



Health Services Research Unit

Newsletter

Spring 2011

SIGNET Trial reports findings

Patients in intensive care units are usually unable to eat, and often have tube feeding into the gut. However, in people who are extremely sick, or who have had gastrointestinal surgery, providing sufficient nutrition via the gut may not be possible. For such patients intravenous (parenteral) feeding is required, but the constituents of that feed have been much debated. The Medical Research Council funded a randomised trial, which involved colleagues from across Scotland, and which examined whether more of the trace element selenium and/or the amino acid glutamine should be contained in intravenous feeding in intensive care. The trial office was in the Health Services Research Unit, and the trial was run between the Universities of Edinburgh and Aberdeen. Fresenius-Kabi and Oxford Nutrition provided funding for the nutrition constituents in the trial.

502 patients from 10 intensive care units in Scotland were recruited into the trial. Selenium and glutamine were added to the intravenous feeding for up to seven days, or until the patient resumed feeding via the gut or died.



We found that neither selenium nor glutamine significantly reduced participants developing a new infection in the first two weeks of the trial, except among those who had received at least five days

of supplementation with selenium. Mortality, lengths of stay in intensive care and hospital, days of antibiotic use and severity of the illness in intensive care were not significantly affected by selenium or glutamine supplementation. The full results from the SIGNET trial have recently been published in the British Medical Journal.

We plan to explore the potential role of selenium further in a bigger trial. We plan to examine whether giving intravenous selenium on its own to patients in intensive care (not just to those patients who require intravenous feeding) affects mortality and infections.

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www.abdn.ac.uk/hsru/

HSRU host visit from German Surgical Trials Network

In September 2010, the Unit (together with HERU) hosted a visit from representatives from the German Surgical Trials Network (known as ChirNet). ChirNet was set up to design and conduct large scale multi-centre clinical trials in surgery across Germany and had received funding from the German Ministry of Research and Education for a visiting programme to learn from existing, well-established international centres of excellence in the conduct of multi-centre clinical trials. The visit to the Unit was part of that programme.

Fourteen individuals from the Network, including representatives from the Universities of Munich, Heidelberg, Berlin, Kiel/Lübeck, Cologne/Witten,

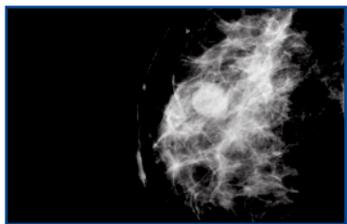


Mainz, Göttingen, and Marburg, attended the two day visit under the leadership of Prof Schumacher from Munich and Dr Seiler from Heidelberg.

Topics discussed over the two-day visit included applying for funding, setting up and running a

trials unit, developing standard operating procedures, deciding which trials to take on, handling complex trials designs and analysis and monitoring procedures. The sessions were lively and interactive and led to a positive action plan for continued collaboration across the two groups. The first evidence of that continued collaboration occurred in November when a sub-group of ChirNet came back to HSRU for a week-long working visit to develop standard operating procedures for their Network under the guidance of Unit staff.

Surveillance mammography following primary breast cancer



There are 45,000 new cases of breast cancer in the UK each year. It is important to know how best to monitor women following treatment of primary breast cancer because approximately 25% of women will experience a recurrence of

their cancer. Tumours detected by mammography are generally smaller and less invasive than those found by clinical examination. However, the evidence for the role and optimal organisation of a surveillance mammography service is uncertain, with professional bodies varying in guidance produced for clinicians.

The National Institute for Health Research Health Technology Assessment Programme funded a project to examine the clinical and cost-effectiveness of different surveillance mammography regimens for detecting ipsilateral breast tumour recurrence and ipsilateral second primary cancer (IBTR) and/or metachronous contralateral breast cancer (MCBC).

We first undertook a survey of UK breast surgeons and radiologists to identify current surveillance practices. This demonstrated that there is considerable variation in the combinations of start, frequency, duration and discharge from surveillance mammography, thus reflecting guideline variations.

Two systematic reviews were then undertaken. The first was to determine the clinical effectiveness of differing surveillance mammography regimens. The findings suggested that surveillance mammography offers a survival benefit compared with a surveillance regimen that does not include surveillance mammography, although the influence of combinations of alternative surveillance strategies remains unclear. The second review considered the diagnostic accuracy of surveillance mammography and suggested that mammography is associated with a high sensitivity and specificity but MRI is the most accurate test for detecting IBTR and MCBC.

We then undertook statistical modelling using individual patient datasets to determine if IBTR and MCBC were risk factors for death (all cause and breast cancer); and to determine whether the size of a subsequent tumour was a risk factor for death, considering the risk factors of the primary tumour. Analyses showed that IBTR has an adverse effect on survival that is independent of known risk factors. Furthermore, in those women experiencing either IBTR or MCBC, the size of the second tumour is important. Women with tumours more than 20mm in diameter were at a significantly greater risk of death than those with no recurrence or those whose tumour was less than 10mm in diameter.

Finally, from our economic evaluation, the strategy with the highest net benefit and, therefore, most likely to be considered cost-effective, was mammographic surveillance alone provided every 12 to 24 months. For women facing a higher likelihood of IBTR or MCBC, more frequent and more intensive surveillance (e.g. surveillance mammography every 12 months) had the highest net benefit. For women with a lower likelihood of IBTR or MCBC, less frequent surveillance mammography had the highest net benefit.

The review will be published as an HTA monograph in 2011.

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Role of drug therapy in the management of symptomatic ureteric stones



Spontaneous Urinary Stone Passage Enabled by Drugs

Kidney stone disease is a common health problem affecting about 1.6 million adults in the UK. In some patients the stone will fall out of the kidney and become lodged in the tube (ureter) between the kidney and bladder. The majority of sufferers experience a sudden episode of prolonged abdominal pain, usually sufficiently severe to need emergency admission to hospital.

The SUSPEND trial aims to determine the clinical and cost-effectiveness of the use of two types of drug for the management of symptomatic urinary stones - alpha blockers (tamsulosin) and calcium channel blockers (nifedipine). The primary clinical outcome of the trial (measured at four weeks) is the spontaneous passage of the stone as measured by the need for further intervention in the treatment of the stone. There is also a primary health economic outcome of incremental cost per quality adjusted life years (QALYs) gained at 12 weeks.

This multi-centre trial, funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme, aims to recruit 1200 participants (randomising 400 to each of the three treatment groups; alpha blockers, calcium channel blockers and placebo). Approximately 16 centres throughout the UK will be involved. Recruitment has recently started, and is due to finish in November 2012.

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Staff news

We welcome Ebenezer Afolabi (Statistician), Katie Banister (Research Fellow), Tracey Davidson (Trial Manager), Anne Duncan (Trial Manager), Mark Forrest (Software Developer), Tara Gurung (Systematic Reviewer), Karen Keenan (Research Fellow), Kirsty Kiezebrink (Research Fellow) and Christiane Pflanz-Sinclair (Trial Manager) to the Unit. Claire Cochran and Louise Campbell have returned from maternity leave.

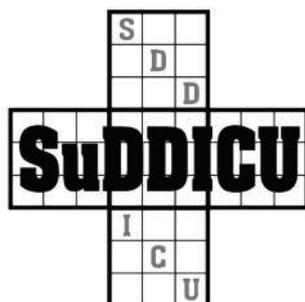
Paola Botello-Pinzon, Susan Campbell, Stephan Dombrowski, Fiona Gammie, David Jenkinson, Shirley Jia, Jim Kerslake, Laura Ternent and Luke Vale have recently left the Unit and we wish them well.

Selective Decontamination of the Digestive tract in critically ill patients treated in Intensive Care Units (the SuDDICU study)

Hospital acquired infections (HAIs) are a major cause of illness and death for patients and markedly increase health care costs. Critically ill patients in an Intensive Care Unit (ICU) are particularly susceptible to these infections and those who acquire HAIs are known to have poor outcomes.

One intervention that has gained interest in ICUs for reducing HAIs is the use of selective decontamination of the digestive tract (SDD). SDD involves the prophylactic application of antibiotics to the mouth, throat and stomach and a short course of intravenous antibiotics. Although the evidence supporting SDD for preventing infections is strong and there is also evidence that SDD saves lives, uptake among health care professionals in the UK is low. Multiple reasons for this have been identified including SDD being counterintuitive to clinicians who believe that antibiotics should be used sparingly (due to the potential of antimicrobial resistance), perceived inadequacies in the current evidence base as most research has been conducted outside the UK and that SDD implementation and delivery might be too difficult in practice.

The National Institute for Health Research Health Technology Assessment Programme (HTA) has awarded a grant to a team led by the Unit to investigate the reasons for low SDD uptake. The aims of the study are to identify (a) specific behaviours involved in delivering SDD, (b) clinicians' key beliefs about SDD and the evidence base, and (c) the next appropriate step in the research:



an effectiveness trial to address evidence gaps or an implementation trial to increase uptake.

The study will use a phased 'multi-lens' approach to investigate SDD from several perspectives using multiple methods based on theories of behaviour:

1. Semi-structured observations of SDD delivery and interviews with key stakeholders to specify the behaviours involved in this clinical procedure;
2. Theory-based Delphi study to identify beliefs of stakeholders in relation to SDD practice and perceptions about future research requirements;
3. National survey of stakeholders based on the Delphi findings to assess current practice, beliefs about SDD and acceptability of next research steps;
4. Semi-structured interviews with international trialists to assess the feasibility of appropriate designs for a randomised controlled trial.

The variable uptake in SDD is also apparent outside the UK. Reflecting the international importance of the topic, partner teams in Canada, Australia and New Zealand are undertaking parallel investigations into the reasons for low uptake in their settings (adopting the UK SuDDICU protocol).

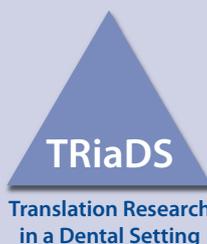
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Translation Research in a Dental Setting

It is well documented that the translation of knowledge into clinical practice is a slow and haphazard process. This is no less true for dental healthcare than other types of healthcare. One common policy strategy to help promote knowledge translation is the production of clinical guidance, but it has been demonstrated that the simple publication of guidance is unlikely to optimise practice.

For dentistry in Scotland, the production of clinical guidance is the responsibility of the Scottish Dental Clinical Effectiveness Programme (SDCEP). TRiADS (Translation Research in a Dental Setting) is a multidisciplinary research collaboration, embedded within the SDCEP guidance development process, which aims to establish a practical evaluative framework for the translation of guidance and to conduct and evaluate a programme of integrated, multidisciplinary research to enhance the science of knowledge translation.

The TRiADS programmatic evaluation employs a standardised process using optimal methods and theory. For each SDCEP guidance document a diagnostic analysis is undertaken alongside the guidance development process. Information is gathered about current dental care activities. Key recommendations and their required behaviours are identified and prioritised. Stakeholder questionnaires and interviews are used to identify and elicit salient beliefs regarding potential barriers and enablers towards the key recommendations and behaviours. Where possible, routinely collected data are used to



measure compliance with the guidance and to inform decisions about whether a knowledge translation intervention is required. Interventions are theory based and informed by evidence gathered during the diagnostic phase and by prior published evidence. They are evaluated using a range of experimental and quasi-experimental study designs, and data collection continues beyond the end of the intervention to investigate the sustainability of an intervention effect. Recent studies include a randomised trial of two strategies to increase adherence to recommended decontamination practice and an interrupted time series of antibiotic prescribing practice.

The TRiADS programmatic approach is a significant step forward towards the development of a practical, generalisable framework for knowledge translation research. The multidisciplinary composition of the TRiADS team enables consideration of the individual, organisational and system determinants of professional behaviour change. In addition the embedding of TRiADS within a national programme of guidance development offers a unique opportunity to inform and influence the guidance development process, and enables TRiADS to inform dental services practitioners, policy makers and patients on how best to translate national recommendations into routine clinical activities.

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HSRU Away Day

An away day was held for Unit staff on 29 September 2010 at the Treetops Hotel in Aberdeen, and focussed on the theme of "best practice". Sessions explored what "best practice" means for the Unit and also generated ideas about how best to achieve and sustain it. The day also provided an opportunity to engage all staff in the ongoing consideration of how the Unit can best equip itself to be viable and sustainable in the future. The format of the day was based on "open space" methodology and was aided by a facilitator.



A number of issues were discussed including: how to maximise creativity in the Unit; professional and career development; communication; our physical and social environment; Unit processes; and planning and partnerships. Feedback from staff suggested that the day was a worthwhile exercise.

A group - the HSRU Improvement and Implementation Group - has been formed within the Unit to manage the development and implementation of the ideas raised.

We have recently updated our website.
You can keep up to date with new developments by visiting
<http://www.abdn.ac.uk/hsru/>

Recent publications

Andrews PJD, Avenell A, Noble DW, Campbell MK, Croal BL, Simpson WG, Vale LD, Battison CG, Jenkinson DJ, Cook JA and the SIGNET Trials Group. Randomised trial of glutamine, selenium, or both, to supplement parenteral nutrition for critically ill patients. *Br Med J* 2011; 342:d1542

Bolland M, Avenell A, Baron J, Grey A, MacLennan GS, Gamble GD, Reid IR. Effect of calcium supplementation on the risk of myocardial infarction and cardiovascular events: a meta-analysis. *Br Med J* 2010;341(c3691)

Cuthbertson BH, Francis J, Campbell MK, McIntyre L, Seppelt I, Grimshaw JM, SuDDICU study group. A study of the perceived risks, benefits and barriers to the use of SDD in adult critical care units (The SuDDICU study). *Trials* 2010;11(117)

Cuthbertson BH, Roughton S, Jenkinson DJ, MacLennan GS, Vale L. Quality of life in the five years after intensive care. *Crit Care* 2010;14(1):R6.

Francis J, Johnston M, Robertson C, Glidewell L, Entwistle VA, Eccles M, Grimshaw JM. What is an adequate sample size? Operationalising data saturation for theory-based interview studies. *Psychol Health* 2010;25(10):1229-45.

Hoddinott P, Allan K, Avenell A, Britten J. Group interventions to improve health outcomes: a framework for their design and delivery. *BMC Public Health* 2010;10:800.

Imamura M, Abrams P, Bain C, Buckley BS, Cardozo L, Cody J, Cook J, Eustice S, Glazener C, Grant A, Hay-Smith J, Hislop J, Jenkinson DJ, Kilonzo M, Mowatt G, Nabi G, N'Dow J, Pickard R, Ternent L, Wallace S, Wardle J, Zhu S, Vale L. Systematic review and economic modelling of the effectiveness and efficiency of non-surgical treatments for women with stress urinary incontinence. *Health Technol Assess* 2010;14(40)

Jia X, Glazener C, Mowatt G, Jenkinson DJ, Fraser C, Bain C, Burr J. Systematic review of the efficacy and safety of using mesh in surgery for uterine or vaginal vault prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2010;21(11):1413-31. DOI: 10.1007/s00192-010-1156-7

Kolehmainen N, MacLennan G, Francis J, Duncan EAS. Clinicians' caseload management behaviours as explanatory factors in patients' length of time on caseloads: a predictive multilevel study in paediatric community occupational therapy. *BMC Health Serv Res* 2010;10:249.

Lourenco T, Grant A, Burr JM, Vale L. The introduction of new interventional procedures in the British National Health Service - a qualitative study. *Health Policy* 2011;100(1):35-42.

Schumm K, Skea Z, McKee L, N'Dow J. 'They're doing surgery on two people': A meta-ethnography of the influences on couples' treatment decision making for prostate cancer. *Health Expect* 2010;13(4):335-49.

Staff profile - Graeme MacLennan

Graeme MacLennan is the Unit Senior Statistician. Graeme manages the statistics team which provides statistical support to all HSRU and CHaRT projects.

Graeme joined the Unit in 1998 as a junior statistician after graduating from University of Aberdeen with a BSc in Mathematics.

Since then he has worked on a range of projects from the Unit portfolio gaining extensive experience in randomised controls trials (RECORD, KAT, PRISM,



STOPPIT, ERUPT), systematic reviews and meta-analyses (benign prostatic enlargement, vaginal prolapse repair) and health psychology (PRIME, GAP). In 2004 he obtained an MSc in Applied Statistics and has been Senior Statistician since 2008.

Graeme's research interests focus on the evaluation of complex interventions, from the development stage through evaluation in randomised trials to evidence synthesis.