Health Services Research Unit

Newsletter Winter 2009/2010

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New trial to investigate prolapse surgery

Pelvic organ prolapse (POP) is the descent from its normal anatomical position of some of the female genital organs (such as the bladder, bowel or womb). This is caused by weakness of the supporting structures or by weak pelvic floor muscles. It is most common in women who have had children and approximately one in ten women will, during their lifetime, need an operation to treat pelvic organ prolapse. There is also a high failure rate after surgery: three in ten women who have an operation will need further surgery. Different types of surgical repair can be used to treat POP, and there is not enough evidence from research to inform which operation is best.

The National Institute for Health Research Health Technology Assessment Programme has awarded a grant to run a multicentre randomised controlled trial in the UK, led by Cathryn Glazener. The aim is to evaluate new techniques which use mesh to reinforce the surgery. As different surgical options are appropriate for women having a primary repair and those having a subsequent operation, this study will comprise two separate RCTs evaluating the two groups of women:

RCT1 - A woman who is having her first repair will be randomised to one of: (i) a standard anterior or posterior prolapse repair, (ii) a standard repair with a biological graft inlay to support the stitches; or (iii) a standard repair with a non-absorbable mesh inlay.

RCT2 - A woman who is having a second or subsequent repair will be randomised to: (iv) a standard anterior or posterior prolapse repair, (v) a standard repair with a non-absorbable mesh inlay, or (vi) a new mesh repair in which the whole prolapse is held up with a large piece of mesh threaded into surrounding tissues using an introducer (mesh kit).

Women who are not eligible for randomisation will also be studied using the same study protocol and methods, in a comprehensive cohort design. Women will be followed up, using examination and questionnaires, for at least two years. Overall, the study aims to recruit 4500 women, half of whom will be randomised, from 15 to 20 centres within the UK. Recruitment started in December 2009.

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Performance assessment and wicked issues: the case of health inequalities

Tackling health inequalities is a policy priority in the UK and performance assessment and target setting is a method for implementing this. As part of a larger Economic and Social Research Council Public Services Programme Study, we set out to understand how contrasting policy and assessment contexts in Scotland, England and Wales were reflected in the ways local individuals conceptualised and devised strategies to tackle health inequalities. The work was led by Lorna McKee together with colleagues in Durham and Cardiff.

The methods included document analysis and two hundred interviews with individuals holding strategic and managerial responsibilities in the NHS, local government and local partnerships. The interviews were carried out in regional centres and ex-mining/industrial hinterland areas to achieve some comparability of context and health status.

Overall, performance assessment made a difference to how narrowing health inequality as a policy for implementation was conceptualised locally and the attention it received. In all three countries health inequalities were receiving more prominence. It was not straightforward to assess, however, how the presence or absence of monitoring affected local actions and budgetary decisions. Progress in the three countries appeared more similar than different and the focus on health inequalities was contingent on performance in other priority areas. Financial stability, safe health care and waiting times dominated attention in all localities. In none of our localities did we find any clear link between performance assessment and systematic learning from the interventions being pursued. There is, therefore, a major challenge to transform systems of accountability into systems for learning and systematically embedding that learning in practice.

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Non-surgical treatment for stress urinary incontinence in women: a systematic review and economic modelling

Stress urinary incontinence (SUI) is the involuntary leakage of urine associated with effort or exertion, or on sneezing or coughing. Estimates of prevalence suggest that over 30% of women aged 40 years and older have SUI. The National Institute for Health Research Health Technology Assessment Programme funded a study which aimed to assess the clinical effectiveness and cost-effectiveness of non-surgical treatments for women with SUI.

The work comprised three elements: (i) a systematic review and meta-analysis of non-surgical treatments for SUI to find out which are most effective, (ii) economic modelling of non-surgical and surgical treatments for SUI to find out which combinations of treatments are most cost-effective, and (iii) a survey of women with SUI to identify outcomes of importance to them.

The systematic review included 88 trials involving 9721 women. Five generic interventions were assessed with many variations and combinations of them: pelvic floor muscle training (PFMT) with or without biofeedback, electrical stimulation, vaginal cones, bladder training and duloxetine (serotonin-norepinephrine reuptake inhibitors). A mixed treatment comparison analysis compared 14 interventions, using data from 55 trials that reported primary outcomes (cure or improvement). Included studies were generally small and had short follow-up periods.

Treatments were on average more effective than no treatment and there was clear evidence that when PFMT was delivered with additional supervisory sessions it was more effective than basic PFMT (median odds ratio 8.36, credible intervals 3.74 to 21.7 for cure). Using this format of PFMT or adding biofeedback to PFMT was also more effective than other treatments. Several other treatment combinations (e.g. PFMT plus biofeedback and bladder training) were promising but there was insufficient evidence to recommend their routine use. Adverse effects were uncommon except when using duloxetine.

The economic model compared cumulative costs and QALYs for a 40-year time horizon for different combinations of non-surgical treatment followed, if necessary, by surgery. Based on cure rates, a pathway of lifestyle changes and PFMT with extra sessions or biofeedback before surgery was the least costly (£1644) and the most effective (16.20 QALYs) and had approximately 70% chance of being considered cost-effective (the other seven strategies modelled cumulatively had less than 30% chance of being considered cost-effective). The cost-effectiveness of the non-surgical treatments was dependent upon whether their short-term effectiveness was sustained.

The survey respondents were a selected sample of women who had previously been in contact with a patient support charity. A Patient Generated Index questionnaire captured different areas affected by SUI, which related to four themes: activities of daily living; sex, hygiene and lifestyle issues; emotional health; and the availability of services. Correlations with the existing standard quality-of-life tools were weak, suggesting that outcomes reported in the available literature on SUI may have limited relevance to the women living with this condition.

The review will be published as an HTA monograph early in 2010.

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Total knee replacement: should the patella be resurfaced or not?

kat
Knee Arthroplasty Trial

Total knee replacement (TKR) is a common and established surgical procedure; however there are variations in the surgical procedures that may affect outcome. The Knee Arthroplasty Trial (KAT), which was funded by the NIHR Health Technology Assessment programme* was designed to determine: a) whether a metal-backed plate for the tibial component is more effective and cost-effective than a single high-density polyethylene component, b) whether it is more effective and cost-effective to resurface the patella and c) whether a mobile bearing between the tibial and femoral components is associated with better outcomes than standard designs without a mobile bearing. The KAT trial recruited 2353 patients from 34 UK centres and involved 116 surgeons.

Within KAT, 1715 patients were randomly allocated to receive patellar resurfacing or not at TKR. The primary outcome measure was the Oxford Knee Score (OKS); secondary measures included SF-12, EQ-5D, costs, cost-effectiveness and need for further surgery.

The mean OKS score was 18 at baseline and 35 at five years in both groups. There was no evidence of a difference between trial groups in OKS at five years (mean difference 0.59; 95% confidence interval -0.58 to 1.76) or any of the other outcome measures. Outcomes were not influenced by whether the patella was domed or anatomic. There was no evidence of a difference in the proportion of patients with knee-related readmissions (resurfaced 12%, non-resurfaced 13%, p=0.54), minor/intermediate reoperation (resurfaced 4.4%, non-resurfaced 5.8%, p=0.27), major reoperation (resurfaced 1.6%, non-resurfaced 2.9%, p=0.08), or further patella-related surgery (resurfaced 1.0%, non-resurfaced 1.9%, p=0.22). Total healthcare costs of the primary operation, subsequent monitoring and revision surgery averaged £7,577 per patient in the patellar resurfacing group and £7,726 per patient in the no patellar resurfacing group: a difference of -£149 (95% CI: -£574, £277, p=0.494).

KAT is larger than any previous RCT or meta-analysis of RCTs of patellar replacement. The conclusion is that over the first five years after TKR, functional outcomes, reoperation rates and healthcare costs appear to be the same irrespective of whether or not the patella is resurfaced.

Data on metal backing and mobile bearing prostheses are currently being analysed.

*Additional funding for research support in clinical centres was received from Howmedica Osteonics; Zimmer; J&J DePuy; Corin Medical; Smith & Nephew Healthcare Ltd; and Biomet Merck Ltd.

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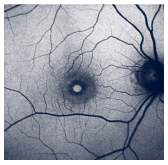
The Full-thickness macular hole and Internal Limiting Membrane peeling Study (FILMS): a randomised controlled trial



A full-thickness macular hole (FTMH) is a common degenerative condition of the eye which, if untreated, can lead to serious loss of vision. Surgery, by means of pars plana vitrectomy and post-operative intraocular tamponade with gas, is effective in closing the hole and improving vision when compared with no treatment. Internal limiting membrane (ILM) peeling was introduced as an additional surgical manoeuvre but there has been uncertainty regarding the optimal procedure.

FILMS (ISRCTN33175422) was funded by the Chief Scientist Office of the Scottish Government Health Directorates and led by Noemi Lois, a consultant ophthalmologist in Aberdeen. The aim of this study was to determine whether, in patients with stage 2 or stage 3 FTHM present for up to 18 months, and with vision of less than or equal to 20/40, macular hole surgery with ILM peeling was superior to surgery without peeling.

FILMS is the largest RCT conducted on this subject. One hundred and forty-one patients from nine centres across the UK and the Republic of Ireland were randomised to receive macular hole surgery with or without ILM peeling. Participants were followed-up in clinic at one, three and six months after surgery. The main outcome was distance visual acuity at six months. Other outcomes included additional measures of vision (near visual acuity at three and six months, contrast sensitivity and reading speed at six months), closure of the macular hole at each time point, complications and re-operation rates, participant reported outcomes as determined by the EQ-5D and the National Eye Institute Visual Function Questionnaire (VFQ-25) at six months and a cost-effectiveness analysis.

One hundred and twenty-seven participants completed the six-month follow up. We found a non-statistically significant difference in distance visual acuity at six months between peel and no peel groups (adjusted difference in means 4.8 (95% CI -0.3 to 9.8), p=0.063). However, there was a statistically significant higher rate of macular hole closure in the ILM peel group at one month with less re-operations performed by six months. The economic evaluation suggested that peeling the ILM is more likely to be considered cost-effective than no ILM peeling. We concluded that macular hole surgery with ILM peeling should become the treatment of choice for patients with stage 2 or stage 3 FTMHs.

We will collect information on the study participants in the longer term. In addition, FILMS will be combined with the results from similar studies conducted internationally.

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Staff profile - Alison McDonald

Alison McDonald joined the Unit in 1993 to work on the Neonatal Examination and Screening Trial (NEST) - a randomised, controlled, switchback trial of alternative policies for low risk infants. Since that time Alison has been involved with several different trials and projects within the Unit, including RECORD (Randomised Evaluation of Calcium and/OR vitamin D), STEPS (Strategies for Trials Enrolment and Participation) and MAPS (Men After Prostate Surgery).

When the Centre for Healthcare Randomised Trials (CHaRT) was established in 2004, Alison became the Senior Trials Manager. She works across the portfolio of CHaRT trials (http://www.charttrials.abdn.ac.uk/trials.shtml). Her role includes overseeing the personnel responsible for the day-to-day running of all CHaRT trials. She provides advice to local investigators on issues of trial conduct and procedures.

Alison is currently a member of several Committees, including the UK Trial Managers' Network (TMN) Steering Group, the Program Committee of the Society for Clinical Trials (SCT), the SCT membership of Clinical Research Associates (CRAs) and Project Managers Committee, the European Clinical Research Infrastructures Network working group on trial monitoring and is a faculty member of the Edinburgh Clinical Trials Management course (ECTMC).

CSO fellowship awarded to Katie Schumm

A CSO Postdoctoral Fellowship has recently been awarded to Katie Schumm and will explore the use of Decision Aids in Randomised controlled Trials (The DART Study). A comprehensive training programme, consisting of short-courses and personal mentoring, will also form an integral component of the fellowship.

The project will focus on the acceptability and usefulness of a trial participation decision aid from both a clinician and patient perspective. The specific objectives are to:

- identify how decision aids are currently used to inform trial participation;
- investigate what patients and clinicians understand about RCT participation;
- define what patients and clinicians perceive as being important information to include in a decision aid to inform trial participation;
- develop a decision aid to inform participation of patients in a RCT;
- assess patients and clinicians views about the acceptability of a trial participation decision aid;
- develop guidance on how to utilise decision aids to inform RCT participation.

The project will use a formal mixed methods approach to explore clinicians' and patients' perspectives about trial participation decision aids.

Katie will collaborate with scientists at the Ottawa Health Research Institute (OHRI), which is home to world experts in decision aid design and development, at key stages of the project to further the decision aid development process.

The fellowship runs from November 2009 to October 2012 and will be conducted in collaboration with researchers in the UK and Canada.

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Unit staff contribute to successful post-graduate teaching

The Health Services Research Unit leads on health services research training as part of a postgraduate programme in Health Services and Public Health Research. The programme includes seven 'core' courses: Health Services Research, Applied Statistics, Epidemiology and Demography, Health Economics, Health Informatics, Managing for Health and Public Health. Students may register for an MSc, Diploma or Certificate qualification. Award of a Diploma or an MSc requires the successful completion of a three or six-month research project respectively.

The aim of the Health Services Research course is to equip students with the skills and information needed to appraise and undertake health services research. At the end of the course students will be able to: design a rigorous evaluation of an innovation in health care; implement such an evaluation with some insight into potential problems and apply the principles of critical appraisal of research evidence to published reports of health services research.

The course is taught in two-hour seminars twice weekly with interactive group sessions providing a key aspect of the learning experience. Students also complete a six month project. Many of the Unit staff contribute to the teaching and student supervision.

The course continues to expand in popularity at both a national and international level, attracting high numbers of UK and overseas students. Whilst many students have background in health (e.g. nursing, nutrition, pharmacy, etc) the course is also highly relevant and welcoming to students holding first degrees in pure or social science who have an interest in expanding their knowledge of health services research.

HSRU staff also contribute to a range of other courses provided within the University, for example Managing for Health.

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Staff news

We welcome to the Unit (from left to right) Mayret Castillo, Emma Hodgson, Eilidh Duncan, Andrew Elders, Alyson Forrest, Pawana Sharma and Stephan Dombrowski, and (not in photo) Fiona Gammie, Julie Murdoch and Kath Starr.

Recent publications

Abrahamsen B, Masud T, Avenell A, Anderson H, Meyer E, Cooper C, Smith H, LaCroix AZ, Torgerson D, Johansen A, Jackson R, Rejnmark L, Wactawski-Wende J, Brixen K, Mosekilde L, Robbins JA, Francis R. **Patient level pooled analysis of 68,500 patients from seven major vitamin D fracture trials in the US and Europe.** Br Med J 2010;340(7738):b5463.

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Epstein D, Bojke L, Sculpher M, REFLUX Trial Group, [Campbell MK], [Ramsay C], [Vale L], [Wileman S]. **Laparoscopic fundoplication compared with medical management for gastro-oesophageal reflux disease: cost effectiveness study.** Br Med J 2009;339(7713):144-156.

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Mowatt G, Zhu S, Kilonzo M, Boachie C, Fraser C, Griffiths TRL, N'Dow J, Nabi G, Cook JA, Vale L. **Systematic review of the clinical and cost-effectiveness of photodynamic diagnosis and urine biomarkers (FISH, ImmunoCyt, NMP22) and cytology for the detection and follow-up of bladder cancer.** Health Technol Assess 2010;14(4).

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