio, studies have to be of a recognised high quality. This can be achieved in two main ways:

- Automatic inclusion if a trial is funded by a grant from the NIHR or one of its partner organisations, e.g. Cancer Research UK. The process of obtaining NIHR grant funding guarantees the high quality of the study
- Adoption of the study on to the portfolio, following the assessment of a study funded by outside sources, e.g. industry, by an NIHR adoption panel.

To support recruitment into portfolio studies, NHS trusts receive funding to provide the appropriate infrastructure. Increasingly, this funding is becoming 'activity' dependent and therefore a trust which recruits more patients into portfolio trials will receive more funding to do so.

Where does lymphoedema clinical research fit into this?

In the last two years there have been a small number of lymphoedema studies which have opened as part of the NIHR portfolio. The author has been fortunate to be a co-investigator in three of these. Two studies have been funded by an NIHR programme grant (Chief Investigator: Professor Nigel Bundred, Manchester), and the third is an industry funded study (Chief Investigator: Professor Christine Moffatt, Derby). The two studies funded by the NIHR programme grant concern lymphoedema of the arm following breast cancer treatment.

The prevention of lymphoedema after axillary node clearance by early external compression (PLACE)

This is a randomised controlled trial aiming to recruit 270 patients across

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seven centres in the UK. The research question addressed is whether early intervention in patients with 'sub-clinical' lymphoedema (as defined by a 4–9% increase in lymphoedema above pre-operative measurements using perometers) can prevent the subsequent development of overt lymphoedema. Patients are randomised to receive 'standard' treatment of advice, elevation and massage or to wear a compression sleeve for one year in addition to standard treatment. The incidence of lymphoedema (defined by an excess limb volume of >10%) at two and five years will be measured.

The use of multifrequency bioimpedance measurement in the early detection of lymphoedema after axillary node clearance (BEA)

This study builds on earlier smaller studies which suggest that bio-impedance measurements can identify patients who are going to develop lymphoedema at a stage before limb volume changes are detected. The aim is to recruit 1100 patients across seven sites in the UK. Patients will be assessed pre and post-operatively with perometer and bioimpedance measurements.

The 'At home evaluation of two pneumatic compression devices in the treatment of leg lymphoedema' (ACE)

This is a randomised, controlled trial of two different intermittent pneumatic compression (IPC) devices, a third generation device compared with a simpler device. These are used by patients at home and are in addition to standard treatment. The primary outcome is the difference in limb volume measurements at 12 and 24 weeks. The plan is to recruit 262 patients across centres in the UK and USA. This is an industry funded study which has been adopted onto the NIHR portfolio.

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These studies represent the beginning of a new era of lymphoedema clinical research in the UK, with large scale multi-centre studies and RCTs providing firmer evidence for the best treatment of patients with lymphoedema. The model of having a number of clinical research investigators who can collaborate with study design, grant application and oversight of trials, working with a 'network' of clinical services who recruit patients into the studies is powerful and should help to answer important clinical questions. This is an exciting time in lymphoedema clinical research in the UK and hopefully there will be more to come. Inevitably, however, the answers to our questions will not appear quickly. For these studies, it will be 3–5 years before the results are available. JL

References

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