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Health Services Research Unit

Newsletter Spring 2013

CATHETER Trial Publishes Findings

The CATHETER trial was a three group, multicentre, randomised controlled trial funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme. Adults (aged ≥16 years) requiring short-term (≤14 days) catheterisation were recruited from 24 NHS hospitals in the UK. Participants were randomised to receive a silver alloy-coated catheter, a nitrofural-impregnated catheter, or a PTFE-coated catheter (control group). Patients undergoing unplanned catheterisation were also included and consent for participation was obtained retrospectively. Data were collected for six weeks after randomisation.

The primary outcome was incidence of symptomatic catheter-associated urinary tract infection (CAUTI), defined as the presence of participant-reported symptoms with clinician prescription of antibiotic for a urinary tract infection at any time up to six weeks after randomisation. Secondary outcomes included incidence of microbiologically confirmed symptomatic CAUTI, incidence of bacteriuria up to three days after catheter removal; changes in health-related quality of life during the six weeks of trial participation; and urethral discomfort related to catheterisation.

7102 participants were randomised, 708 of whom subsequently were not catheterised, did not confirm consent, or withdrew, and were not included in the primary analyses. 6394 were included in the analysis. Results showed that 271/2144 (12.6%) of the control group participants had incidence of CAUTI compared with 263/2097 (12.5%) of participants allocated to the silver alloy catheter (difference –0.1% [95% CI –2.4 to 2.2]), and 228/2153 (10.6%) of participants allocated a nitrofural catheter (–2.1% [–4.2 to 0.1]). The proportion of participants reporting catheter-related discomfort was higher in the nitrofural group compared with the other groups.

We concluded that silver alloy-coated catheters were not effective for the reduction of incidence of symptomatic CAUTI. The reduction we noted in CAUTI associated with nitrofural-impregnated catheters was less than our pre-stated minimum level of clinical effectiveness (a 3.3% absolute reduction). Routine use of antimicrobial-impregnated catheters was not supported by this trial. The report was recently published in the Lancet:

Pickard R, Lam T, MacLennan G, et al. *Lancet* 2012; 380: 1927-35.

For further information contact Graeme MacLennan, email g.maclennan@abdn.ac.uk, telephone 01224 438147.

Conference Report: Improving Quality in Healthcare: Translating Evidence into Practice

TRiaDS
Translation Research in a Dental Setting

The inaugural Translation Research in a Dental Setting (TRiaDS) Conference was held on 7th November 2012 at the John McIntyre Conference Centre in Edinburgh. Co-organised by the Health Services Research Unit and NHS Education for Scotland (NES), the one day international event focussed on approaches to the translation of evidence into practice and attracted 112 delegates including clinicians, policy-makers, academics and educators from across the UK, North America and mainland Europe. Michael Matheson, Scottish Government Minister for Public Health and Sport, delivered the keynote speech on the importance of translating research findings into clinical practice. In addition, international experts in the field of knowledge translation including Professors Jeremy Grimshaw, Michel Wensing and Martin Eccles shared their expertise and insights through interactive presentations and discussion sessions. The conference programme included parallel sessions with presenters from NICE, the UK Cochrane Centre, Scottish Dental Clinical Effectiveness Programme, Healthcare Improvement Scotland, NES and the Universities of Aberdeen, Leicester, Leeds and University College London as well as poster presentations sponsored by the Scottish Dental Practice Based Research Network. Conference delegates branded the event a huge success: "*Excellent conference with great speakers*". Feedback also suggests that there is a real appetite for similar events in the future.

From left: Prof Craig Ramsay, Michael Matheson MSP, Dr Lindsay Burley, Prof Jan Clarkson, Dr David Felix

New study funded to evaluate vault and uterine prolapse surgery: the VUE study

Around 1 in 10 women will need prolapse surgery at some point in their lives. Prolapse occurs when the pelvic organs (such as the bladder, bowel or womb) come down into, or out of, the vagina. This is caused either by weakness of the tissues which usually support these organs or by weak pelvic floor muscles. It is most common in women who have had children.

For women with a uterine (womb) prolapse or a vault prolapse (top of the vagina, in a woman who has had her womb removed previously), there are many different operations. There is a high failure rate after surgery: a quarter of women who have had their womb removed will need a vault repair later. However, there is not enough evidence from research to identify which operation is best for these two types of prolapse. Many operations have been tried, but have not been extensively evaluated, especially in terms of how well they improve prolapse symptoms.

VUE is a multi-centre trial funded by the National Institute for Health Research Health Technology Assessment Programme which will be carried out in around 40 hospitals in the UK. A total of 800 eligible women having surgery for uterine or vault prolapse will be randomised to one of two trials:

1. Uterine trial: vaginal hysterectomy compared with an operation to hold up the uterus without removing it
2. Vault trial: hold up the vault from below (the vaginal route) compared with holding it up via the abdomen (tummy)

Women will have a routine physical examination before surgery and complete a baseline questionnaire. Further symptom questionnaires will be completed 6 and 12 months after surgery. The women will be examined and reviewed in outpatients at 12 months after surgery. Our main interest is in the cure or improvement of prolapse symptoms, as reported by the women themselves.

For further information, contact Lynda Constable, email l.constable@abdn.ac.uk, telephone 01224 438174.

Evaluating therapeutic interventions for the removal of ureteric stones: the TISU trial

Urinary stone disease is very common with an estimated general population prevalence of 2–3%. When urinary stones move from the kidney into the ureter (the tube connecting the kidney to the bladder), they cause severe debilitating pain, short-term impairment of quality of life and use substantial NHS resources.

Most ureteric stones pass spontaneously (with painkillers and fluids) sometimes aided by medication. However, a fifth to a third of cases require active "stone removal" due to failure to pass the stone, continuing pain, infection or obstruction to urine drainage. The two most common active interventions are **extracorporeal shockwave lithotripsy** (a machine - a lithotripter - fragments the stone by passing focussed shock-waves through the body towards the stone) and **ureteroscopic stone treatment** (where the stone is removed using a ureteroscope). Whilst both interventions appear to be effective in stone clearance, they differ in invasiveness, anaesthetic requirement, treatment setting, the number of procedures required to clear the stone, complications, patient reported outcomes (such as severity, duration of pain), and cost.

Our team has been funded by the National Institute for Health Research Health Technology Assessment Programme HTA programme to undertake a multicentre trial to determine the clinical and cost effectiveness of lithotripsy as first treatment option, compared with ureteroscopic retrieval for ureteric stones.

We plan to recruit and randomly allocate 1000 adults with a ureteric stone requiring an active intervention across 17 UK secondary care units to lithotripsy or uteroscopic treatment. Our primary outcomes measured at 6 months will be: 1) clinical resolution of the stone episode - defined as no further intervention required to facilitate stone passage; and 2) incremental cost per quality adjusted life year based on responses to the health status measure EQ5D.

For further information, contact Ruth Thomas, email r.e.thomas@abdn.ac.uk, telephone 01224 438172.

Staff profile: Shaun Treweek

Shaun Treweek joined the Unit in January 2013 to take up a post as Professor of Health Services Research. Shaun has almost 20 years' experience as a health services researcher specialising in trial methodology. He is active in the field of pragmatic trial design, the design and pre-trial testing of complex interventions, improved recruitment interventions for trials and theory-based methods to assess the implementation potential of interventions. Before joining the Unit, Shaun was at the University of Dundee where he was latterly Assistant Director of the Tayside Clinical Trials Unit.

Prior to Dundee, Shaun spent six years in Oslo working at the Norwegian Knowledge Centre for the Health Services, which is where he initially developed his interest in trial methodology and systematic reviews. He retains active links with the Norwegians and currently works on two European Community funded projects with his Oslo-based colleagues.

For further information, contact Shaun Treweek, email streweek@mac.com, telephone 01224 438145.

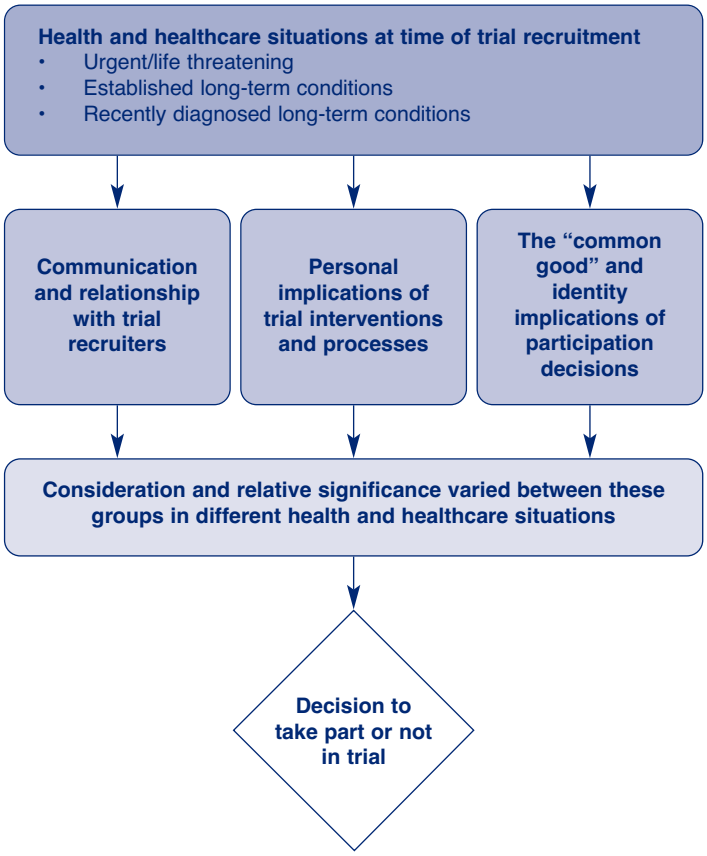
What makes people participate in clinical trials?

It is well known that recruitment to trials can be difficult. In recent years a number of in-depth qualitative studies have been published that have outlined patients' experiences of recruitment and participation in trials. To understand the collective insights from these studies we had, in 2007, undertaken a meta-ethnography of relevant studies (a formal synthesis method which centres on the construction of interpretations cumulatively across qualitative studies). This meta-ethnography had synthesised relevant papers published between 1996 and 2005. More recently, we undertook a second meta-ethnography, this time using studies published between 2005 and 2010. This allowed us the opportunity to: a) compare findings with those from the first meta-ethnography; and b) explore the methodological implications for the updating of meta-ethnographies.

The two syntheses were broadly compatible, but the conceptual model developed in the second more clearly highlighted how key aspects of context, recruitment approach and person approach can interact to influence trial recruitment. In particular the way potential participants were situated in terms of their health states and treatment junctures (and their perceptions about these at the time of trial recruitment) was particularly salient. Their sense of their situation at the time of being approached about trial participation influenced their judgements, particularly around the implications of trial participation for the "common good" (their desire to help others) and their own "identity" in relation to participating (what their non/participation might say about them). It could also mediate the influence of their communication and relationship with trial recruiters and of the nature of the trial interventions and processes.

Our work highlights the need for trialists to consider potential participants' health and healthcare situations when designing recruitment approaches. This study also provided the first empirical insights into the updating process that we are aware of for meta-ethnographies.

Conceptual model: Factors influencing trial participation



For further information, contact Sharon McCann, email s.k.mccann@abdn.ac.uk, telephone 01224 438154.

Target differences in sample size calculations – the DELTA study

The randomised controlled trial (RCT) is widely considered to be the gold standard study for comparing the effectiveness of health interventions. Central to the validity of a RCT is the calculation of the number of participants needed (the sample size). This provides reassurance that the trial will identify a difference of a particular magnitude if such a difference exists. The value used to determine the sample size can be considered the "target difference". Despite its importance, specification of the target difference, as opposed to statistical approaches to calculating the sample size, has been greatly neglected. DELTA, funded by the Medical Research Council's Methodology Research Programme, involved a comprehensive review of potential methods, two surveys of current practice amongst trialists, and production of a guidance document to inform the design of future studies.

DELTA
Difference ELicitation in TriAls

The search identified 11,485 potentially relevant studies; 1,445 papers were full-text assessed with 776 included in the review. Seven methods were identified – anchor, distribution, health economic, opinion-seeking, pilot study, review of evidence base and standardised effect size; each with important variations in implementation. The surveys showed substantial differences in awareness, use and willingness to recommend the various methods amongst trialists. Guidance regarding specification of the target difference and the use of potential methods, including reporting standards for trial protocol and main results papers, was developed.

There is a clear need for greater use of formal methods to determine the target difference and better reporting of its specification. While no single method provides a perfect solution to a difficult question, methods are available to inform specification of the target difference and should be used whenever feasible. Raising the standard of RCT sample size calculations and the corresponding reporting of them, would aid health professionals, patients, researchers and funders in judging the strength of the evidence and ensure better use of scarce resources.

For further information, contact Jonathan Cook, email j.a.cook@abdn.ac.uk, telephone 01224 438166.

Elucigene FH20 and LIPOchip for the diagnosis of familial hypercholesterolaemia: a systematic review and economic evaluation

Familial hypercholesterolaemia (FH) is genetic condition in which affected individuals have raised cholesterol from birth, leading to early development of atherosclerosis and coronary heart disease, and high risk of premature death. In the UK the prevalence of FH is about 1 in 500, affecting around 120,000 people. Current guidelines on the identification and management of FH recommend DNA testing using comprehensive genetic analysis (CGA). It has been suggested that use of assay systems (such as Elucigene FH20 or LIPOchip) targeted to detect the most common FH mutations in a population might either replace CGA or be used as a pre-screen. We undertook a systematic review, commissioned by NICE's Diagnostics Assessment Programme, with the aim of assessing the diagnostic accuracy, effect on patient outcomes and cost-effectiveness of Elucigene FH20 and LIPOchip for the diagnosis of FH.

Fifteen studies were included to assess diagnostic accuracy against a reference standard of CGA. Sensitivity ranged from 44% to 52% for Elucigene FH20 and from 33.3% to 94.5% for various versions of LIPOchip in detecting FH-causing mutations in patients with a clinical diagnosis of FH.

As targeted tests designed to detect a limited number of genetic mutations, Elucigene FH20 and LIPOchip are unable to detect all known cases of FH, in contrast with CGA. CGA was found to be the most effective test in terms of sensitivity and quality-adjusted life year (QALY) gain. Elucigene FH20 and LIPOchip were also cost-effective; however because of inferior sensitivity compared with CGA, these tests offered cost savings but at the expense of large QALY losses compared with CGA.

In the light of our findings, new NICE guidance, issued in December 2012, stated that:

- Elucigene FH20 and LIPOchip are not recommended for the confirmation of a clinical diagnosis in people with FH because greater health benefits can be achieved cost-effectively through the use of CGA.
- Elucigene FH20 and LIPOchip are not recommended for cascade testing relatives of people with confirmed FH because targeted sequencing is less expensive and can be used for all relatives with no loss in health benefits.

For further information, contact Graham Mowatt, email g.mowatt@abdn.ac.uk, telephone 01224 438090.

Recent publications

(1) Campbell MK, Piaggio G, Elbourne DR, Altman DG, CONSORT Group. The CONSORT 2010 statement: extension to cluster randomised trials. *BMJ* 2012;345:e5661.

(2) Cook JA, Ramsay CR, Carr AJ, Rees JL, UKUFF Trial Group. A questionnaire elicitation of surgeons' belief about learning within a surgical trial. *PLoS One* 2012;7(11): e49178.

(3) Dombrowski S, Sniehotta F, Avenell A, Johnston M, MacLennan G, Azuara-Blanco A. Identifying active ingredients in complex behavioural interventions for obese adults with obesity-related co-morbidities or additional risk factors for co-morbidities: A systematic review. *Health Psychology Review* 2012;6(1):7-32.

(4) Ford JA, Jones R, Elders A, Mulatero C, Royle P, Stewart F, Todd R, Mowatt G. Denosumab for treatment of bone metastases secondary to solid tumours: systematic review and network meta-analysis. *Eur J Cancer* 2013;49(2):416-30.

(5) Glazener C, Elders A, MacArthur C, Lancashire RJ, Herbison P, Hagen S, Dean N, Bain C, Toozs-Hobson P, Richardson K, McDonald A, McPherson G, Wilson D, ProLong Study Group. Childbirth and prolapse: long term associations with the symptoms and objective measurement of pelvic organ prolapse. *Br J Obstet Gynaecol* 2013;120(2):161-8.

(6) Kolehmainen N, MacLennan G, Ternent L, Duncan EAS, Duncan EM, Ryan S, McKee L, Francis J. Using shared goal setting to improve access and equity: a mixed methods study of the Good Goals intervention in children's occupational therapy. *Implementation Science [serial on the Internet]* 2012;7:76.

(7) McPherson G, Campbell M, Elbourne D. Use of Randomisation in Clinical Trials: A Survey of UK Practice. *Trials* 2012;13:198.

(8) Pickard R, Lam T, MacLennan G, Starr K, Kilonzo M, McPherson G, Gillies K, McDonald A, Walton K, Buckley B, Glazener C, Boachie C, Burr J, Norrie J, Vale L, Grant A, N'Dow J. Types of urethral catheter for reducing symptomatic urinary tract infections in hospitalised adults requiring short-term catheterisation: multicentre randomised controlled trial and economic evaluation of antimicrobial- and antiseptic-impregnated urethral catheters (the CATHETER trial). *Health Technol Assess* 2012;16(47):1-197.

(9) Ramsay C, Pickard R, Robertson C, Close A, Vale L, Armstrong N, Barocas DA, Eden CG, Fraser C, Gurung T, Jenkinson D, Jia X, Lam TB, Mowatt G, Neal DE, Robinson MC, Royle J, Rushton SP, Sharma P, Shirley MDF, Soomro N. Systematic review and economic modelling of the relative clinical benefit and cost-effectiveness of laparoscopic surgery for removal of the prostate in men with localised prostate cancer. *Health Technol Assess* 2012;16(41):1-313.

(10) Treweek S, Barnett K, MacLennan G, Bonetti D, Eccles MP, Francis J, Jones C, Pitts NP, Ricketts I, Weal M, Sullivan F. E-mail invitations to general practitioners were as effective as postal invitations and were more efficient. *J Clin Epidemiol* 2012;65(7):793-7.

Staff News

We welcome the following people to the Unit: Juwera Ali and Sreekath Cherukuri (Programmers), Clare Cooper (Health Psychology research fellow), Joanne Coyle (WISE OWLS research fellow), Vikki Entwistle (Professor in Health Services Research and Ethics) and Shaun Treweek (Professor in Health Services Research).

Karen McLeod, Ted Bassinga, Gillian Murray-Dickson, Mayret Castillo and Kieran Rothnie have recently left the Unit and we wish them well.

Editorial team: Moira Cruickshank and Caroline Burnett. The Health Services Research Unit is funded by the Chief Scientist Office of the Scottish Government Health Directorates. However, the views expressed in this publication are those of the authors alone. The projects undertaken within the Heath Services Research Unit receive funding from a number of different funding bodies.

This newsletter is produced twice yearly by the Health Services Research Unit, University of Aberdeen, Health Sciences Building, Foresterhill, Aberdeen, AB25 2ZD. Telephone: 01224 438412. Fax: 01224 438165. Email: mcruickshank@abdn.ac.uk. WWW: http://www.abdn.ac.uk/hsru/