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APPENDIX 1

HSRU PROJECTS

HEALTH CARE ASSESSMENT PROJECTS

A.1

A placebo controlled randomised trial of intravenous lidocaine in accelerating gastrointestinal recovery after colorectal surgery (ALLEGRO)

Investigators

Graeme MacLennan, HSRU; John Norrie, Hugh Paterson, Ken Fearon, Irwin Foo, University of Edinburgh; Susan Nimmo, Doug Speake, Angie Balfour, Lothian NHS Board; Robert Arnott, PPI

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £376,988 (£933,150)

Summary

ALLEGRO is a research study investigating if Intravenous (IV) Lidocaine improves recovery of gut function after colorectal surgery for NHS patients.

Lidocaine (a local anaesthetic) used intravenously (through the vein) has been shown to reduce pain and inflammation after surgery and seems to help other aspects of recovery that may be important for return of gut function, for example reducing nausea and vomiting.

ALLEGRO is a multicentre randomised controlled trial, funded by NIHR HTA Programme.

The Allegro study aims to find out if IV Lidocaine can help improve the recovery of gut function in patients after bowel surgery compared to placebo (or dummy) IV in 562 participants. The primary outcome is how quickly gut function returns.

ALLEGRO is led by Mr Hugh Paterson, based at University of Edinburgh.

Current status

Ongoing

Publications and presentations

None

A.2

A pragmatic group sequential placebo controlled randomised trial to determine the effectiveness of Glyceryl trinitrate for retained placenta. (GOT-IT)

Investigators

Graeme MacLennan, Gladys McPherson, Graeme Scotland, HSRU; John Norrie, Dr Fiona Dennison, Prof Jane Norman, Dr Julia Lawton, University of Edinburgh; Mrs Sheonagh Brook-Smith, NHS Lothian; Mrs Mathilde Peace, Lothian Maternity Services Liaison Committee; Mrs Cynthia Clarkson, National Childbirth Trust; Mrs Jane Brewin, Tommy's; Prof Dame Tina Lavender, University of Manchester

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £227,433 (£1,671,968)

Summary

A retained placenta (RP) is a complication after a normal birth, which affects nearly 11,000 women in the UK a year. The recommended treatment for RP is a surgical procedure - manual removal of placenta (MROP). This is a painful and unpleasant procedure for the women, involving an additional stay in hospital, and is an additional cost for the NHS.

GOT-IT is a multi-centre randomised controlled blinded trial, funded by the NIHR HTA Programme, investigating whether treatment with oral Glyceryl trinitrate (GTN) is an effective treatment for retained placenta which will lead to a reduction in the number of women requiring manual removal of the placenta. Women with retained placenta will be randomised to either GTN or placebo.

GOT-IT will randomise 1100 women.

The trial is led by Dr Fiona Dennison based at the University of Edinburgh.

Current status

Ongoing

Key publications

Denison, FC, Norrie, J, Lawton, K, Norman, JE, Scotland, G, McPherson, G, McDonald, A, Forrest, M, Hudson, J, Peace, M, Clarksson, C, Brook-Smith, S, Morrow, S, Hallowell, N, Hodges, L, Carruthers, KF A pragmatic group sequential placebo controlled randomised trial to determine the effectiveness of glyceryl trinitrate for retained placenta (GOT-IT): a study protocol. *BMJ Open* 2017;7(9):e017134

A.3

A randomised controlled trial comparing the clinical effectiveness and cost-effectiveness of laparoscopic cholecystectomy compared with observation/conservative management for preventing recurrent symptoms and complications in adults with uncomplicated symptomatic gallstones (C-GALL)

Investigators

Craig Ramsay, Miriam Brazzelli, Katie Gillies, Graeme MacLennan, Alison Avenell, HSRU; Dr Irfan Ahmed, Dr Bernard Croal ,NHS Grampian; Rodolfo Hernandez, Peter Murchie, University of Aberdeen; Jane Blazeby, University of Bristol

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £1,381,052 (£1,397,962)

Summary

Gallstone disease (cholelithiasis) is one of the most common gastrointestinal disorders in industrialised societies. In the UK and North America, the number of surgical procedures for gallstone disease increased between 1950s and 1990s, reflecting both the rise in prevalence of gallstone disease and the use of cholecystectomy as the treatment of choice.

The aim of the C-GALL trial is to assess the clinical and cost effectiveness of laparoscopic cholecystectomy with observation/conservative management for preventing recurrent symptoms and complications in adults (aged 18 and over) presenting with uncomplicated symptomatic gallstones in a secondary care setting and considered suitable for cholecystectomy.

This NIHR Health Technology Assessment (HTA) programme funded trial is a multi-centre randomised controlled trial aiming to recruit 430 participants across 20 secondary care sites in the UK. Trial participants are followed-up for 18 months and the patient outcome is quality of life bodily pain which is measured using a questionnaire (SF-36) that is completed at entry into the trial (baseline) and then at 3, 9, 12 and 18 months. The primary economic outcome measure will be incremental cost per QALY.

The C-GALL trial is led by Professor Irfan Ahmed (NHS Grampian) and Professor Craig Ramsay (University of Aberdeen). C-GALL opened to recruitment in August.

Current status

Ongoing

Publications and presentations

None

A.4

A randomised controlled trial of the effectiveness, and cost-effectiveness, of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) for trauma (UK REBOA)

Investigators

Graeme MacLennan, Dwayne Boyers, Jan Jansen, Marion Campbell, HSRU; Karim Brohi, Tim Harris, Barts & London School of Medicine & Dentistry; Jonny Morrison, NHS Greater Glasgow & Clyde; Robert Lendrum, Alfred Hospital & Monash University; Nigel Tai, Defence Medical Services/Royal London Hospital; Chris Moran, Nottingham University Hospital NHS Trust; Mark Midwinter, Royal Centre for Defence, QE Hospital; Fional Lecky, Sheffield University

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £1,058,662 (£1,183,000)

Summary

Each year around 5400 people in England and Wales die after being severely injured – for example, in a road traffic collision, or as a result of a major fall. The leading cause of preventable death following injury is uncontrolled bleeding, which usually requires immediate surgery. However, some patients die before they can reach an operating theatre.

REBOA (which stands for Resuscitative Endovascular Balloon Occlusion of the Aorta) is a new technique which could help with this. REBOA involves passing a small inflatable balloon into the aorta (the main artery) to stop the bleeding until a patient can be taken to an operating theatre.

The UK-REBOA study, funded by the NIHR HTA programme, aims to compare standard major trauma centre care with REBOA versus standard major trauma care alone. We expect to recruit approximately 120 patients in this study, across 10 Major Trauma Centres, over four years.

The primary outcome is mortality at 90 days.

UK-REBOA is led by Dr Jan Jansen based at the University of Alabama and HSRU, University of Aberdeen.

Current status

Ongoing

Publications and presentations

None

A.5

A randomised controlled trial to determine the effectiveness of bridging from emergency to regular contraception (Bridge-it)

Investigators

Graeme MacLennan, HSRU; John Norrie, Sharon Cameron, Anna Glasier, James Trussell, University of Edinburgh; Andrew Radley, NHS Tayside; Lisa McDaid, University of Glasgow; Paula Baraister, Kings College Hospital NHS; Judith Stephenson, UCL Partners

Source and amount of HSRU funding (total funding)

NIHR HTA Commissioned Call £212,536 (1,026,802)

Summary

Emergency contraception (EC) can prevent pregnancy for women following unprotected sex or burst condoms etc. Most women who use EC in the UK go to a pharmacy for it. It is really important that women start a regular method of contraception after EC if they don't want to become pregnant. However, most pharmacies cannot usually provide contraception (except condoms) without a prescription. This means that to start regular contraception (e.g. implant, pill etc) women must go to a GP or family planning clinic. Getting an appointment can take time and some women fall pregnant during this time.

Bridge-it, funded by the NIHR HTA, is a cluster randomised crossover trial involving approximately 26 pharmacies in 3 UK regions - London (South and Central), Lothian and Tayside recruiting a total of 2080 women aged 16 and over presenting for EC. The primary objective of the trial is to determine whether offering women attending a pharmacy for EC a 3 month supply of progestogen only pill (POP) plus the offer to attend a local Sexual Reproductive Health (SRH) service results in increased uptake of effective contraception, compared to standard care (which usually includes verbal advice to visit a GP & SRH service) and whether the intervention reduces abortion rates. Participants will be surveyed by text/phone at 4 and 12 months to ask about methods of contraception they have been using and where they got it from, if they used EC again and about any pregnancies they may have had.

If we find a difference in contraceptive use or numbers of unintended pregnancies amongst women who got the POP, we will calculate the costs or savings of this to the NHS. During the study we will also interview women and pharmacists about how providing the POP from the pharmacy might work in everyday practice.

The Bridge-it Trial is led by Dr Sharon Cameron based at the University of Edinburgh.

Current status

Ongoing

Publications and presentations

None

A.6

A Randomised controlled trial to Evaluate the effectiveness and cost benefit of prescribing high dose Fluoride toothpaste in preventing and treating dental Caries in high-risk older adults (REFLECT)

Investigators

Craig Ramsay, Dwayne Boyers, HSRU; Martin Tickle, Stephen Birch, Yin-Ling Lin, Iain Pretty, Helen Worthington, Tanya Walsh, University of Manchester; Michael Donaldson, Northern Ireland Health & Social Care Board; Paul McGarry, PPI; Jan Clarkson, University of Dundee

Source and amount of HSRU funding (total funding)

NIHR HTA £826,812 (2,063,056)

Summary

A Randomised controlled trial to Evaluate the effectiveness and cost benefit of prescribing high dose fluoride toothpaste in preventing and treating dental Caries in high-risk older adults (Reflect trial).

Recent research has found that many more people are keeping their own teeth for longer. Although this is a good thing it also means that when people begin to suffer with decay, the treatments required are more complex and expensive and may be very costly. There is a need to help people keep their own teeth free from decay as long as possible.

Since the 1970's fluoride toothpaste has been widely used to prevent tooth decay. Standard fluoride toothpaste, available to buy on the high street, contains around 1400 parts per million (ppm) of fluoride. High dose fluoride toothpaste, containing 5000ppm fluoride, is available by prescription from the dentist and is increasingly provided to patients judged to be at risk of decay.

In 2016 prescriptions of high dose fluoride toothpaste cost the NHS over £20 million and these costs are increasing rapidly. However, there is a lack of evidence to demonstrate that this toothpaste benefits patients and is cost-effective for the NHS.

The Reflect study is a multicentre randomised controlled trial funded by the NIHR HTA Programme. The trial will compare prescription of 5000 ppm fluoride toothpaste, used as advised by the participant's dentist, plus usual care, with usual care only (any advice given by the dentist will be to use standard, off-the-shelf, fluoride toothpaste). The study will run for 3 years and aims to recruit approximately 1200 people aged 50 years and over, who have a high risk of caries, from NHS dental practices in Northern Ireland, Scotland and England.

The primary clinical outcome is the number and proportion of individuals requiring restoration or extraction or endodontic treatment due to caries evaluated at 36 months.

The Reflect trial is led by Professor Martin Tickle based at the University of Manchester.

Current status

Ongoing

Publications and presentations

None

A.7

Abdominal massage for bowel dysfunction effectiveness research (AMBER)

Investigators

Shaun Treweek, HSRU: John Norrie, University of Edinburgh, Dr Doreen McClurg, Suzanne Hagen, Helen Mason, Glasgow Caledonian University; Anton Emmanuel, University College London Hospitals NHS Foundation Trust; Christine Norton, King's College London; Peter Donnan, University of Dundee; Fiona Harrie, University of Stirling; Paul Smith, Spinal Injuries Association

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £19,090 (£741,763)

Summary

Neurogenic bowel dysfunction (NBD: constipation and/or faecal incontinence) is common in people with multiple sclerosis (MS) and is rated as the most severe impact of their disease/injury, above wheelchair dependence. Despite this, current treatment options are limited.

AMBER is a multicentre trial involving 10 centres across the UK and is funded by the National Institute for Health Research and aims to find out whether abdominal massage can help improve the symptoms of NBD in these patients. A small study has already shown that it is possible for patients or carers to perform abdominal massage and in some cases this helped the patient with their symptoms. A larger study is now required to confirm the results one way or another. We will measure the results of treatment after 6 and 24 weeks. We are primarily interested in whether patients in the intervention group (receiving optimized bowel care and abdominal massage) have had more of an improvement in their NBD symptoms at 24 weeks after they start the study than the control group (receiving optimized bowel care only). We also want to find out how bad the constipation and bowel symptoms are, how much this affects their life and if they have any problems with their bladder. We will also measure the costs of the treatments and any costs to the patient and their family, and balance these against any benefits of the intervention treatment.

AMBER is led by Doreen McClurg at Glasgow Caledonian University, the recruitment target is 200 patients and recruitment will start in 2015.

Current status

Ongoing

Key publications

McClurg, D, Goodman, K, Hagen, S, Harris, F, Treweek, S, Emmanuel, A, Norton, C, Coggrave, M, Doran, S, Norrie, J, Donnan, P, Mason, H, Manoukian, S Abdominal massage for neurogenic bowel dysfunction in people with multiple sclerosis (AMBER — Abdominal Massage for Bowel Dysfunction Effectiveness Research): study protocol for a randomised controlled trial. *Trials* 2017;18:150

A.8**Aberdeen Technology Assessment Reviews (TARs) contract (2016-2021)****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £2,624,984 (£2,624.984)

Summary

HSRU, in collaboration with HERU and the section of Population Health within the University of Aberdeen is one of the nine independent academic centres in the UK commissioned to undertake technology assessment reviews (TARs) for NICE and also TARs and short reports for other NHS customers. NICE carry out appraisals of health technologies at the request of the Department of Health and provides guidance to the NHS on the clinical and cost effectiveness of selected new and established technologies. Guidance produced by NICE on health technologies is mandatory in England and Wales and applied selectively in Scotland (via the Scottish Health Technology Group and the Scottish Medicines Consortium) and Northern Ireland. The University of Aberdeen is the only academic centre in Scotland to hold a TAR contract and HSRU has been involved in the contract since 2001. The TAR work involves preparing a critique of the clinical effectiveness and cost effectiveness evidence submitted to NICE by the pharmaceutical companies in support of their cases to have new or existing drugs reimbursed by the NHS as well as broader evidence syntheses that, apart from a systematic review of current clinical effectiveness evidence, may include the development of an economic model to estimate the cost-effectiveness of alternative therapeutic or diagnostic interventions.

In 2014, the TAR contract was successfully renewed for the 2016-2021 period. The previous TAR contract covered the 2011-2016 period.

Current status

Ongoing

Key publications

See Appendix 2 Publications for a list of publications related to this contract.

A.9

Ablative therapy for men with localised prostate cancer: a systematic review and economic evaluation

Investigators

Craig Ramsay, Graeme MacLennan, HSRU; Dr Thomas Lam, NHS Grampian; Prof James N'Dow, Dr Sara MacLennan, Academic Urology Group, University of Aberdeen; Dr Rob Pickard, Prof Luke Vale, Prof Stephen Rushton, Mr Mark Foster, Newcastle University; Mr Axel Merseburger, Hannover Medical School, Germany; Mr Axel Heidenreich, University Hospital Aachen, Germany

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £175,619 (£292,253)

Summary

This NIHR HTA-funded project sought to determine the clinical benefits and cost-effectiveness of ablative therapy for men with localised prostate cancer. Ablative treatments considered were: brachytherapy; cryotherapy; high intensity focused-ultrasound (HIFU); vascular-targeted photodynamic therapy (PDT); transperineal radiofrequency interstitial tumour ablation (RITA) therapy; and laser ablation therapy. Traditional treatment options included surgical removal of the prostate; radical prostatectomy (RP), use of external beam radiotherapy (EBRT) to destroy the cancer, or active surveillance.

For primary ablative therapy, neither cryotherapy nor HIFU had sufficiently robust data to enable any definitive conclusions to be made. The effectiveness data on brachytherapy was more robust and there was some evidence that cancer-specific outcomes in the short-term were either better or equivalent to either EBRT or RP, with comparable adverse effect profiles apart from a possible increased risk of dysuria and urinary retention. The findings on focal ablative therapy were mostly derived from data on focal cryotherapy, which suggested that cancer-specific outcomes were at least comparable to full-gland cryotherapy, and there was a suggestion that urinary incontinence outcome may be better following focal cryotherapy compared with whole gland cryotherapy. In terms of the cost benefit analysis, the findings suggest that of all the ablative interventions, HIFU is the most likely to be considered cost-effective when assessed against threshold values for a cost per QALY that society might be willing to pay. However, there were considerable uncertainties within the analyses.

For salvage ablative therapy following primary EBRT, lack of reliable and robust data prevented any meaningful conclusions to be made, in comparison with salvage RP.

Overall, the findings of this assessment indicate that there is insufficient evidence to help inform recommendations on the use of ablative therapies in the UK NHS and that further research is needed. For further details see: <http://www.nets.nihr.ac.uk/projects/hta/1013601>.

Current status

Completed

Key publications

Ramsay, CR, Adewuyi, T, Gray, J, Hislop, J, Shirley, MDF, Jayakody, K, MacLennan, GS, Fraser, C, MacLennan, SJ, Brazzelli, M, N'Dow, J, Pickard, R, Robertson, C, Rothnie, K, Rushton, SP, Vale, LD, Lam, T Ablative therapy for localised prostate cancer: systematic review and economic evaluation. *Health Technol Assess* 2015;19(49)

A.10

Aflibercept BRVO: Aflibercept for treating visual impairment due to macular oedema secondary to branch retinal vein occlusion

Investigators

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Aflibercept for treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO). The clinical evidence submitted by the company (Bayer Pharma AG) responsible for manufacturing Aflibercept (Eylea) consisted of one RCT involving Aflibercept, VIBRANT, and eight studies involving relevant comparator treatments (laser photocoagulation therapy, ranibizumab or dexamethasone). The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released a technology appraisal guidance (TA409, September 2016). Aflibercept is recommended by NICE as an option, within its marketing authorisation, for treating visual impairment in adults caused by macular oedema after branch retinal vein occlusion, only if the company provides Aflibercept in line with the commercial access agreement with NHS England. <https://www.nice.org.uk/guidance/ta409>

Current status

Completed

Key publications

Scott, N, Cummins, E, Cruickshank, M, Fraser, C, Lois, N, Brazzelli, M. Aflibercept for treating visual impairment due to macular oedema secondary to branch vein occlusion: a single technology appraisal. . *Evidence Review Group report in support of the NICE STA Programme*. . University of Aberdeen: Health Services Research Unit; 2016. <https://www.nice.org.uk/guidance/ta409/documents/committee-papers-3>

A.11**Aflibercept CNV: Aflibercept for treating myopic choroidal neovascularisation****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Fast Track Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Aflibercept for treatment of myopic choroidal neovascularisation (mCNV). The clinical evidence submitted by the company (Bayer Pharma AG) responsible for manufacturing Aflibercept (Eylea) consisted of one RCT assessing Aflibercept versus sham-controlled injections. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released a technology appraisal guidance (TA486, November 2017). Aflibercept is currently recommended by NICE, within its marketing authorisation, as an option for treating visual impairment because of myopic choroidal neovascularisation in adults, only if the company provides Aflibercept in line with the commercial access agreement with NHS England. If patients and their clinicians consider both Aflibercept and ranibizumab to be suitable treatments, the least costly should be used, taking into account anticipated administration costs, dosage and price per dose. <https://www.nice.org.uk/guidance/ta486>

Current status

Completed

Key publications

Brazzelli, M, Cummins, E, Fielding, S, Cruickshank, M, Fraser, C, Azuara-Blanco, A. Aflibercept for treating myopic choroidal neovascularisation. Fast track appraisal: cost comparison case. *Evidence Review Group Report in support of NICE Fast Track Appraisal Programme*. London: National Institute for Health and Care Excellence; 2017. <https://www.nice.org.uk/guidance/ta486/documents/committee-papers>

A.12

Aflibercept DMO: Aflibercept for treating diabetic macular oedema

Investigators

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Aflibercept for treatment of diabetic macular oedema (DMO) in adults. The clinical evidence submitted by the company (Bayer Pharma AG) responsible for manufacturing Aflibercept (Eylea) consisted of two phase III RCTs, VISTA and VIVID, which compared Aflibercept with laser photocoagulation therapy for DMO. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released a technology appraisal guidance (TA346, July 2015). Aflibercept is currently recommended by NICE as an option for treating visual impairment caused by diabetic macular oedema only if (i) the eye has a central retinal thickness of 400 micrometres or more at the start of treatment and (ii) the company provides Aflibercept in line with the commercial access agreement with NHS England. <https://www.nice.org.uk/guidance/ta346>

Current status

Completed

Key publications

Fielding, S, Cummins, E, Cruickshank, M, Fraser, C, Lois, N, Brazzelli, M. Aflibercept for treating diabetic macular oedema. *Evidence Review Group Report in support of the NICE STA Programme*. University of Aberdeen: Health Services Research Unit; 2014 URL:

<https://www.nice.org.uk/guidance/ta346/documents/macular-oedema-diabetic-aflibercept-committee-papers4>

A.13**Aflibercept solution for injection for the treatment of wet age-related macular degeneration****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Aflibercept for the treatment of adults suffering from wet age-related macular degeneration (wet AMD). The clinical evidence submitted by the company (Bayer Pharma AG) responsible for manufacturing Aflibercept (Eylea) consisted of two RCTs comparing Aflibercept with ranibizumab and 10 RCTs involving either Aflibercept or ranibizumab. Aflibercept proved to be a safe and cost-effectiveness option for the treatment of wet AMD in adults. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released a technology appraisal guidance (TA294, July 2013). Aflibercept is currently recommended by NICE as an option for treating wet age-related macular degeneration only if i) Aflibercept is used in accordance with the recommendations for ranibizumab in and, ii) the manufacturer provides Aflibercept in line with the commercial access agreement with NHS England. <https://www.nice.org.uk/guidance/ta294>

Current status

Completed

Key publications

Cummins, E, Fielding, S, Johnston, R, Rothnie, K, Stewart, F, Lois, N, Burr, J, Brazzelli, M. Aflibercept solution for injection for the treatment of wet age-related macular degeneration. *Evidence Review Group report in support of NICE STA Programme*. University of Aberdeen: Health Services Research Unit; 2013 URL: <https://www.nice.org.uk/guidance/ta294/documents/macular-degeneration-wet-agerelated-aflibercept-1st-line-evaluation-report2>

A.14

Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia

Investigators

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia. The clinical evidence submitted by the company (Sanofi Ltd) responsible for manufacturing Alirocumab (Praluent) consisted of ten phase III RCTs comparing Alirocumab with placebo, ezetimibe or ezetimibe plus a statin. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released a technology appraisal guidance (TA393, June 2016). Alirocumab is currently recommended as an option for treating primary hypercholesterolaemia or mixed dyslipidaemia only if (i) low-density lipoprotein concentrations are persistently above specified thresholds despite maximal tolerated lipid-lowering therapy, and (ii) the company provides Alirocumab in line with the commercial access agreement with NHS England. <https://www.nice.org.uk/guidance/ta393>

Current status

Completed

Key publications

Scotland, G, Neilson, A, Javanbakht, M, Fielding, S, Cruickshank, M, Sharma, P, Fraser, C, Simpson, W, Brazzelli, M. Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia. *Evidence Review Group report in support of the NICE STA Programme*. University of Aberdeen: Health Services Research Unit; 2015. <https://www.nice.org.uk/guidance/ta393/documents/committee-papers>

A.15**An open randomised trial of the Arabin pessary to prevent preterm birth in twin pregnancy, with health economics and acceptability (STOPPIT-2)****Investigators**

Graeme MacLennan HSRU; John Norrie, Prof Jane Norman, Sarah Stock, Joel Smith, Sarah Cunningham-Burley, University of Edinburgh; Steven Thornton, University of Exeter; Andrew Shennan, King's College London; Jane Denton, Multiple Births Foundation; Mark Kilby, University of Birmingham; Phillip Bennett, Neil Marlow, Imperial College London; Stephen Robson, University of Newcastle upon Tyne

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £241,178 (£987,974)

Summary

STOPPIT-2 is a multi-centre randomised controlled trial, funded by the NIHR HTA Programme investigating whether the Arabin cervical pessary prevents preterm birth in women with a twin pregnancy and a short cervix. Patients with a short cervix (≤ 30 mm) who agree to participate in the treatment phase of the study will be randomised to either treatment with the Arabin cervical pessary or to standard care (no additional treatment).

STOPPIT-2 will randomise 500 participants.

The primary endpoint of the trial is birth before 34+0 weeks following the spontaneous onset of labour.

STOPPIT-2 is led by Professor Jane Norman based at the University of Edinburgh.

Current status

Ongoing

Publications and presentations

None

A.16

Brentuximab Vedotin is recommended by NICE for treatment of relapsed or refractory systemic anaplastic large cell lymphoma (sALCL)

Investigators

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the clinical and cost-effectiveness of Brentuximab vedotin for treating relapsed or refractory anaplastic large cell lymphoma (sALCL). The clinical effectiveness evidence submitted by the company (Takeda UK Ltd) responsible for manufacturing Brentuximab vedotin (Adcetris) consisted of one Phase II, open-label, single-arm, multi-centre trial examining the efficacy and safety of Brentuximab vedotin in patients with relapsed or recurrent sALCL after treatment failure of at least one prior therapy. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released clinical guidance (TA478, October 2017). Brentuximab vedotin is currently recommended as an option for treating relapsed or refractory systemic anaplastic large cell lymphoma only if (i) patients have an Eastern Cooperative Oncology Group performance status of 0 or 1 and (ii) the company provides Brentuximab vedotin in line with the commercial access agreement with NHS England. <https://www.nice.org.uk/guidance/ta478>

Current status

Completed

Key publications

Boyers, D, Cruickshank, M, Jacobsen, E, Cooper, D, Fraser, C, Culligan, D, Scotland, G. Brentuximab vedotin for relapsed or refractory systemic anaplastic large cell lymphoma. *Evidence Review Group report in support of NICE STA programme*. University of Aberdeen: Health Services Research Unit; 2017. <https://www.nice.org.uk/guidance/ta478/documents/committee-papers-2>

A.17**Clinical and cost-effectiveness of cholecystectomy versus observation/conservative management for adults presenting with uncomplicated symptomatic gallstones or cholecystitis****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

This NIHR HTA evidence synthesis assessed the clinical and cost effectiveness of cholecystectomy compared with observation/conservative management in patients with uncomplicated symptomatic gallstones (biliary colic or cholecystitis). Two good quality RCTs conducted in Norway and involving 201 participants were included in the assessment. The results showed that 88% of people initially randomised to surgery and 45% of people initially randomised to observation eventually underwent cholecystectomy during the 14-year follow-up period. Participants randomised to surgery experienced more surgery-related complications and showed a slight, non-significant, increase in the rate of all-cause mortality than those who were treated conservatively. In contrast, participants allocated to observation had more episodes of cholecystitis, but few other gallstone-related complications (e.g. common bile duct stones, acute pancreatitis). Fifty five percent of people randomised to observation did not require surgery during the long term follow-up and 12% of people randomised to cholecystectomy did not undergo the scheduled operation. The results of the economic evaluation showed that, on average, the surgery strategy was more costly but more effective than the conservative management strategy. The result of the incremental cost-effectiveness analysis indicated that the conservative management strategy had a 51% chance of being considered cost-effective when the society's willingness to pay for a QALY was £20,000 and 46% when the society's willingness to pay was £30,000. There was, however, uncertainty around some parameters used in the model. Approximately 70,000 cholecystectomies are performed every year in the UK. The results of this assessment suggest that surgery could probably be avoided in a proportion of people with symptoms but no complications. However, the paucity of the current evidence and the uncertainty about some of the findings of this assessment, clearly indicate that a well-designed, NHS-based, long-term RCT is needed.

<https://www.ncbi.nlm.nih.gov/pubmed/25164349>

Current status

Completed

Key publications

Brazzelli, M, Cruickshank, M, Kilonzo, M, Ahmed, I, Stewart, F, McNamee, P, Elders, A, Fraser, C, Avenell, A, Ramsay, C Clinical effectiveness and cost-effectiveness of cholecystectomy compared with observation/conservative management for preventing recurrent symptoms and complications in adults presenting with uncomplicated symptomatic gallstones or cholecystitis: a systematic review and economic evaluation. *Health Technol Assess* 2014;18:55

A.18**Collagenase clostridium histolyticum for the treatment of Dupuytren's contracture****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

This NIHR HTA-funded evidence synthesis assessed the clinical and cost-effectiveness of collagenase clostridium histolyticum (CCH) injections, within its licensed indication, as an alternative to surgery (including fasciectomy, dermofasciectomy, open fasciotomy and needle fasciotomy) for the treatment of adults presenting with Dupuytren's disease. Dupuytren's disease is a slowly progressive condition of the hand, characterised by formation of nodules in the palm which gradually develop into fibrotic cords. Contracture of the cords produces fingers' deformities. Surgery is recommended for moderate and severe contractures but complications and/or recurrences are frequent. CCH has been developed as a minimally invasive alternative to surgery in some patients. The project considered clinical evidence from five RCTs comparing collagenase with placebo (493 participants), 3 RCTs comparing various surgical procedures (334 participants), 2 non-randomised studies comparing collagenase with surgery (105 participants), 5 non-randomised comparative studies assessing various surgical procedures (3571 participants) and 15 case series on the use of collagenase (3154 participants). An economic model was developed to estimate the costs and consequences of CCH versus alternative surgical procedures. The current NICE guidance (TA459, published July 2017) recommends CCH as an option for treating Dupuytren's contracture with a palpable cord in adults only if all the following apply:

- There is evidence of moderate disease (functional problems and metacarpophalangeal joint contracture of 30° to 60° and proximal interphalangeal joint contracture of less than 30° or first web contracture) plus up to two infected joints.
- Percutaneous needle fasciotomy is not considered appropriate, but limited fasciectomy is considered appropriate by the treating hand surgeon.
- The choice of treatment (CCH or limited fasciectomy) is made on an individual basis after discussion between the responsible hand surgeon and the patient about the risks and benefits of the treatments available.
- One injection is given per treatment session by a hand surgeon in an outpatient setting.

<https://www.nice.org.uk/guidance/ta459>

Current status

Completed

Key publications

Brazzelli, M, Cruickshank, M, Tassie, E, McNamee, P, Robertson, C, Elders, A, Fraser, C, Hernandez, R, Lawrie, D, Ramsay, CR Collagenase clostridium histolyticum for the treatment of Dupuytren's contracture: systematic review and economic evaluation *Health Technol Assess* 2015;19(90)

A.19**Comparative study of new imaging technologies for the diagnosis of glaucoma (GATE)****Investigators**

Augusto Azuara-Blanco, Craig Ramsay, Jen Burr, Kirsty McCormack, Rodolfo Hernandez, Luke Vale, Joanne Coyle, HSRU; Prof Ted Garway-Heath, Moorfields Eye Hospital; Rupert Bourne, Hinchingsbrooke/Moorfields/Addenbrooke's Hospitals; Mark Batterbury, Royal Liverpool University Hospital

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £321,350 (£406,690)

Summary

Many healthy subjects are unnecessarily referred from the community to hospital eye services to rule out glaucoma.

The GATE study, funded by NIHR-HTA, evaluated the diagnostic performance of imaging tests at identifying, among patients referred to hospital, those who have glaucoma or are at risk and those who do not have any eye disease. Participants were imaged with four new diagnostic tests: MRA and GPS analysis using the Heidelberg Retina Tomograph (HRT-III), Scanning laser polarimetry (GDx-ECC) and Optical Coherence Tomography (Spectralis). We compared the imaging results with a clinical diagnosis of glaucoma by an experienced consultant ophthalmologist (reference standard). An economic modelling evaluation assessed the cost-effectiveness of adopting imaging as a triage test compared to current practice.

In total, 955 individuals were recruited. Glaucoma was diagnosed by the clinician in 17% of participants and no evidence of glaucoma was found in 32% of participants. Overall, 38% of GATE participants were discharged from secondary care after their first visit to hospital eye services.

The study concluded that automated imaging can be effective to aid glaucoma diagnosis among individuals referred from the community to hospital eye services. An alternative pathway for patients referred from community to hospital eye services with possible glaucoma, using a triage test that includes imaging, IOP and VA, appears to be cost-effective compared with current practice.

Current status

Completed

Key publications

Azuara-Blanco, A, Banister, K, Boachie, C, McMeekin, P, Gray, J, Burr, J, Bourne, R, Garway-Heath, D, Batterbury, M, Hernandez, R, McPherson, G, Ramsay, CR, Cook, JA Automated imaging technologies for the diagnosis of glaucoma: a comparative diagnostic study for the evaluation of the diagnostic accuracy, performance as triage tests and cost-effectiveness (GATE study). *Health Technol Assess* 2016;20:8

Banister, K, Boachie, C, Bourne, R, Cook, JA, Burr, J, Ramsay, CR, Garway-Heath, D, Gray, J, McKeekin, P, Hernandez, R, Azuara-Blanco, A Can automated imaging with HRT for disc and GDx-ECC and Spectralis OCT for retinal nerve fiber layer analysis aid glaucoma detection? *Ophthalmology* 2016;123(5):930-38

A.20

Comparison of LAser, Surgery and foam Sclerotherapy (CLaSS)

Investigators

Seonaidh Cotton, Luke Vale, Jen Burr, Craig Ramsay, Marion Campbell, Jill Francis, HSRU; Julie Brittenden, Kevin Cassar, Dept of Surgery, University of Aberdeen; Mike Gough, Leeds General Infirmary; Paul Bachoo, NHS Grampian; Andrew Mavor, Leeds General Infirmary; Prof Julian Scott, University of Leeds; Prof Peter McCollum, University of Hull; Ian Chetter, Hull NHS Trust

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £1,100,665 (£1,129,665)

Summary

The treatment of patients with varicose veins results in a considerable workload and financial burden to the NHS. Visible varicose veins occur in up to 40% of men and 32% of women.

Foam sclerotherapy (foam) and endovenous laser ablation (EVLA) have emerged as alternative treatments to surgery for patients with varicose veins, but uncertainty exists regarding their clinical and cost-effectiveness in the medium and long-term. This is important because if varicose veins recur, further treatments may be required.

CLASS is a national multi-centre NIHR HTA-funded trial designed primarily to assess the clinical and cost-effectiveness of three treatment modalities: a) foam; b) EVLA with subsequent foam to varicosities when required; and c) surgery. Primary outcome measures include disease-specific quality of life (QoL), measured by the Aberdeen Varicose Vein Questionnaire (AVVQ) and generic QoL, measured by EQ-5D, SF-36 at 6 months, and cost-effectiveness as cost per quality adjusted life year (QALY) gained.

A total of 798 adult patients with symptomatic primary varicose veins were recruited into the trial and randomised to one of the treatment options. At six weeks and six months after treatment, participants were reviewed at an outpatient clinic where the study outcomes are assessed. Six month follow-up is complete. Follow-up to 5 years is ongoing.

Current status

Ongoing

Key publications

Brittenden, J, Cotton, SC, Elders, A, Ramsay, CR, Norrie, J, Burr, J, Campbell, B, Bachoo, P, Chetter, I, Gough, M, Earnshaw, J, Lees, T, Scott, J, Baker, SA, Francis, J, Tassie, E, Scotland, G, Wileman, S, Campbell, MK A randomized trial comparing treatments for varicose veins. *N Engl J Med* 2014;371(13):1218-27

Tassie, E, Scotland, G, Brittenden, J, Cotton, SC, Elders, A, Campbell, MK, Campbell, B, Gough, M, Burr, JM, Ramsay, CR, CLASS Study Team Cost-effectiveness of ultrasound-guided foam sclerotherapy, endovenous laser ablation or surgery as treatment for primary varicose veins from the randomized CLASS trial. *Br J Surg* 2014;101(12):1532-40

A.21**Complex designs in randomised clinical trials – a case study in dentistry****Investigators****Beatriz Goulao, Graeme MacLennan, Craig Ramsay, HSRU****Source and amount of HSRU funding (total funding)**

£None

Summary

Oral health research is often a source of challenging data: statistical errors in the design, analysis and conclusions of dental research are frequently reported; when clinical outcomes are collected, they have an inherently hierarchical structure (e.g. teeth nested within people who are often nested within dental practices) with often non-normal distributions that can be challenging to analyse and present; outcome assessment becomes a challenge due to measurement errors and reliability of the data collected.

The PhD will address challenges in split-plot designs and the difficulty and costs of measuring clinical gingival bleeding in a large scale, multicentre pragmatic RCT by investigating the methodological implications for different ways of clinically measuring gingival bleeding and by assessing the diagnostic performance of several new self-reported measures.

The thesis will be focused on the following objectives:

- Conduct a systematic review to identify split-plot designs used in healthcare research and describe their methodology and develop guidance on its report.
- Develop simulation methods to calculate a sample size in a split-plot design under a variety of assumptions and provide guidance on how to do it.
- Assess the diagnostic performance of a set of new self-reported bleeding questions compared to clinical bleeding on probing and update a systematic review about the diagnostic performance of other self-reported bleeding measures.
- Assess the statistical implications of collecting repeated clinical bleeding measures in the IQaD RCT and inform future trials based on this.

Supervision: Prof Craig Ramsay and Mr Graeme MacLennan**Current status**

Ongoing

Key publications

Goulao, B, MacLennan, G, Ramsay, C The split-plot design was useful for evaluating complex, multi-level interventions but there is need for improvement in its design and report. *J Clin Epidemiol* 2017: <https://doi.org/10.1016/j.jclinepi.2017.10.019> (published ahead of print).

A.22

CSAW: Can Shoulder Arthroscopy Work? Is arthroscopic sub-acromial decompression (ASAD) more effective than arthroscopy only for shoulder pain?

Investigators

Joanne Coyle, Jonathan Cook, HSRU; Dr David Beard, Dr Stephen Gwilym, Dr Andrew Judge, Mrs Cushla Cooper, Prof Andrew Carr, Nuffield Dept of Orthopaedics, University of Oxford

Source and amount of HSRU funding (total funding)

Arthritis Research UK £7,804 (£199,964)

Summary

CSAW is a multicentre randomised controlled trial, funded by Arthritis Research UK, comparing two surgical procedures (Arthroscopic Sub-acromial Decompression Surgery, and Arthroscopy of the shoulder) with a non-operative management with specialist reassessment, in patients who have had sub-acromial pain of at least three months duration.

The trial aimed to answer two main questions; firstly, should bone spurs be removed and secondly, is arthroscopic surgery a useful way to treat this type of shoulder pain.

The trial had a primary patient reported outcome, the Oxford Shoulder Score (OSS). CSAW recruited 313 participants who were followed-up for 12 months.

The Trial is led by Professor David Beard based at the University of Oxford.

Current status

Ongoing

Publications and presentations

None

A.23

Dapagliflozin for the treatment of type 2 diabetes

Investigators

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's single technology appraisal process, was to review the evidence for the clinical and cost-effectiveness of Dapagliflozin in combination with other glucose-lowering therapies for treating type 2 diabetes in adults. The clinical evidence submitted by the company (Bristol-Myers Squibb and AstraZeneca) responsible for manufacturing Dapagliflozin (Forxiga) consisted of 5 RCTs: 3 in patients with type 2 diabetes inadequately controlled with metformin alone and 2 in patients with type 2 diabetes inadequately controlled with insulin with or without oral antidiabetic drugs. Of the 3 trials of Dapagliflozin as an add-on to metformin, two were placebo controlled with follow-up of 24 weeks and one compared Dapagliflozin with a sulfonylurea for up to 52 weeks of follow-up. The 2 trials of Dapagliflozin as an add-on to insulin were both placebo controlled. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released clinical guidance (TA288, June 2013). Dapagliflozin in a dual therapy regimen in combination with metformin was initially recommended as an option for treating type 2 diabetes, only if (i) a sulfonylurea was contraindicated or not tolerated or (ii) the person was at significant risk of hypoglycaemia or its consequences. Dapagliflozin in combination with insulin with or without other antidiabetic drugs was recommended as an option for treating type 2 diabetes. <http://guidance.nice.org.uk/ta288>

NICE updated and replaced this guidance in November 2016 (TA418).

Current status

Completed

Key publications

Cummins, E, Scott, N, Rothnie, K, Waugh, N, Fraser, C, Philip, S, Brazzelli, M. Dapagliflozin for the treatment of type 2 diabetes: A Single Technology Appraisal. *Evidence Review Group report in support of NICE STA programme*. University of Aberdeen: Health Services Research Unit; 2013.

<https://www.nice.org.uk/guidance/ta288/documents/diabetes-type-2-dapagliflozin-evaluation-report2>

A.24

Difference Elicitation in TriAls (DELTA)

Investigators

Joanne Coyle, Luke Vale, Craig Ramsay Cynthia Fraser, HSRU, Prof Doug Altman, University of Oxford; Prof Andrew Briggs, Prof John Norrie, University of Glasgow; Prof Peter Fayers, University of Aberdeen; Dr Brian Buckley, National University of Ireland/Bowel & Bladder Foundation; Prof Ian Harvey, University of East Anglia

Source and amount of HSRU funding (total funding)

MRC £131,655 (£152,877)

Summary

The randomised controlled trial (RCT) is widely considered to be the gold standard study for comparing the effectiveness of health interventions. From both a scientific and ethical standpoint, selecting an appropriate target difference is of crucial importance. Given its importance, determination of the target difference, as opposed to statistical approaches to calculating the sample size, has been greatly neglected. A variety of approaches have been proposed for formally determining what an important difference should be (such as the "minimum clinically important difference") though the current state of the evidence is unclear particularly with regards to informing RCT design. This UK MRC funded project sought to provide an overview of the current evidence through three main components: (i) a systematic review of methods for identifying a target difference developed within and outside the health field to assess their usefulness for various forms of RCTs; (ii) a survey of trialists; and (iii) development of a structured guidance document to aid the design of future trials.

The results were:

1. The search identified seven methods were identified – anchor, distribution, health economic, opinion-seeking, pilot study, review of evidence base (RoEB) and standardised effect size; each with important variations in implementation.
2. a. 180 responses to the Society of Clinical Trials survey were received representing 13 countries. Awareness of methods ranged from 69 (38%) for health economic method to 162 (90%) for pilot study.
b. Of the sixty-one surveys sent out to UK trialist groups, thirty-four (56%) responses were received. Awareness ranged from 33 (97%) for the RoEB and pilot methods, to only 14 (41%) for the distribution method. Based upon the most recent trial all bar three groups (30 - 91%) used a formal method.

Guidance was developed on the use of each method and reporting of the sample size calculation in a trial protocol and results paper. The study concluded that there is a clear need for greater use of formal methods to determine the target difference and better reporting of its specification.

Current status

Completed

Key publications

Cook, JA, Hislop, J, Adewuyi, T, Harrild, K, Altman, DG, Ramsay, CR, Fraser, C, Buckley, B, Fayers, P, Briggs, A, Harvey, I, Norrie, JD, Fergusson, DA, Ford, I, Vale, L. Assessing methods to specify the target difference for a randomised controlled trial: DELTA (Difference Elicitation in TriAls) review. *Health Technol Assess* 2014;18:28

A.25

Do Non-steroidal Anti-inflammatory drugs (NSAIDs) reduce the appearance of sacroiliac joint bone marrow oedema on MRI, in spondyloarthritis? (DyNAMISM)

Investigators

Lorna Aucott, Mark Forrest, HSRU; Gareth Jones, Gary Macfarlane, University of Aberdeen; Raj Sengupta, Royal National Hospital for Rheumatic Diseases, Bath; Alexander Bennett, Defence Medical Rehabilitation Centre, Surrey

Source and amount of HSRU funding (total funding)

Arthritis Research UK £238,855 (£468,196)

Summary

Magnetic Resonance Imaging (MRI) is commonly used to look for inflammation in the sacroiliac joints (the joints where the spine meets the pelvis), something which is a key feature of axial spondyloarthritis (axSpA). Many patients with axSpA take non-steroidal anti-inflammatory drugs (NSAIDs) to help manage their pain. The use of NSAIDs may hide the appearance of inflammation in the sacroiliac joints when viewed on MRI. If this is true, it (a) may prevent some patients from receiving the correct diagnosis; and (b) may mean that some patients are unable to be given the most appropriate medication for their disease.

DyNAMISM, funded by Arthritis Research UK (ARUK) will investigate whether, among male patients with axSpA, the use of NSAIDs reduces the appearance of inflammation in the sacroiliac joints when viewed with MRI. This will allow us to investigate whether a 'NSAIDs free' period helps doctors make a diagnosis of axSpA and whether patients can tolerate a short period without their NSAIDs, although other pain medication may be taken during this period if required.

Approximately 500 participants across the UK will take part. After stopping taking any NSAIDs for one week, participants have an MRI scan of their sacroiliac joints. After the scan, participants restart their usual NSAIDs medication. Depending on the results of the first scan, some participants will be asked to return for a second scan six weeks later. Participants provide a blood sample and complete questionnaires at each study visit.

DyNAMISM is led by Dr Gareth Jones based at the University of Aberdeen.

Current status

Ongoing

Publications and presentations

None

A.26**Early Detection of Neovascular Age-related macular degeneration (EDNA)****Investigators**

Craig Ramsay, Joanne Coyle, Graham Scotland, Katie Banister, HSRU; Usha Chakravarthy, Ruth Hogg, Queens University Belfast; Sobha Sivaprasad, Moorfields Eye Hospital NHS Trust; Jonathan Cook, University of Oxford; Heinrich Heimann, Royal Liverpool & Broadgreen University Hospitals NHS Trust

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £863,779 (£2,096,031)

Summary

“Wet” or neovascular age-related macular degeneration (nAMD) is a leading cause of sight loss in older people.

EDNA, which is a diagnostic accuracy study, aims to find out the best test(s), and how often patients should be tested, to reliably detect the start of nAMD with high specificity and sensitivity. The study is funded by the NIHR HTA Programme.

We are evaluating five non-invasive diagnostic tests which are easily performed and routinely carried out in the NHS secondary care setting and which fall into two groups; functional and morphological.

The functional tests are visual acuity, Amsler test and self-reported quality of sight. The morphological tests are fundus examination and optical coherence tomography (OCT). We will compare these test results with a reference standard measurement of a fluorescein angiogram (FFA).

We enrolled 562 patients attending eye clinics in NHS hospitals across the UK who had a recent diagnosis of nAMD in one eye only and we will monitor the unaffected eye during routine clinic appointments for three years.

The primary outcome will be the sensitivity and specificity of the five index tests for the diagnosis of nAMD.

The study is led by Professor Usha Chakravarthy based at Queens University Belfast.

Current status

Ongoing

Publications and presentations

None

A.27**Effectiveness in Angle-closure Glaucoma of Lens Extraction (Eagle)****Investigators**

Jen Burr, John Norrie, Craig Ramsay, Luke Vale, HSRU; PI: Mr Augusto Azuara-Blanco, NHS Grampian; Tin Aung, Singapore National Eye Centre; Paul Foster, UCL Institute of Ophthalmology; David Friedman, The John Hopkins Hospital; Jimmy Lai, United Christian Hospital; Da-Wen Lu, Tri-Service General Hospital; Catherine Lui, Taipei Veterans General Hospital; Winifred Nolan, Sandwell and West Birmingham Hospital; Jovina See, National University Hospital; David Wong, University of Hong Kong

Source and amount of HSRU funding (total funding)

NIHR EME Programme £913,170 (£1,651,812)

Summary

EAGLE was an MRC funded international multi-centre pragmatic randomised controlled trial (RCT) aiming to establish whether removal of the lens of the eye (lens extraction) for newly diagnosed Primary Angle Closure Glaucoma (PACG) results in better patient reported health, vision, lower intraocular pressure (IOP) and other outcomes compared with standard management.

22 specialist centres in the UK and nine International centres (two in Singapore, two in Hong Kong, two in Malaysia and one in Australia) participated.

Research coordinators in each centre recruited 419 people newly diagnosed with PACG who met the eligibility criteria. EAGLE patient follow-up consisted of several visits to the hospital for data collection (physical clinical measures and questionnaires) at 6, 12, 24 and 36 month post randomisation. Regular clinic follow-up continued as clinically indicated between study outcome visits.

The study concluded that initial treatment with lens extraction for PACG and PAC is more effective and cost-effective than laser iridotomy after three years and should be considered as an alternative to current practice.

Current status

Completed

Key publications

Azuara-Blanco, A, Burr, J, Ramsay, CR, Cooper, D, Foster, P, Friedman, D, Scotland, G, Javanbakht, M, Cochran, C, Norrie, J The effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma: a randomized controlled trial (EAGLE) *Lancet* 2016;388:1389-97

Javanbakht, M, Azuara-Blanco, A, Burr, J, Ramsay, C, Cooper, D, Cochran, C, Norrie, J, Scotland, G Early lens extraction with intraocular lens implantation for the treatment of primary angle closure glaucoma: an economic evaluation based on data from the EAGLE trial. *BMJOpen* 2017;7(1):e013254

A.28**ELECTric Tibial nerve stimulation to Reduce Incontinence in Care homes (ELECTRIC)****Investigators**

John Norrie, Shaun Treweek, Graeme MacLennan, HSRU; Prof Jo Booth, Helen Mason, Suzanne Hagen, Maggie Lawrence, Dawn Skelton, Doreen McClurg, Glasgow Caledonian University; Christine Norton, Kings College London; Daneille Harari, Guy's and St Thomas' NHS Foundation Trust; Paul Edwards, BUPA UK Care Services; Claire Goodman, University of Hertfordshire; Andrew Lowndes, PPI

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £266,946 (£1,244,477)

Summary

Bladder problems, including urinary incontinence, are common in older people who live in a care home. There are few options to treat the causes of urinary incontinence and so older people who have urinary incontinence wear absorbent pads to catch the leakage. Transcutaneous posterior tibial nerve stimulation, also called TPTNS, has been shown to reduce urinary incontinence in community-living older women and adults with neurogenic bladder dysfunction (including multiple sclerosis, Parkinson's and stroke).

The ELECTRIC trial, which is funded by NIHR HTA Programme, will investigate the clinical effectiveness of a programme of transcutaneous posterior tibial nerve stimulation to treat urinary incontinence in care home residents and the associated costs and consequences. 500 participants with urinary incontinence will be recruited from care homes in Scotland and England and will be randomised to a programme of TPTNS or sham stimulation. The primary outcome is volume of urinary incontinence leaked over a 24 hour period at 6 weeks post randomisation.

Recruitment to the study will start in early 2018

The ELECTRIC trial is led by Professor Jo Booth based at Glasgow Caledonian University.

Current status

Ongoing

Publications and presentations

None

A.29**Eluxadoline for treating irritable bowel syndrome with diarrhoea****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the submission of the pharmaceutical company on the evidence for the clinical and cost-effectiveness of Eluxadoline for treating irritable bowel syndrome with diarrhoea. The clinical evidence submitted by the company (Allergan) responsible for manufacturing Eluxadoline (Truberzi) consisted of one phase II and two phase III RCTs comparing Eluxadoline with placebo. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released a technology appraisal guidance (TA471, August 2017). Eluxadoline is currently recommended as an option for treating irritable bowel syndrome with diarrhoea in adults only if (i) the condition has not responded to other pharmacological treatments (for example, antitomotility agents, antispasmodics, tricyclic antidepressants), or (ii) pharmacological treatments are contraindicated or not tolerated, and (iii) it is started in secondary care.

<https://www.nice.org.uk/guidance/ta471>

Current status

Completed

Key publications

Cummins, E, Ayansina, D, Sharma, P, Fraser, C, Shimonovich, M, McLean, M, Brazzelli, M. Eluxadoline for treating irritable bowel syndrome with diarrhoea. *Evidence Review Group report in support of NICE STA programme*. University of Aberdeen: Health Services Research Unit; 2016.

<https://www.nice.org.uk/guidance/ta471/documents/committee-papers-2>

A.30

Enzalutamide for treating metastatic hormone-relapsed prostate cancer not previously treated with chemotherapy

Investigators

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Enzalutamide for treating metastatic, hormone-relapsed prostate cancer for people not previously treated with chemotherapy. The clinical evidence submitted by the company (Astellas) responsible for manufacturing Enzalutamide (Xtandi) consisted of a single large, international, multicentre trial of Enzalutamide versus placebo. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released clinical guidance (TA377, January 2016). Enzalutamide is currently recommended, within its marketing authorisation, as an option for treating metastatic hormone-relapsed prostate cancer: (i) in people who have no or mild symptoms after androgen deprivation therapy has failed, and before chemotherapy is indicated and (ii) only when the company provides Enzalutamide in line with the commercial access agreement with NHS England. <https://www.nice.org.uk/guidance/ta377>

Current status

Completed

Key publications

Robertson, C, Cummins, E, Fielding, S, Lam, T, Fraser, C, Ramsay, C. Enzalutamide for treating metastatic hormone-relapsed prostate cancer not previously treated with chemotherapy. *Evidence Review Group report in support of the NICE STA Programme*.

Health Services Research Unit: University of Aberdeen; 2015.

<https://www.nice.org.uk/guidance/ta377/documents/prostate-cancer-metastatic-hormonerelapsed-enzalutamide-id683-committee-papers-2>

A.31

Evaluating the behavioural intervention, organisational and health economic evidence base for adult obesity management

Investigators

Alison Avenell, HSRU; Prof Marie Johnston, Jo Hart, Dr Falko Sniehotta, School of Psychology, University of Aberdeen; Dr Susan Michie, Department of Psychology, UCL; Prof Phil Hannaford, Department of GP&PC, University of Aberdeen

Source and amount of HSRU funding (total funding)

CSO £362,630 (679,500)

Summary

This research included systematic reviews of trials of adult obesity management examining the most effective long-term interventions, behaviour change techniques to use, the effectiveness of group-based interventions, the best length and frequency for follow-up for interventions, the effectiveness of interventions given by community pharmacies, the effectiveness of interventions in older people. Two studies with patients, providers of services and policy makers, particularly examining the effects of group approaches. Examination of preferences for types of lifestyle intervention. Examination of Scottish health records for obesity related disease risk, prior to the evaluation of alternative approaches to obesity management. Pilot studies of group based lifestyle behaviour change programme, developed from this research.

Using lifestyle behaviour change techniques based on psychological control theory, social cognitive theory, and social comparison theory, improves weight loss. Group-based obesity management is as least as effective as that delivered to the individual. Incentives, such as financial incentives, should be researched to aid weight loss. Simple advice on healthy eating and physical activity, with limited support, are unlikely to produce at least 5-10% long-term weight loss. This degree of long-term weight loss requires more intensive programmes particularly with a focus on a reduction in calorie intake and lifestyle behaviour change support. The NHS has limited capacity for this type of support for weight management in obesity. NHS staff need greater training in lifestyle behaviour change techniques and working with groups. Scarce NHS resources need to be targeted at those at highest risk of obesity-related disease, who are most likely to benefit from these programmes.

Current status

Ongoing

Key publications

Dombrowski, S, Sniehotta, F, Avenell, A, Johnston, M, MacLennan, G 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 Psychol Rev* 2012;6(1):7-32

Dombrowski, S, Knittle, K, Avenell, A, Araujo-Soares, V, Sniehotta, F Long term maintenance of weight loss with non-surgical interventions in obese adults: systematic review and meta-analyses of randomised controlled trials. *Br Med J* 2014;348:g264

Ryan, M, Yi, D, Avenell, A, Douglas, F, Aucott, L, van Teijlingen, E, Vale, LD Gaining pounds by losing pounds: preferences for lifestyles to reduce obesity. *Health Econ Policy Law* 2015;10(2):161-82

Aucott, L, Philip, S, Avenell, A, Sattar, N, Wild, S Patterns of weight change after the diagnosis of type 2 diabetes in Scotland and their relationship with glycaemic control, mortality and cardiovascular outcomes: a retrospective cohort study. *BMJ Open* 2016;6:e010836

Stewart, F, Avenell, A Behavioural Interventions for Severe Obesity Before and/or After Bariatric Surgery: a Systematic Review and Meta-analysis. *Obes Surg* 2016;26(6):1203-14

Best, D, Avenell, A, Bhattacharya, S How effective are weight-loss interventions for improving fertility in women and men who are overweight or obese? A systematic review and meta-analysis of the evidence. *Hum Reprod Update* 2017;23(6):681-705

Best, D, Avenell, A, Bhattacharya, S, Stadler, G New debate: is it time for infertility weight-loss programmes to be couple-based? *Hum Reprod* 2017: <https://doi.org/10.1093/humrep/dex313> (published ahead of print)

Ma, C, Avenell, A Effects of weight loss interventions for adults who are obese on mortality, cardiovascular disease and cancer: a systematic review and meta-analysis. *BMJ* 2017 (in press)

A.32**EVAR: The clinical and cost-effectiveness of protocols using contrast-enhanced ultrasound and/or colour duplex ultrasound in the long-term surveillance of endovascular abdominal aortic aneurysm repair****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The primary aim of this NIHR HTA-funded project is to assess the current evidence for the clinical effectiveness and cost-effectiveness of surveillance imaging strategies following endovascular repair (EVAR) of an abdominal aortic aneurysm. EVAR is a minimally invasive technique but is associated with potential complications, thus patients require lifelong surveillance following the procedure. Computed tomography angiography (CTA) is widely used but carries the risk of repeated exposure to radiation and to a toxic contrast agent. The use of ultrasound has been suggested as a possible, safer alternative. The imaging technologies under evaluation are colour duplex ultrasound (CDU) or contrast-enhanced ultrasound (CEU), alone or in conjunction with plain film X-ray, compared with computed tomography angiography (CTA). We are conducting a systematic review of the literature; considering data from national and international registries and relevant clinical databases; developing a model based economic evaluation to represent possible alternative surveillance strategies modelled at varying surveillance intervals; and recording the personal experience of two patient representatives. The results of the project will inform clinical practice and policy on the optimal surveillance strategy after EVAR. <https://www.journalslibrary.nihr.ac.uk/programmes/hta/157801/#/>

Current status

Ongoing

Key publications

Brazzelli, M, Hernandez, R, Sharma, P, Robertson, C, Shimonovich, M, MacLennan, G, Fraser, C, Jamieson, R, Vallabhaneni, S The clinical and cost-effectiveness of protocols using contrast-enhanced ultrasound and/or colour duplex ultrasound in the long-term surveillance of endovascular abdominal aortic aneurysm repair: an evidence synthesis and economic evaluation. *Health Technol Assess* 2017 (accepted for publication)

A.33**Explanatory comparative study of conventional Total Knee Arthroplasty versus Robotic assisted Bi-UniCompartmental Knee Arthroplasty (TRUCK)****Investigators**

Mark Forrest, HSRU; Mark Blyth, NHS Greater Glasgow & Clyde; Phil Rowe, University of Strathclyde; Iain Anthony, Bryn Jones, Angus MacLean, NHS Greater Glasgow and Clyde

Source and amount of HSRU funding (total funding)

NIHR EME Programme £164,750 (£587,112)

Summary

Osteoarthritis (OA) is the most common form of joint disease. It causes pain and stiffness and affects at least 8 million people in the UK imposing a considerable economic and personal burden. The knee is one of the most common sites affected by OA. Knee Replacement, or Arthroplasty, is the current surgical treatment of choice for end stage OA of the knee.

TRUCK is an explanatory randomised controlled trial funded by MRC and NIHR EME to compare a novel robotic assisted surgical technique (Bi-Unicompartmental Knee Arthroplasty) against a standard surgical technique (Total Knee Arthroplasty) in patients with osteoarthritis of both the medial and lateral compartments of the knee.

TRUCK aims to recruit 94 participants.

The primary outcome is the percentage of patients with a bi-phasic (normal) moment curve during gait (level walking) measured at 1 year.

TRUCK is led by Mr Mark Blyth based at Glasgow Royal Infirmary.

Current status

Ongoing

Publications and presentations

None

A.34**Ezetimibe for treating primary (heterozygous-familial and non-familial) hypercholesterolaemia****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia. The clinical evidence submitted by the company (Merck Sharp & Dohme Ltd) responsible for manufacturing Ezetimibe (Ezetrol) consisted of 25 RCTs of either Ezetimibe versus placebo, or Ezetimibe plus a statin versus a matching statin dose. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released clinical guidance (TA385, February 2016). Ezetimibe monotherapy is currently recommended as an option for treating primary (heterozygous-familial or non-familial) hypercholesterolaemia in adults who cannot tolerate statin therapy or for whom initial statin therapy is contraindicated. In adults who have started statin therapy, Ezetimibe is currently recommended when (i) serum total or low-density lipoprotein cholesterol concentration is not appropriately controlled either after appropriate dose titration of initial statin therapy or because dose titration is limited by intolerance to the initial statin therapy, and (ii) a change from initial statin therapy to an alternative statin is being considered. <https://www.nice.org.uk/guidance/ta385>

Current status

Completed

Key publications

Scotland, G, Javanbakht, M, Scott, N, Cruickshank, M, Sharma, P, Fraser, C, Simpson, W, Brazzelli, M. Ezetimibe for treating primary (heterozygous-familial and non-familial) hypercholesterolaemia. . *Evidence Review Group report in support of the NICE STA Programme*. University of Aberdeen: Health Services Research Unit; 2015. <https://www.nice.org.uk/guidance/ta385/documents/committee-papers>

A.35**Female Urgency, Trial of Urodynamics as Routine Evaluation; a superiority randomised clinical trial to evaluate the effectiveness and cost effectiveness of invasive urodynamic investigations in management of women with refractory overactive bladder symptoms (FUTURE)****Investigators**

Graeme MacLennan, HSRU; John Norrie, University of Edinburgh; Mohammed Abdel-fattah, NHSG; M Drake, Bristol University; Chris Chapple, Simon Dixon, Chris Hillary, University of Sheffield; A Mostafa, University of Aberdeen; Niki Cotteril, Andrew Gammie, Dr H Hashim, North Bristol NHS Trust; Ash Monga, University Hospitals Southampton NHS Trust; Karen Brown, Newcastle Upon Tyne Hospitals NHS Foundation Trust; Karen Ward, Central Manchester University Hospitals NHS Trust

Source and amount of HSRU funding (total funding)

NIHR HTA Commissioned Call £1,453,772 (£1,529,679)

Summary

Overactive bladder (OAB) affects 12-14% of the adult female population in the UK. Although rarely life-threatening, OAB can have a considerable negative impact on patients' quality of life, restricting their social life and ability to work, and up-to social isolation in severe cases. OAB is first treated with lifestyle changes (such as reducing caffeine intake); pelvic floor exercises; bladder training and certain medications. Unfortunately these treatments do not work in 25-40% of patients (i.e. refractory OAB). These patients may be offered second line treatments such as injections of BOTOX into the bladder wall or SNM (an implant in the buttock which aim to regulate the bladder nerves in the lower spine).

Before recommending second line treatments, doctors are advised to perform a diagnostic invasive test called "Urodynamics" to confirm the diagnosis. Patients often find Urodynamics embarrassing and uncomfortable and in almost 40% of patients, Urodynamics does not show the underlying cause of the bladder problem and therefore it is unable to guide doctors and patients in their decision making.

The FUTURE study, funded by NIHR HTA Programme, is a randomised controlled trial that aims to recruit 1096 women to assess whether routinely performing Urodynamics, in addition to the standard comprehensive clinical assessment, improves the outcome of treatments in women with refractory OAB compared to comprehensive clinical assessment only. We also want to assess whether doing the test on everybody makes the best use of NHS resources.

The primary outcome measure is participant reported success at 15 months post randomisation (approximately 12 months post treatment) as measured by the Patient Global Impression of Improvement – Index.

The FUTURE study is led by Mr Mohamed Abdel-fattah based at the University of Aberdeen.

Current status

Ongoing

Publications and presentations

None

A.36**FOCUS (Focusing On Clozapine Unresponsive Symptoms)****Investigators**

Graeme MacLennan, HSRU; Prof Anthony Morrison, Mr Rory Byrne, Dr Paul French, Greater Manchester West NHS Foundation Trust; Prof Andrew Gumley, University of Glasgow; Prof Douglas Turkington, University of Newcastle; Prof David Kingdon, University of Southampton; Dr Matthias Schwannauer, University of Edinburgh; Prof Linda Davies, University of Manchester; Prof Thomas Barnes, Imperial College London; Ms Suzy Johnston, The Cairn of Mental Health

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £113,771 (£1,745,263)

Summary

The FOCUS trial, is a randomised controlled trial, funded by the NIHR HTA Programme, assessing whether cognitive behaviour therapy (CBT) is an effective treatment for individuals who have experience of psychosis and whose symptoms have been unresponsive to the anti-psychotic medication 'clozapine'. We have recruited 487 participants to the trial across five sites in the UK: Hampshire, Manchester, Newcastle, Glasgow and Edinburgh.

Eligible participants who consented to take part were randomly allocated to either treatment as usual, which means they continued on with their usual care OR treatment as usual plus CBT. Those participants who were allocated to CBT were offered up to 30 sessions of CBT over the course of 9 months. In addition, all participants were asked to meet with a research assistant for a follow up appointment at 9 months and 21 months.

The primary outcome is the Positive and Negative Syndrome Scale (PANSS), a 30-item rating scale designed to provide a comprehensive assessment of psychopathology in adult patients with schizophrenia.

The project started on the 1 December 2012 and is led by Professor Tony Morrison based at the University of Manchester and Greater Manchester West Mental Health Foundation Trust.

Current status

Ongoing

Publications and presentations

None

A.37**Full thickness macular hole and Internal Limiting Membrane peeling Study (FILMS)****Investigators**

Jen Burr, John Norrie, Luke Vale, HSRU; Noemi Lois, NHS Grampian

Source and amount of HSRU funding (total funding)

CSO £149,250 (202,338)

Summary

A full-thickness macular hole (FTMH) is a common retinal condition associated with impaired vision. The CSO funded FILMS trial has reported six month outcomes in a leading eye journal, Investigative Ophthalmology and Visual Science. This study was a randomised controlled trial recruiting 141 participants with macular hole (stages 2 and 3). The study investigated whether internal limiting membrane peeling compared with no peeling improved the success of macular hole surgery with regards to visual function, closure of the macular hole, quality of life and cost-effectiveness. The findings demonstrated no evidence of difference in distance visual acuity (primary outcome of the study) between ILM peel and no ILM peel groups at six months after macular hole surgery but initial ILM peeling was more likely to close the hole and reduce the need for further surgery. The study concluded that ILM peeling would seem the treatment of choice for idiopathic stage 2-3 FTMH and is likely to be a cost-effective use of resources.

Current status

Completed

Publications and presentations

None

A.38**Graduated compression as an Adjunct to Pharmacoprophylaxis in Surgery (GAPS)****Investigators**

Graeme MacLennan, HSRU; Alun Davies, Joseph Shalhoub, Karen Dhillon, Imperial College London; Christopher Baker, Imperial College Healthcare NHS Trust; Gerard Stansby, University of Newcastle Upon Tyne; Beverley Hunt, King's College London; Tamara Everington, Hampshire Hospitals NHS Trust; David Epstein, University of Grenada; Manjit Gohel, Cambridge University Hospital NHS Trust; Andrew Bradbury, University of Birmingham; Annya Stephens-Boal, Lifeblood: the thrombosis charity; David Warwick, University of Southampton

Source and amount of HSRU funding (total funding)

NIHR HTA Open £227,213 (£1,972,411)

Summary

When a person is in hospital for an operation, they often spend a lot of time in bed, putting them at risk of deep vein thrombosis (DVT). DVT is where a blood clot develops in a deep vein in one or both of the legs, causing pain, swelling and long term complications such as leg ulcers. If a DVT is not treated, then there is a risk that part of the blood clot could break off and become stuck in one of the lungs, blocking blood supply (pulmonary embolism, PE). Together, these two conditions are known as venous thromboembolism (VTE), which is a leading cause of death and disability worldwide. The importance to preventing patients from developing VTE is widely recognized. The main strategies in place involve anticoagulant medications (which thin the blood so it cannot form the harmful clots) and mechanical devices such as elasticated compression stockings (which apply continuous pressure to the legs, helping to maintain bloodflow). Evidence for using elastic stockings to prevent VTE has been challenged, with a lack of evidence for the additional benefits of elastic stockings over and above the benefit of blood-thinning. If elastic stockings reduce VTE over and above blood thinners, these benefits need to be weighed against the disadvantages, such as discomfort, restricting blood flow to the leg, blistering, cost and staff needing to help patients to put them on.

The GAPS study, funded by NIHR HTA Programme, aims to compare whether patients who wear elastic stockings, as well as taking anticoagulant medication have a lower chance of developing VTE than patients who take anticoagulant medications only. Participants are randomly allocated to one of two groups: 1) Graduated compression to wear during their hospital stay, as well as taking low molecular weight heparin OR 2) low molecular weight heparin only.

Current status

Ongoing

Key publications

Shalhoub, J, Norrie, J, Baker, C, Bradbury, CW, Dhillon, K, Everington, T, Gohel, MS, Hamady, Z, Heatley, F, Hudson, J, Hunt, BJ, Stephens, A, Warwick, D, Davies, AN Graduated Compression Stockings as an Adjunct to Low Dose Low Molecular Weight Heparin in Venous Thromboembolism Prevention in Surgery: A Multicentre Randomised Controlled Trial. *Eur J Vasc Endovasc Surg* 2017;53(6):880-85

A.39**Hysterectomy or Endometrial Ablation Trial for Heavy menstrual bleeding: A multicentre randomised controlled trial comparing laparoscopic supra-cervical hysterectomy with second generation endometrial ablation for the treatment of heavy menstrual bleeding (HEALTH)****Investigators**

Graeme MacLennan, Joanne Coyle, Graeme Scotland, Kirsty McCormack, HSRU; Prof S Bhattacharya, DAHS, University of Aberdeen; Dr Kevin Cooper, Dr Mark Wittaker, Dr Jed Hawke, Dr Kevin Phillips, Dr Robert Hawthorne, Dr Mark Roberts, NHS Grampian

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £1,195,628 (£1,427,325)

Summary

HEALTH is a multi-centre trial, funded by the NIHR HTA Programme, comparing surgical options for the management of women with heavy menstrual bleeding (HMB). The primary aim of this study is to compare the clinical and cost effectiveness of laparoscopic supra-cervical hysterectomy (LASH) with second generation endometrial ablation (EA).

HEALTH will recruit 648 women. Trial participants will be followed-up for 12 months.

The co-primary (clinical) outcomes will be a) Menorrhagia Mult-Attribute QoL Scale (MMAS), a condition-specific QoL outcome ranging from 0-100 based upon 6 domains, measured at 15 months after randomisation, and b) patient satisfaction, measured on a six point scale (from "totally satisfied" to "totally dissatisfied") measured at 15 months after randomisation.

The trial is led by Professor Siladitya Bhattacharya based at the University of Aberdeen and Professor Kevin Cooper based at Aberdeen Royal Infirmary.

Current status

Ongoing

Key publications

Cooper, K, McCormack, K, Breeman, S, Wood, J, Scott, N, Clark, J, Philip, K, Hyde, A, McDonald, A, Forrest, M, Wileman, S, Scotland, G, Norrie, J, Bhattacharya, S HEALTH: laparoscopic supra-cervical hysterectomy versus second generation endometrial ablation for the treatment of heavy menstrual bleeding: study protocol for a randomized controlled trial. *Trials* 2017 (submitted for publication)

A.40**Ibrutinib for treating relapsed or refractory chronic lymphocytic leukaemia****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Ibrutinib for treating relapsed or refractory chronic lymphocytic leukaemia. The clinical evidence submitted by the company (Janssen) responsible for manufacturing Ibrutinib (Imbruvica) focused on the results of a single large multicentre randomised controlled trial comparing Ibrutinib with ofatumumab in patients with chronic lymphocytic leukaemia, who have received at least one prior treatment. The submission also presented data from four non randomised and non-controlled studies of Ibrutinib. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released clinical guidance (TA429, January 2017). Ibrutinib alone is currently recommended within its marketing authorisation as an option for treating chronic lymphocytic leukaemia in adults: who have had at least 1 prior therapy or who have a 17p deletion or TP53 mutation, and in whom chemoimmunotherapy is unsuitable and only when the company provides Ibrutinib in line with the commercial access agreement with NHS England.

<https://www.nice.org.uk/guidance/ta429>

Current status

Completed

Key publications

Cummins, E, Culligan, D, Cooper, D, Fraser, C, Robertson, C, Ramsay, CR. Ibrutinib for treating relapsed or refractory chronic lymphocytic leukaemia *Evidence Review Group report in support of the NICE STA Programme*. University of Aberdeen: Health Services Research Unit; 2016.

<https://www.nice.org.uk/guidance/ta429/documents/committee-papers-2>

A.41**Interrupted times series (ITS) evaluation****Investigators**

Jemma Hudson, Craig Ramsay, HSRU; Shona Fielding, University of Aberdeen

Source and amount of HSRU funding (total funding)

£None

Summary

Interrupted times series (ITS) evaluation designs involve monitoring particular populations, administrative units, or groups of health professionals for a period of time prior to implementation of an intervention (e.g., patient safety programme implementation; national guidelines dissemination, prescribing policy reorganisation in hospitals), and subsequently for a period of time following the intervention. The general objective in ITS studies is to examine whether the data series observed post-intervention differs in important aspects from that in the pre-intervention period. Robust evaluation methodology is vital, but analysis of such designs varies from study to study and there is little published guidance on the design strengths and weaknesses, or contexts in which the design should be considered exist. These uncertainties are hindering the quality and reporting of results as well as the spread of many improvement interventions where randomisation is not feasible. This PhD addresses the following broad research questions:

- What design and analysis approaches to ITS data are being used in healthcare and how are they reported?
- What methods should be used when analysing an ITS and what aspects should be reported?

Supervision: Prof Craig Ramsay and Dr Shona Fielding

Current status

Ongoing

Publications and presentations

None

A.42**Interventions for the treatment of painful bladder syndrome (i.e. interstitial cystitis)****Investigators**

Miriam Brazzelli, HSRU; Luke Vale, University of Newcastle

Source and amount of HSRU funding (total funding)

NIHR HTA £20,000 (£20,000)

Summary

This NIHR HTA-funded project will assess the current evidence for the clinical effectiveness of interventions for the treatment of painful bladder syndrome (i.e. interstitial cystitis) in adults. There is currently no definitive cure for painful bladder syndrome and treatment options, which aim to alleviate symptoms, include pharmacological therapy, surgery, supportive/conservative therapies, and lifestyle recommendations. We will conduct a network meta-analysis to estimate treatment effects for different clinical interventions. The results of this project will inform clinical practice and policy on the most effective options for treating the symptoms of painful bladder and help to identify future primary research opportunities for the NHS. In addition, the findings of this project will contribute to the development of a series of systematic reviews, which will focus on specific categories of intervention (i.e., intravesical therapy, pharmacological interventions, surgical interventions, conservative interventions) and will be published in the Cochrane Library.

<https://www.journalslibrary.nihr.ac.uk/programmes/hta/165901/#/>

Current status

Ongoing

Publications and presentations

None

A.43**Investigation of NICE technologies for Enabling Risk-Variable-Adjusted-Length Dental Recall Trial (Interval)****Investigators**

Craig Ramsay, Graeme MacLennan, HSRU; Prof Nigel Pitts, Prof Jan Clarkson, Dr Debbie Bonetti, Prof Ruth Freeman, Prof David Ricketts, University of Dundee; Prof Helen Worthington, University of Manchester; Dr Marjon van der Pol, HERU, University of Aberdeen; Tony Anderson, Dr Wendy McCombes, Dr Linda Young, NHS Education for Scotland; Prof Frederick Burke, Dr Deborah White, University of Birmingham; Prof Gail Douglas, University of Leeds; Robert Elford, Patient Rep; Dr Ronald Gorter, University of Amsterdam; Richard Herbert, University of Cardiff; Dr Penny Hodge, University of Glasgow; Prof Gerry Humphris, University of St Andrews; Dr Theodorus Mettes, Radboud University Nijmegen Medical Centre; Prof Ian Needleman, UCL Eastman Dental Institute; Margaret Ross, University of Edinburgh

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £702,121 (£3,300,510)

Summary

The INTERVAL trial, funded by NIHR HTA, is a UK multi-centre randomised controlled trial evaluating the effectiveness and cost effectiveness of three dental recall strategies, including one advocated by the recent NICE guidance, on maintaining oral health.

An NIHR-HTA funded feasibility phase started in June 2009 and recruited across 10 dental practices in the UK. After the initial 18 month feasibility study, the trial continued to full recruitment of 2372 participants across 50 dental practices.

The primary outcome is the mean proportion of site bleeding on probing at 4 years follow-up.

The INTERVAL trial is led jointly by Professor Jan Clarkson and Professor Nigel Pitts from the University of Dundee.

Current status

Ongoing

Publications and presentations

None

A.44**Knee Arthroplasty Trial (KAT)****Investigators**

Marion Campbell, HSRU; David Rowley, University of Dundee; Ray Fitzpatrick, University of Oxford; David Murray, Nuffield Orthopaedic Centre; Richard Morris, Royal Free Hospital School of Medicine; Alistair Gray, University of Oxford; Jill Dawson, Chris Dodd, Nuffield Orthopaedic Centre; Paul Gregg, University of Newcastle upon Tyne; Ian Learmonth, University of Bristol; James Hutchison, University of Aberdeen; David Hamblen, University of Glasgow; David Marsh, Queens University Belfast

Source and amount of HSRU funding (total funding)

NIHR HTA £369,860 (£369,860)

Summary

The KAT trial, funded by the NIHR HTA Programme is the largest randomised trial of knee replacement surgery ever undertaken, in which the effects of patellar resurfacing, mobile bearings and metal backing were investigated. A total of 116 surgeons in 34 UK centres participated and 2352 participants were randomised. At a median of 10 years of follow-up we can be more than 95% confident that patella resurfacing is cost-effective, despite there being no significant difference in clinical outcomes. We found no definite advantage or disadvantage of mobile bearings in OKS, quality of life, reoperation and revision rates or cost-effectiveness. We found improved functional results for metal-backed tibias: complication, reoperation and revision rates were similar. The metal-backed tibia was cost-effective, particularly in the elderly.

The KAT trial is led by Professor David Murray based at the University of Oxford.

Follow-up to 20 years post-randomisation is ongoing.

Current status

Ongoing

Key publications

Dakin, H, Gray, A, Fitzpatrick, R, MacLennan, G, Murray, D Rationing of total knee replacement: A cost-effectiveness analysis on a large trial dataset. *BMJ Open* 2012;2(1):e000332

Breeman, S, Campbell, MK, Dakin, H, Fiddian, N, Fitzpatrick, R, Grant, A, Gray, A, Johnston, L, MacLennan, GS, Morris, RW, Murray, DW, Group, KT Five year results of a randomised controlled trial comparing mobile and fixed bearing total knee replacement. *Bone Joint J* 2013;95-B(4):486-92

Murray, DW, MacLennan, GS, Breeman, S, Dakin, HA, Johnston, L, Campbell, MK, Gray, AM, Fiddian, N, Fitzpatrick, R, Morris, RW, Grant, AM, KAT Trial Group A randomised controlled trial of the effectiveness and cost-effectiveness of different knee prostheses - the KAT trial. *Health Technol Assess* 2014;18:19

A.45**Male synthetic sling versus Artificial urinary Sphincter for men with urodynamic stress incontinence after prostate surgery: Evaluation by Randomised controlled trial (MASTER)****Investigators**

Graeme MacLennan, Charis Glazener, Craig Ramsay, Kirsty McCormack, Alison McDonald, Gladys McPherson, HSRU; Prof Paul Abrams, North Bristol NHS Trust; Prof Marcus Drake, University of Bristol; Prof Rob Picard, Newcastle University; Ms Mary Kilonzo, HERU, University of Aberdeen; Sir Alexander Macara, Patient and public involvement representative

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £1,079,794 (£1,619,356)

Summary

Male synthetic sling versus Artificial urinary Sphincter for men with urodynamic stress incontinence after prostate surgery: Evaluation by Randomised controlled trial (MASTER).

Around one in five patients who undergo prostate surgery (for cancer or benign disease) need to use incontinence pads because of leaking urine. The male synthetic sling (male sling) is an alternative to the artificial urinary sphincter (AUS) for people with urodynamic stress incontinence after prostate surgery, but there is limited evidence of relative effectiveness and cost-effectiveness to guide choice. We aim to resolve this by directly comparing the rate of incontinence at 12 months.

MASTER is a multicentre randomised controlled trial, funded by the NIHR HTA Programme.

The MASTER trial aims to compare male sling surgery with artificial urinary sphincter surgery in 360 men with urodynamic stress incontinence after prostate surgery, over 3 years.

The primary outcome is clinical and cost effectiveness of the male sling compared with an artificial urinary sphincter using the participant's report of incontinence at 12 months.

Current status

Ongoing

Key publications

Abrams, P, Shearer, K The MASTER trial: artificial urinary sphincter versus male sling. *Trends Urol Mens Health* 2015;6(2):37-38

Constable, L, Cotterill, N, Cooper, D, Glazener, C, Drake, MJ, Forrest, M, Harding, C, Kilonzo, M, MacLennan, G, McCormack, K, McDonald, A, Mundy, A, Norrie, J, Pickard, R, Ramsay, C, Smith, R, Wileman, S, Abrams, P Male synthetic sling versus artificial urinary sphincter trial for men with urodynamic stress incontinence after prostate surgery (MASTER): study protocol for a randomised controlled trial. *Trials* 2017 (submitted for publication)

A.46**Management of the open abdomen****Investigators**

Graeme MacLennan, Gladys McPherson, Graham Mowatt, James Kerlake, HSRU; Amin Amin, Dunfermline; Karen Ritchie, Joanne Abbott, HIS Glasgow; Kathy Rowan, Intensive Care National Audit and Research Centre, London; Victoria Axe, Bruce Campbell, Hannah Patrick, NICE, London; Gordon Carlson, Salford; Heather Newton, Truro

Source and amount of HSRU funding (total funding)

Department of Health via University of Sheffield £259,616 (£519,232)

Summary

Patients undergoing laparotomy for abdominal sepsis and trauma are frequently managed by leaving the abdomen temporarily open (laparostomy). Negative pressure wound therapy (NPWT) has become popular means of managing laparostomy wounds as it is said to facilitate nursing care and delayed primary wound closure, but the evidence to support it is poor and concerns have recently been expressed about the risk of intestinal fistulation from exposed bowel, leading to an increased risk of death. A prospective observational study of 578 patients being treated with an open abdomen in 105 hospitals in the UK was undertaken between 1st January 2010 and 31st June 2011. The project was funded by the National Institute for Health and Clinical Excellence (NICE).

Current status

Completed

Key publications

Carlson, GL, Patrick, H, Amin, AI, McPherson, G, MacLennan, G, Afolabi, E, Mowatt, G, Campbell, B Management of The Open Abdomen: a national Study of Clinical Outcome and Safety of Negative Pressure Wound Therapy. *Ann Surg* 2013;257(6):1154-59

Oral presentations

MacLennan, G, Carlson, GL, Patrick, H, Amin, AI, McPherson, G, Afolabi, E, Mowatt, G, Campbell, B. A national audit of the management of the open abdomen. *Association of Surgeons of Great Britain and Ireland, Liverpool, May 9-11 2012*

A.47**MRC Search Filters Performance Project (MRC SFP)****Investigators**

Cynthia Fraser, Charles Boachie, HSRU: Carol Lefebvre, Cochrane Collaboration; Jenny Harbour, Lynne Smith, Healthcare Improvement Scotland; Julie Glanville, Sophie Beal, Steven Duffy, York Health Economics Consortium

Source and amount of HSRU funding (total funding)

MRC £18,584 (£93,031)

Summary

One information retrieval tool used by information professionals is the methodological search filter to identify specific study designs such as randomized controlled trials. Search filters can help to optimize retrieval by maximizing sensitivity (i.e. identifying as high a proportion as possible of relevant records) whilst achieving adequate precision (minimizing the number of irrelevant records to be assessed). As search filters proliferate, it is unclear how searchers evaluate and choose between available filters.

A series of reviews was undertaken to establish the methods that have been used to measure and report search filter performance. A web-based questionnaire elicited information professionals' views on what measures are most useful in choosing between available filters.

Filter performance comparison studies most commonly reported highest sensitivity, highest precision and optimal/balanced filter strategies. Tables were the most frequently used method of reporting the results of filter performance comparisons but graphs may be more useful. Respondents used a variety of ways to help in selection: not only referring to reported performance (sensitivity and specificity in particular) but also relied on advice of colleagues and the providence of the filters.

Results from this study will inform the development of a search filter performance website.

Current status

Completed

Key publications

Beale, S, Duffy, S, Glanville, J, Lefebvre, C, Wright, D, McCool, R, Varley, D, Boachie, C, Fraser, C, Harbour, J, Smith, L. Choosing and using methodological search filters: searchers' views. *Health Info Libr J* 2014;31(2):133-47

Harbour, J, Fraser, C, Lefebvre, C, Glanville, J, Beale, S, Boachie, C, Duffy, S, McCool, R, Smith, L Reporting methodological search filter performance comparisons: a literature review. *Health Info Libr J* 2014;31:176-94

Lefebvre, C, Glanville, J, Beale, S, Boachie, C, Duffy, S, Fraser, C, Harbour, J, McCool, R, Smith, L Assessment of methodological search filter performance to improve efficiency of evidence information retrieval: systematic reviews and qualitative study. *Health Technol Assess* 2017 (in press)

A.48**MRS/MRI: Systematic review of the diagnostic accuracy and cost-effectiveness of magnetic resonance spectroscopy and enhanced magnetic resonance imaging techniques in aiding the localisation of prostate abnormalities for biopsy****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

This NIHR HTA-funded evidence synthesis aimed at assessing the diagnostic accuracy and cost-effectiveness of magnetic resonance spectroscopy (MRS), enhanced dynamic contrast-enhanced MRI (DCE-MRI), and diffusion weighted MRI (DW-MRI) in localising prostate abnormalities for biopsy in men with prior negative biopsy for whom harbouring malignancy was still suspected. In the UK prostate cancer is the most common cancer in men and the second most common cause of cancer death in men after lung cancer.

This project included a systematic review of diagnostic accuracy to compare the accuracy of MRS, DCE-MRI and DW-MRI with T2-weighted magnetic resonance imaging (T2-MRI) and transrectal ultrasound-guided biopsy (TRUS) against histopathology (biopsied tissues) as reference standard; and an economic model to assess the cost-effectiveness of using alternative MRI/MRS sequences for directing TRUS-guided biopsies compared with an extended-cores TRUS-guided approach.

Fifty-one studies involving over 10,000 men were included in this assessment. MRS had higher sensitivity and specificity than T2-MRI. Few studies reported DCE-MRI or DW-MRI. The cost-effectiveness of MRS compared with T2-MRI and TRUS was sensitive to several key parameters. If MRS and DW-MRI can be shown to have high sensitivity for detecting moderate/high-risk cancer, while avoiding the need for men with no cancer/low-risk disease undergoing biopsy, they could represent a cost-effective approach to diagnosis. However, owing to the relative paucity of reliable data, further studies are required. In particular, comparisons of the individual and combined components of a multiparametric magnetic resonance (MR) approach (MRS, DCE-MRI and DW-MRI) with both a MR-biopsy session and an extended TRUS-guided biopsy scheme would be useful.

<http://www.nets.nihr.ac.uk/projects/hta/0914601>

Current status

Completed

Key publications

Mowatt, G, Scotland, G, Boachie, C, Cruickshank, M, Ford, J, Fraser, C, Kurban, L, Lam, TB, Padhani, AR, Royle, J, Scheenen, TW, Tassie, E The diagnostic accuracy and cost-effectiveness of magnetic resonance spectroscopy and enhanced magnetic resonance imaging techniques in aiding the localisation of prostate abnormalities for biopsy: a systematic review and economic evaluation. *Health Technol Assess* 2013;17(20)

A.49**Multiple frequency bioimpedance devices for fluid management in people with chronic kidney disease having dialysis****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

Chronic kidney disease (CKD) is a long-term condition that often requires dialysis treatment. During dialysis, it is important to optimise the volume of fluid to be removed, to avoid underhydration or overhydration. People having dialysis are, therefore, assigned a 'target weight', which is commonly assessed using clinical methods such as weight gain between dialysis sessions, pre- and post-dialysis blood pressure and patient-reported symptoms. These methods, however, are not precise and measurement using bioimpedance devices is becoming common practice. This NIHR HTA-funded evidence synthesis assessed the clinical and cost-effectiveness of multiple frequency bioimpedance devices for fluid management in people with chronic kidney disease having dialysis. The devices being considered as an alternative to standard clinical assessment in the UK were: BCM - Body Composition Monitor, BioScan 920-II, BioScan touch i8, InBody S10, and MultiScan 5000. The assessment was conducted according to current methodological standards and a de novo economic model was developed to assess the cost-effectiveness of use of the specified devices versus standard clinical assessment. The current NICE guidance (DG29, published June 2017), which is based upon the findings of this assessment, states that there is insufficient evidence to recommend the adoption of the BCM – Body Composition Monitor to guide fluid management in people with chronic disease having dialysis in the NHS. Further evidence is recommended to show the evidence of using the BCM – Body Composition Monitor on outcomes. <http://www.nice.org.uk/guidance/dg29>

Current status

Completed

Key publications

Scotland, G, Cruickshank, M, Jacobsen, E, Cooper, D, Fraser, C, Shimonovich, M, Marks, A, Brazzelli, M Multiple frequency bioimpedance devices for fluid management in people with chronic kidney disease having dialysis: A systematic review and economic evaluation. *Health Technol Assess* 2017 (accepted for publication)

A.50**Nitrites in Acute Myocardial Infarction (NIAMI)****Investigators**

Graeme MacLennan, Jen Burr, HSRU; Prof Michael Frenneaux, Dr Dana Dawson, Prof Tom Redpath, University of Aberdeen; Dr Stuart Cook, MRC CSC; Prof Juan-Carlos Kaski, SGUL; Dr Pitt Lim, St George's Hospital

Source and amount of HSRU funding (total funding)

MRC £170,224 (£1,234.151)

Summary

Cardiovascular diseases (CVD) are the main cause of death in the UK, accounting for almost 200,000 deaths per year. One of the manifestations of CVD is acute myocardial infarction (MI or heart attack). There are estimated to be approximately 125,000 acute MIs in the UK per year. Whilst early reperfusion (restoring of blood flow to the heart) plays an important role in reducing the infarct size (area of dead tissue resulting from failure of blood supply), the reperfusion process itself causes injury. Effective therapy aimed at reducing this reperfusion injury has the potential to substantially to reduce the risk of developing heart failure after an MI. There is evidence from animal models to suggest that an injection of sodium nitrite prior to reperfusion may reduce the reperfusion injury.

NIAMI is a multi-centre, double-blind, randomised trial, funded by the MRC, evaluating sodium nitrite injection versus placebo. The primary outcome is the difference in final infarct size between sodium nitrite and placebo groups measured using Magnetic Resonance Imaging (MRI) 6-8 days following the acute myocardial infarction and corrected for area at risk. Secondary endpoints include plasma creatine kinase and Troponin I over 72 hours and LV ejection fraction and LV end systolic volume index at 10-14 days and 6 months.

The inclusion criteria were: men aged ≥ 18 years, women aged ≥ 55 years and women aged < 55 years (of childbearing potential who are sterilised, or have had a hysterectomy or have effective contraception); presenting within 12 hours of the onset of chest pain who have ST segment elevation of more than 1mm elevation in limb leads or 2mm elevation in two contiguous chest leads with occlusion of the culprit related artery (TIMI grade 0 or TIMI grade 1) for whom the clinical decision has been made to treat with primary percutaneous coronary intervention (PCI). A total of 229 patients were recruited and randomised to either 5ml low-dose sodium nitrite or saline (placebo) given intravenously over 5 minutes immediately prior to the primary PCI.

The study concluded that intravenous sodium nitrite administered immediately prior to reperfusion in patients with acute STEMI did not reduce infarct size.

Current status

Completed

Key publications

Siddiqi, N, Neil, CJ, Bruce, M, MacLennan, G, Cotton, S, Papadopoulo, SA, Feelisch, M, Bunce, N, Lim, P, Hildick-Smith, D, Horowitz, JD, Madhani, M, Boon, N, Kaski, JC, Dawson, D, Frenneaux, MP Intravenous sodium nitrite in acute ST-elevation myocardial infarction: a randomized controlled trial (NIAMI). *Eur Heart J* 2014;35(19):1255-62

A.51

Open mesh repairs in adults presenting with a clinically diagnosed unilateral, primary inguinal hernia

Investigators

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

This NIHR HTA-funded evidence synthesis assessed the clinical and cost effectiveness of open mesh repairs in adults presenting with a clinically diagnosed unilateral, primary inguinal hernia who are operated in an elective setting. The assessment was conducted to current methodological standards and focused on evidence from randomised controlled trials comparing the effects of open pre-peritoneal mesh repair versus Lichtenstein mesh repair with particular attention to postoperative chronic pain. A fully probabilistic economic model was developed to assess the cost-effectiveness of these open mesh procedures. Comprehensive sensitivity analyses were used to address uncertainty.

Although with some uncertainty, people who underwent the open preperitoneal repair returned to work and normal activities earlier than those who underwent the Lichtenstein repair. In general, the open preperitoneal repair was associated with fewer episodes of pain, fewer recurrences and fewer complications than the Lichtenstein repair. The open preperitoneal mesh repair showed to improve patient QoL through a reduction in chronic pain, early complications and recurrences and appeared to be the most cost-effective option. However, evidence on the long-term effects was limited and there was some uncertainty with regard to the parameters used to populate the economic model. Further research was suggested to determine the long-term clinical effectiveness as well as the most cost effective option of open mesh procedures for primary inguinal hernia.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4781117/>

Current status

Completed

Key publications

Sharma, P, Boyers, D, Scott, N, Hernandez, R, Fraser, C, Cruickshank, M, Ahmed, I, Ramsay, C, R., Brazzelli, M The clinical effectiveness and cost-effectiveness of open mesh repairs in adults presenting with a clinically diagnosed primary unilateral inguinal hernia who are operated in an elective setting: systematic review and economic evaluation. . *Health Technol Assess* 2015;19(92)

Boyers, D, Hernandez, R, Sharma, P, Scott, N, Fraser, C, Cruickshank, M, Ahmed, I, Ramsay, C, Brazzelli, M 'Primary inguinal hernia: changing open repair technique likely cost-effective. *HERU Policy Briefing* 2017.

https://www.abdn.ac.uk/heru/documents/Policy_Briefs/HERU_PB_February_2017.pdf

A.52**Open urethroplasty versus endoscopic urethrotomy (OPEN)****Investigators**

Graeme MacLennan, Glayds McPherson, Joanne Coyle, HSRU; Prof Rob Pickard, Dr Tim Rapley, Dr Mark Deverill, Prof Elaine McColl, Prof Luke Vale, Newcastle University; Prof Anthony Mundy, University College London; Mr Steve Payne, Manchester Royal Infirmary; Mr Nick Watkin, St George's Hospital London; Prof James N'Dow, Academic Urology Unit, University of Aberdeen; Mr Barclay Stewart, Service User Representative

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £297,163 (£1,253,564)

Summary

Urethral stricture is a narrowing of the urethra caused by scarring after injury or infection. It is the commonest cause of difficulty passing urine in younger and middle aged men. The prevalence is approximately 200 per 100,000 men in their 20s rising to 900 per 100,000 men in their 70s. Urethral strictures affect about 62,000 men in the UK at any one time. In the NHS in England this corresponds to 17,000 hospital admissions annually, 16,000 bed-days and 12,000 operations at a cost in excess of £10M.

The OPEN trial, funded by the NIHR HTA Programme, is a multicentre randomised trial comparing open urethroplasty with endoscopic urethrotomy in men with recurrent bulbar urethral strictures. The trial aims to recruit 210 men. The primary outcome is the area under curve (AUC) for serial repeated measurement of International Consultant on Incontinence Modular Questionnaire Male Form (ICIQ-Male SF) questionnaire over 24 months following randomisation.

Current status

Ongoing

Key publications

Stephenson, R, Carnell, S, Johnson, N, Brown, R, Wilkinson, J, Munday, A, Payne, S, Watkin, N, N'Dow, J, Sinclair, D, Rees, R, Barclay, S, Cook, J, Goulao, B, MacLennan, G, McPherson, G, Jackson, M, Rapley, T, Shen, J, Vale, L, Norrie, J, McColl, E, Pickard, R Open urethroplasty versus endoscopic urethrotomy - clarifying the management of men with recurrent urethral stricture (the OPEN trial): study protocol for a randomised controlled trial. *Trials* 2015;16:600

A.53**Optical coherence tomography for the diagnosis, monitoring, and guiding of treatment for neovascular age-related macular degeneration: a systematic review and economic evaluation****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

This NIHR HTA-funded project sought to determine the optimal role of Optical coherence tomography (OCT) in: (i) the diagnosis of people newly presenting with suspected neovascular age-related macular degeneration (nAMD) and (ii) in monitoring those previously diagnosed with the disease. Both the more recently introduced spectral domain OCT (SD-OCT) and the time domain OCT (TD-OCT) were assessed against a reference standard of fundus fluorescein angiography (FFA). Based on a small body of evidence of variable quality, OCT had high sensitivity and moderate specificity for diagnosis, and relatively high sensitivity but low specificity for monitoring. For the diagnosis of newly suspected nAMD cases, the pooled sensitivity and specificity estimates for TD-OCT were 88% (95% CI; 46% to 98%) and 78% (95% CI; 64% to 85%) respectively. For the monitoring of those previously diagnosed with nAMD, the pooled sensitivity and specificity estimates for TD-OCT and SD-OCT combined were 85% (95% CI; 72% to 93%) and 48% (95% CI; 30% to 67%) respectively. The findings suggest that although OCT is a reasonable sensitive test, using it as the only test for monitoring patients with nAMD would, potentially, result in a substantial proportion of patients with inactive disease receiving treatment unnecessarily, due to its low specificity. In the economic modelling, strategies using OCT test results alone to make diagnosis and/or monitoring treatment decisions were unlikely to be a cost-effective use of resources. The most cost-effective strategy was FFA alone, interpreted by an ophthalmologist, for diagnosis combined with a nurse or technician-led stepwise approach for monitoring.

Current status

Completed

Key publications and presentations

Mowatt, GM, Hernandez, R, Castillo, M, Lois, N, Elders, A, Fraser, C, Amoaku, W, Burr, JM, Lotery, A, Ramsay, C, Azuara-Blanco, A Optical coherence tomography (OCT) for the diagnosis of neovascular age-related macular degeneration: a systematic review. *Health Technol Assess* 2014;18:69

Oral presentations

Lois, N. Diagnostic Accuracy of OCT in the diagnosis and monitoring of nAMD. *13th International AMD and Retina Congress* 2013

A.54**Optimising Pelvic floor exercises to Achieve Longterm benefits. Multicentre randomised trial of the effectiveness and cost-effectiveness of basic versus biofeedback-mediated intensive pelvic floor muscle training for female stress or mixed urinary incontinence (OPAL)****Investigators**

Graeme MacLennan, Charis Glazener, Alison McDonald, Gladys McPherson, Andy Elders, HSRU; Prof Suzanne Hagen, Dr Doreen McClurg, Dr Joanne Booth, Glasgow Caledonian University; Dr Mohamed Abdelfattah, DAHS, University of Aberdeen; Dr Wael Agur, NHS Ayrshire & Arran; Dr Carol Bugge, University of Stirling; Dr Sarah Dean, Universities of Exeter; Dr Jean Hay-Smith, University of Otago, NZ; Mary Kilonzo, HERU, University of Aberdeen; Dr Brian Buckley, Independent; Dr Karen Guerrero, NHS Greater Glasgow & Clyde; Mrs Lyndsay Wilson, Service user

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £457,082 (£1,970,785)

Summary

Opal is a multi-centre trial, funded by the NIHR HTA Programme comparing basic pelvic floor muscle training (PFMT) versus biofeedback-mediated intensive PFMT. The aim of the study is to investigate whether biofeedback-mediated intensive PFMT is more effective and cost-effective than basic PFMT for the treatment of female stress or mixed urinary incontinence.

OPAL will recruit 600 participants. Follow-up will continue for two years.

The trial is led by Prof Suzanne Hagen based at Glasgow Caledonian University.

Current status

Ongoing

Publications and presentations

None

A.55**OPTIMISTIC. Observational prolonged trial in myotonic dystrophy type 1 to improve stamina, a target identification collaboration****Investigators**

Shaun Treweek, HSRU; Tom Heskes and Elena Marchiori, Radboud University, The Netherlands; Hanns Lochmuller, Michael Trenell, Kate Bushby and Volker Straub, University of Newcastle Upon Tyne; Benedikt Schoser, Angela Schuller and Simone Thiele, Ludwig-Maximilians-Universitaet Muenchen, Germany; Guillaume Bassez and Jean-Yves Hogrel, Assistance Publique – Hopitaux De Paris, France; Darren Monckton, University of Glasgow; Peter Donnan, University of Dundee; Michale Catt, CATT-SCI Limited, UK; Ameli Schwalber, Sara Stober, Andrea Wohner, Karin Rosenits, Barbara Heisserer, Juliane Dittrich, Moritz Eckert, Nari Heitkamp, Katrin Zimmerman, Andrea Schwalber, Concentris Research Management GmbH, Germany

Source and amount of HSRU funding (total funding)

EU (FP7) £29,584 (£2,370,000)

Summary

Myotonic dystrophy type1 (DM1) is a rare, inherited chronic progressive disease as well as an autosomal dominant multisystemic disorder. It is probably the most common adult form of muscular dystrophy, with a prevalence of approximately 10 per 100,000 people affected. DM1 has often been a neglected disease, with progress in the development of management and therapies lacking behind that of other conditions.

OPTIMISTIC is a multi-centre, randomised trial designed to compare an intervention comprising cognitive behavioural therapy plus graded exercise therapy against standard care. Participants will be recruited from myotonic dystrophy clinics and neuromuscular centres in France, Germany, the Netherlands and the UK. OPTIMISTIC aims to recruit 296 individuals to achieve a sample size of 208 individuals for analysis.

The project is led by Baziel van Engelen at Radboud University, the Netherlands, is ongoing and recruitment is expected to finish by the middle of 2015.

More details on OPTIMISTIC are available at <http://optimistic-dm.eu>

Current status

Ongoing

Key publications

Van Engelen, B, OPTIMISTIC Consortium, [Treweek, S]. Cognitive behaviour therapy plus aerobic exercise training to increase activity in patients with myotonic dystrophy type 1 (DM1) compared to usual care (OPTIMISTIC). *Trials* 2015;16:224

A.56**Pembrolizumab for treating advanced or recurrent PD-L1 positive non-small-cell lung cancer after progression with platinum-based chemotherapy****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Pembrolizumab for the treatment of adults with advanced or recurrent PD-L1 positive non-small cell lung cancer i) whose disease has progressed after platinum-containing doublet chemotherapy and ii) whose disease has progressed on both platinum-containing doublet chemotherapy and targeted therapy for epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) positive tumours. The clinical effectiveness evidence submitted by the company (Merck Sharp & Dohme Ltd) responsible for manufacturing Pembrolizumab (Keytruda) consisted of three RCTs: KEYNOTE-010, a phase II/III head-to-head RCT that compared pembrolizumab with docetaxel; KEYNOTE-001 (Parts C and F) a phase I trial due to its initial dose escalation, which evolved into multiple phase II-like sub-studies through a series of expansion cohorts that assessed the effects and safety of pembrolizumab (no comparator); and LUME-LUNG-1, a phase III trial that compared docetaxel plus nintedanib with docetaxel plus placebo. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released clinical guidance (TA428, January 2017). Pembrolizumab is currently recommended, within its marketing authorisation, as an option for treating locally advanced or metastatic PD-L1-positive non-small-cell lung cancer in adults who have had at least one chemotherapy (and targeted treatment if they have an epidermal EGFR or ALK positive tumour), only if: i) Pembrolizumab is stopped at 2 years of uninterrupted treatment and no documented disease progression, and ii) the company provides Pembrolizumab in line with the commercial access agreement with NHS England.

<https://www.nice.org.uk/guidance/TA428>

Current status

Completed

Key publications

Brazzelli, M, Hawkins, N, McKeekin, N, Goulao, B, Cooper, D, Sharma, P, Fraser, C, Nicolson, M, Wu, O. Pembrolizumab after platinum chemotherapy for treating advanced, recurrent, PD-L1 positive, non-small cell lung cancer. . *Evidence Review Group report in support of the NICE STA* University of Aberdeen: Health Services Research Unit; 2016. <https://www.nice.org.uk/guidance/ta428/documents/committee-papers-3>

A.57**PHOTodynamic versus white light-guided treatment of non-muscle invasive bladder cancer: A randomised trial of clinical and cost-effectiveness (The PHOTO Trial)****Investigators**

Craig Ramsay, Graeme MacLennan, HSRU; Rob Pickard, Luke Vale, Rakesh Heer, Newcastle University; John Kelly, UCHL; Emma Hall, Institute for Cancer Research; James N'Dow, University of Aberdeen; Ghulam Nabi, University of Dundee; Param Mariappan NHS Lothian; Jo Cresswell, South Tees NHS Trust; Rhidian Hurle, ABM University LHB; Hugh Mostafid, Hampshire Hospitals; Ernest Taylor, Independent

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £767,068 (£2, 380,539)

Summary

Bladder cancer is the most frequently occurring tumour of the urinary system. Although many early bladder cancers are readily treatable with transurethral resection of bladder tumour (TURBT) it remains one of the most costly cancers to manage on a per patient basis because of its high prevalence, high recurrence rate, need for adjuvant treatments and the requirement for long-term cystoscopic surveillance. The total cost of treatment and 5-year follow-up of patients with Non Muscle Invasive Bladder Cancer (NMIBC) diagnosed during 2001–02 in the United Kingdom was £64 million. From a patient perspective, there often are considerable anxieties about recurrences, surgery and progression requiring additional therapies with potential mortality and long term morbidity (e.g. radical surgery). More efficient management strategies to reduce NMIBC recurrence and hence decrease both the burden to patients and costs to the NHS are urgently needed.

PHOTO is a multicentre randomised controlled phase III trial funded by the NIHR HTA Programme.

The PHOTO trial seeks to determine the efficacy of using photo-dynamic diagnosis (PDD) guided by a fluorescent tumour marker under blue light, instead of conventional white light, for TURBT in intermediate and high risk non-muscle invasive bladder cancer, and whether its implementation is worthwhile for the NHS.

The primary clinical outcome is time to recurrence, for each of the two treatment strategies, with a principal point of interest at 3 years.

The PHOTO trial aims to recruit 533 participants with suspected new diagnosis of intermediate/high risk NMIBC from at least 30 UK hospital sites. Participants will be followed up regularly for 3 years.

The PHOTO trial is led by Dr Rakesh Heer based at the University of Newcastle and managed by CHaRT in collaboration with the Institute of Cancer Research Clinical Trials Unit.

Current status

Ongoing

Publications and presentations

None

A.58**Point-of-care tests (CoaguChek system, INRatio2 PT/INR monitor and ProTime Microcoagulation system) for the self-monitoring of the coagulation status of people receiving long-term vitamin K antagonist therapy compared with standard UK practice****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

This NIHR HTA-funded project assessed the clinical and cost effectiveness of point-of-care coagulometers for the self-monitoring of the coagulation status (self-testing and self-management) in people receiving long-term vitamin K antagonist therapy. Three devices (CoaguChek system, INRatio2 PT/INR monitor and ProTime Microcoagulation system) were considered as an alternative to standard monitoring practice in the UK and the assessment was conducted according to current methodological standards. A de novo economic model was developed to assess the cost-effectiveness of self-monitoring versus standard primary or secondary care clinic monitoring. Current NICE guidance (DG14, published September 2014), which is based upon the results of this assessment, recommends the use of the CoaguChek XS system and InRatio2 PT/INR monitor for the self-monitoring of coagulation status in adults and children taking long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease if:

- They prefer this form of testing and
- They or their carers are both physically and cognitively able to self-monitor effectively.

The guidance points out that there is greater uncertainty of clinical benefit for the InRatio2 PT/INR monitor than for the CoaguChek XS system but the precision and accuracy of both monitors are comparable to laboratory-based INR testing. <https://www.nice.org.uk/guidance/dg14>

Our report was also reviewed by the Scottish Health Technologies Group to inform NHS Scotland (Health Improvement Scotland, Evidence note 57)

http://healthcareimprovementscotland.org/our_work/technologies_and_medicines/shtg_-_evidence_notes/evidence_note_57.aspx

Current status

Completed

Key publications and presentations

Sharma, P, Scotland, G, Cruickshank, M, Tassie, E, Fraser, C, Burton, C, Croal, B, Ramsay, C, Brazzelli, M Is self-monitoring an effective option for people receiving long-term vitamin K antagonist therapy? A systematic review and economic evaluation. *BMJ Open* 2015;5(6):e007758

Sharma, P, Scotland, G, Cruickshank, M, Tassie, E, Fraser, C, Burton, C, Croal, B, Ramsay, C, Brazzelli, M Point-of-care tests (CoaguChek system, INRatio2 PT/INR monitor and ProTime Microcoagulation system) for the self-monitoring of the coagulation status of people receiving long-term vitamin K antagonist therapy compared with standard UK practice. *Health Technol Assess* 2015;19(48)

Scotland, G Is self-monitoring a cost-effective option for people receiving long-term vitamin K antagonist (Warfarin) therapy? *HERU Policy Briefing* September 2015. https://www.abdn.ac.uk/heru/documents/Policy_Briefs/HERU_PB_Sept_2015.pdf

Oral presentations

Sharma, P, Scotland, G, Cruickshank, M, Tassie, E, Fraser, C, Burton, C, Ramsay, C, Brazzelli, M. Assessment of diagnostic tests and the impact on decision making: self-monitoring of oral anticoagulation therapy. *Health Technology Assessment International (HTAi), Annual Meeting, Oslo, 13-17 June 2015*

A.59**Progression Evaluation in Glaucoma (PEG)****Investigators**

Katie Banister, Craig Ramsay, HSRU; Prof A Azuara-Blanco, Queen's University Belfast

Source and amount of HSRU funding (total funding)

Glaucoma Society £35,595 (£40,000)

Summary

Glaucoma is a slowly progressing eye disease caused by damage to the optic disc and this can lead to permanent peripheral vision impairment if not treated.

Our recent diagnostic accuracy study (the GATE study), evaluated whether automated imaging technologies can be used to aid glaucoma diagnosis in hospital services and recruited nearly 1000 patients who had been newly referred for possible glaucoma.

The PEG study, funded by the International Glaucoma Association, aims to understand more about what happens to patients' vision after their referral from the community as they are monitored or treated in hospital eye services. PEG will investigate the progression of glaucoma in a subset of the GATE cohort who had glaucoma or were diagnosed as at risk of glaucoma (glaucoma suspects and ocular hypertension) over 4 years of routine monitoring and treatment in hospital eye services. We will investigate whether any of the characteristics of the person (e.g. age, gender, intraocular pressure, measurements of the retina and optic disc taken at baseline from the GATE study) can predict which patients will have progressive disease.

Current status

Ongoing

Publications and presentations

None

A.60**PROlapse Surgery: Pragmatic Evaluation and randomised Controlled Trial (PROSPECT)****Investigators**

Graeme MacLennan, Charis Glazener, Luke Vale, Alison McDonald, Gladys McPherson, HSRU; Mr Anthony Smith, St Mary's Hospital, Manchester; Dr Christine Bain, NHS Grampian; Dr Robert Freeman, Plymouth Hospitals NHS Trust; Dr Kevin Cooper, NHS Grampian; Prof Adrian Grant, IAHS; Dr Suzanne Hagen, Glasgow Caledonian University

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £2,424,327 (2,424,327)

Summary

PROSPECT is a NIHR HTA funded trial of surgical options for the management of anterior and/or posterior vaginal wall prolapse (the PROSPECT trial). The aim is to evaluate new techniques which use mesh to reinforce the surgery because these have not yet been properly evaluated. 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.

Women who are not eligible for randomisation will also be studied using the same study protocol and methods in a comprehensive cohort design.

PROSPECT recruited over 3000 women, half of whom were randomised, from 35 UK centres. In women who were having a primary repair, there was evidence of no benefit from the use of mesh inlay or biological graft compared with standard repair in terms of efficacy, QoL or adverse effects (other than mesh complications) in the first two years following prolapse surgery. The trials in women having a secondary repair was too small to be conclusive.

Current status

Ongoing

Key publications

Independent Review Group on Transvaginal Mesh Implants (Glazener, C. The Scottish Independent Review of the Use, Safety and Efficacy of Transvaginal Mesh Implants in the Treatment of Stress Urinary Incontinence and Pelvic Organ Prolapse in Women. *Interim Report (2015); Final report (2017)*. Edinburgh: The Scottish Government.

Glazener, C, Breeman, S, Elders, A, Hemming, C, Cooper, K, Freeman, R, Smith, A, Hagen, S, Montgomery, I, Kilonzo, M, Boyer, M, McDonald, A, McPherson, G, MacLennan, G, Norrie, J Clinical effectiveness and cost-effectiveness of surgical options for the management of anterior and/or posterior vaginal wall prolapse: two randomised controlled trials within a comprehensive cohort study - results from the PROSPECT Study. *Health Technol Assess* 2016;20(95)

Glazener, C, Breeman, S, Elders, A, Hemming, C, Cooper, K, Freeman, RF, Smith, A, Reid, F, Hagen, S, Montgomery, I, Kilonzo, M, Boyers, D, McDonald, A, McPherson, G, MacLennan, G, Norrie, J Mesh, graft or standard repair for women having primary anterior or posterior 1 prolapse surgery? Two randomised controlled trials (the PROSPECT Study). *Lancet* 2016;389(10067):381-92

A.61**Quantitative Fibronectin to help Decision making in women with symptoms of Preterm Labour (QUIDS)****Investigators**

Graeme MacLennan, HSRU; John Norrie, Sarah Stock, Jane Norman, University of Edinburgh; Asma Khalil, St George's University of London; Rachel Morris, University of Birmingham; Lesley Jackson, NHS Greater Glasgow & Clyde; Kathleen Boyd, University of Glasgow; Andrew Shennan, King's College London; Susan Harper-Clarke, PPI

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £201,928 (£719,822)

Summary

The clinical diagnosis of preterm labour that leads to delivery is notoriously challenging. Up to 80% of women who have signs and symptoms of preterm labour remain pregnant after 7 days.

A test called quantitative fetal Fibronectin (qfFN) may help improve diagnosis of preterm labour. The lower the concentration of fFN in the sample, the less likely preterm delivery is to occur. Currently, the fFN test which is part of standard care, provides a positive or negative result. The ability to measure the absolute amount of fibronectin is new and has the potential to more accurately rule out preterm labour.

The main aim of QUIDS, funded by NIHR HTA Programme, is to see if qfFN can accurately rule out spontaneous preterm delivery within 7 days of testing. We will use our findings to develop decision support tool, to help women and clinicians assess how likely preterm delivery is, and decide whether to start treatment or not.

We plan to recruit 1600 women who will be eligible to have the fFN test. We anticipate that recruitment will last 12 months and around 15 sites will be involved in the UK.

QUIDS is led by Dr Sarah Stock based at the University of Edinburgh.

Current status

Ongoing

Publications and presentations

None

A.62**Radium-223 dichloride for treating metastatic hormone relapsed prostate cancer with bone metastases (ID576) Single Technology Appraisal****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Radium-223 dichloride for the treatment of metastatic castration resistant prostate cancer. The clinical evidence submitted by the company (Bayer Health Care) responsible for manufacturing Radium-223 dichloride (Xofigo) consisted of one international, multicentre, double-blind phase three randomised controlled trial (RCT) sponsored by the company. Evidence from a smaller phase-two, international multicentre, double-blind RCT was presented in a supportive role. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released clinical guidance (TA412, September 2016). Radium-223 dichloride is currently recommended as an option for treating hormone-relapsed prostate cancer, symptomatic bone metastases and no known visceral metastases in adults only if i) they have already had docetaxel or docetaxel is contraindicated or is not suitable for them; ii) the company provides Radium-223 dichloride in line with the commercial access agreement with NHS England. <https://www.nice.org.uk/guidance/ta412>

Current status

Completed

Key publications

Robertson, C, Lam, T, Stewart, F, Scott, N, Cummins, E, Ramsay, C. Radium-223 dichloride for treating metastatic hormone relapsed prostate cancer with bone metastases. *Evidence Review Group Report in support of the NICE STA Programme*. University of Aberdeen: Health Services Research Unit; 2013

Scotland, G, Hernandez, R, Robertson, C, Scott, N, Fraser, C. Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases (men who have not received docetaxel and for whom docetaxel is contraindicated or not suitable). *ERG critique of the company submission for re-consideration of current CDF technologies under the new proposed CDF criteria*. University of Aberdeen: Health Services Research Unit; 2016. <https://www.nice.org.uk/guidance/ta412/documents/committee-papers>

A.63**Randomised Evaluation of Laproscopic Surgery for reflux (REFLUX)****Investigators**

Craig Ramsay, Adrian Grant, Marion Campbell, HSRU; Iain Martin, Dept of Surgery, University of Leeds; Mark Sculpher, Centre for Health Economics, University of York; Zygmunt Krukowski, Dept of Surgery, Aberdeen Royal Hospitals NHS Trust; Robert Heading, Centre for Liver & Digestive Disorders, University of Edinburgh; Ara Darzi, Minimal Access Surgical Unit, St Mary's Hospital, London; Ian Russell, Dept of Health Sciences, University of York

Source and amount of HSRU funding (total funding)

NHS HTA Programme £879,153 (£,1,105,903)

Summary

The REFLUX trial, funded by the NIHR HTA, is a multi-centre randomised trial comparing a policy of relatively early laparoscopic surgery with a continued best medical management policy for people with more severe gastro-oesophageal reflux disease (GORD).

810 people with GORD were recruited from 21 centres across the UK - 357 into the randomised component, and 453 into the patient preference component of the trial. The one year results showed benefits for fundoplication in terms of condition-specific measures of outcome and of the EQ-5D at one year post-surgery. Extended follow-up to five years was carried out to evaluate the longer term clinical effectiveness and cost-effectiveness of early laparoscopic surgery compared with continued medical management.

After five years, early laparoscopic surgery continued to provide better relief of GORD symptoms and a better quality of life than medical management. Adverse effects of surgery were uncommon and generally observed soon after surgery. A small proportion had re-operations. There was no evidence of long term adverse symptoms caused by surgery. Despite being initially more costly, a surgical policy is highly likely to be more cost-effective for such patients suffering from chronic GORD.

Current status

Completed

Key publications

Grant, AM, Boachie, C, Cotton, S, Faria, R, Bojke, L, Epstein, D, Ramsay, CR, Corbacho, B, Sculpher, M, Krukowski, ZH, Heading, RC, Campbell, MK, REFLUX Trial Group Clinical and economic evaluation of laparoscopic surgery compared with medical management for gastro-oesophageal reflux disease - 5-year follow-up of multicentre randomised trial (The REFLUX Trial). *Health Technol Assess* 2013;17(22):1-166

Grant, AM, Faria, R, Cotton, S, Boachie, C, Bojke, L, Epstein, D, Ramsay, CR, Corbacho, B, Sculpher, M, Krukowski, Z, Heading, RC, Campbell, MK, Group, RT Minimal access surgery compared with medical management for gastro-oesophageal reflux disease - clinical and economic evaluation based on five year follow-up of multicentre randomised controlled trial (The REFLUX Trial). *Br Med J* 2013;346:f1908

A.64**Randomised trial of vitamin D and calcium for the secondary prevention of osteoporosis related fractures in the elderly (RECORD)****Investigators**

Marion Campbell, Adrian Grant, HSRU; Cyrus Cooper, MRC Environmental Epidemiology Unit; Fraser Anderson, Roger Francis, Dept of Geriatric Medicine, University of Newcastle upon Tyne; David Torgerson, Centre for Health Economics, University of York

Source and amount of HSRU funding (total funding)

MRC £None (£103,874)

Summary

Osteoporotic fractures are a major cause of ill-health in older people. The most promising prevention strategy for the elderly, amongst whom most fractures occur, is supplementation with a combination of vitamin D and calcium. Evidence for vitamin D alone is much weaker, but if clinically effective this would be more appropriate and cost effective. The aim of this placebo-controlled randomised controlled trial (with factorial design) was, therefore, to evaluate the effects of vitamin D and calcium alone and in combination on new fractures, health care resources, and quality of life.

Current status

Completed

Key publications

Avenell, A, MacLennan, GS, Jenkinson, DJ, McPherson, GC, McDonald, A, Pant, PR, Grant, AM, Campbell, MK, Anderson, FH, Cooper, C, Francis, RM, Gillespie, WJ, Robinson, CM, Torgerson, DJ, Wallace, WA, RECORD Trial Group Long-Term Follow-Up for Mortality and Cancer in a Randomized Placebo-Controlled Trial of Vitamin D3 and/or Calcium (RECORD Trial). *J Clin Endocrinol Metab* 2012;97(2):614-22

Rejnmark, L, Avenell, A, Masud, T, Anderson, F, Meyer, HE, Sanders, KM, Salovaara, K, Cooper, C, Smith, HE, Jacobs, ET, Torgerson, D, Jackson, RD, Manson, JE, Brixen, K, Mosekilde, L, Robbins, JA, Francis, RM, Abrahamsen, B Vitamin D with calcium reduces mortality: patient level pooled analysis of 70,528 patients from eight major vitamin D trials. *J Clin Endocrinol Metab* 2012;97(8):2670-81

Bristow, SM, Bolland, MJ, MacLennan, GS, Avenell, A, Grey, A, Gamble, GD, Reid, IR Calcium supplements and cancer risk: a meta-analysis of randomised trials. *Br J Nutr* 2013;110(8):1384-93

Ford, J, MacLennan, GS, Avenell, A, Bolland, M, Grey, A, Witham, M, RECORD Trial Group Cardiovascular disease and vitamin D supplementation; trial analysis, systematic review and meta-analysis. *Am J Clin Nutr* 2014;100(3):746-55

MacLennan, G, McDonald, A, McPherson, G, Treweek, S, Avenell, A Advance telephone calls ahead of reminder questionnaires increase response rate in non-responders compared to questionnaire reminders only: The RECORD Phone Trial. *Trials* 2014;15:13

A.65**Ranibizumab for the treatment of choroidal neovascularisation associated with pathological myopia****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please see A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Ranibizumab for treating choroidal neovascularisation associated with pathological myopia. The main source of clinical evidence submitted by the company (Novartis) responsible for manufacturing Ranibizumab (Lucentis) consisted of one phase III trial comparing Ranibizumab with verteporfin photodynamic therapy (vPDT) in people with visual impairment caused by choroidal neovascularisation secondary to pathological myopia. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released clinical guidance (TA298, November 2013). Ranibizumab is currently recommended by NICE as an option for treating visual impairment due to choroidal neovascularisation secondary to pathological myopia when the manufacturer provides Ranibizumab in line with the commercial access agreement with NHS England.

<https://www.nice.org.uk/guidance/ta298>

Current status

Completed

Key publications

Cummins, E, Fielding, S, Cruickshank, M, Fraser, C, Lois, N, Brazzelli, M. Ranibizumab for the treatment of choroidal neovascularisation associated with pathological myopia. A Single Technology Appraisal. *Evidence Review Group report in support of NICE STA programme*. University of Aberdeen: Health Services Research Unit; 2013. <https://www.nice.org.uk/guidance/ta298/documents/choroidal-neovascularisation-pathological-myopia-ranibizumab-evaluation-report2>

A.66**RAPID Trial. Development of interventions to reduce patient delay with symptoms of acute coronary syndrome: identifying optimal content and mode of delivery****Investigators**

Shaun Treweek, HSRU: Dr Barbara Farquharson, Prof Brian Williams, Ms Nadine Dougall, Dr Stephan Dombrowski, University of Stirling; Dr Karen Smith, Dr John McGhee, Clare Jones, University of Dundee

Source and amount of HSRU funding (total funding)

CSO £3,438 (£221,668)

Summary

Acute Coronary Syndrome is serious and delay to treatment, in particular patient decision time, is a critical factor in reducing mortality and achieving optimal benefit from current treatment strategies. Previous interventions to reduce patient decision time have been largely unsuccessful. However, most interventions have failed to incorporate relevant psychological theory or to use established behaviour change techniques (BCTs).

This CSO funded study will develop a theory-based intervention by (i) identifying the content (i.e. BCTs) most likely to be effective, based on existing evidence (Systematic Review) and consensus amongst subject experts (Delphi study) and (ii) identifying the most effective way of delivering that content by comparing two modes of delivery (text only and text plus visual) with a control in an intervention modelling experiment, measuring effect on intention to seek help immediately.

RAPID is led by Barbara Farquharson at the University of Stirling.

Current status

Ongoing

Key publications

Farquharson, B, Dombrowski, S, Pollack, A, Johnston, M, Treweek, S, Williams, B, Smith, K, Dougall, N, Jones, C, Pringle, S Reducing patient delay with symptoms of acute coronary syndrome: a research protocol for a systematic review of previous interventions to investigate which behaviour change techniques are associated with effective interventions. *Open Heart* 2014;1(1):e000079

Farquharson, B, Johnston, M, Smith, K, Williams, B, Treweek, S, Dombrowski, SU, Dougall, N, Abhyankar, P, Grindle, M Reducing patient delay in Acute Coronary Syndrome (RAPiD): research protocol for a web-based randomized controlled trial examining the effect of a behaviour change intervention. *J Adv Nurs* 2017;73(5):1220-34

A.67**REBALANCE: Systematic review and integrated report on the quantitative, qualitative and economic evidence base for the management of severe obesity [classes II and III obesity (BMI \geq 35kg/m²)]****Investigators**

Alison Avenell, HSRU; Paul Aveyard, University of Oxford; Jennifer Logue, University of Glasgow; Laura Webber, UK Health Forum; Drew Walker, NHS Tayside; Su Sethie, NHS England

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £524,213 (£530,873)

Summary

There is little systematic review evidence to inform weight management programmes for adults with severe obesity (body mass index of 35kg/m² or over). People with severe obesity are likely to need more assistance with weight loss and more likely to have medical, psychological and social problems related to their obesity.

This 20 month long project is funded by the National Institute of Health Research Health Technology Assessment Programme. This is a collaborative project between the Health Services Research Unit and Health Economics Research Unit (University of Aberdeen), Prof Marijn De Bruin, Health Psychology (University of Aberdeen), Prof Paul Aveyard, Department of Primary Health Care Sciences (University of Oxford) and Dr Laura Webber and Dr Lise Retat (UK Health Forum).

The project comprises a series of systematic reviews of randomised and non-randomised trials, qualitative research and health economic studies, to develop an economic model and inform the management of adults with severe obesity. We will examine the effectiveness and cost-effectiveness of different approaches to helping change lifestyles, and compare lifestyle approaches to bariatric surgery. We will use new methods to examine the behaviour change techniques which are most able to support people.

Current status

Ongoing

Publications and presentations

None

A.68**Reducing Asthma Attacks in Children using Exhaled Nitric Oxide as a biomarker to inform treatment strategy - a randomised trial (RAACENO)****Investigators**

Graeme MacLennan, Heather Morgan, HSRU; Steve Turner, Shona Fielding, Aileen Neilson, David Price, University of Aberdeen; Mike Thomas, University of Southampton; Erol Gaillard, University of Leicester; Johan de Jongste, Marielle Pijnenberg, Erasmus University Medical Centre, Netherlands

Source and amount of HSRU funding (total funding)

NIHR EME Programme £1,467,091 (£1,531,931)

Summary

The focus of this study is childhood asthma exacerbations, which are common, potentially life-threatening and are a considerable financial burden to healthcare systems. Annually in the UK 150,000 children see their family doctor for an asthma exacerbation and 25,000 are hospitalised. One third of the £1 billion NHS budget for asthma is spent on provision for unscheduled care of which about one half is for childhood exacerbations. Exacerbations are relatively infrequent and short-lived but their importance to patients is emphasised in the Global Initiative for Asthma whose major goals include "to prevent asthma exacerbations".

Previous studies undertaken that looked at Fractional exhaled Nitric Oxide (FeNO) as a biomarker, suggest that its use to guide asthma treatment could help reduce the number of children with an asthma exacerbation.

This study will compare outcomes between two clinical management strategies. Asthma treatment guided by "symptoms only" (i.e. standard care) in the control arm while FeNO levels and symptoms will be used to guide asthma treatment in the intervention arm. This study will add to the current understanding of the relationship between FeNO, sputum eosinophilia and asthma exacerbation and also add to the research base for the management of children with asthma symptoms treated with inhaled corticosteroids.

This randomised multi-centre study, is funded by the NIHR EME Programme, will recruit 502 participants over 22 months. Children or young persons aged 6-16 years, have asthma, attend hospital asthma clinics, are treated with inhaled corticosteroids, and have had an asthma attack treated with steroid tablets in the past year are eligible to take part. We will be recruiting children in approximately 25 hospitals around the UK.

The primary outcome is asthma exacerbation (attack) which will be assessed at the 3, 6, 9 and 12 month follow-up visits, and confirmed with data held in medical records.

RAACENO is led by Professor Steve Turner based at the University of Aberdeen.

Current status

Ongoing

Publications and presentations

None

A.69**Safety & tolerability of the combination of simvastatin plus rifaximin in patients with decompensated cirrhosis: a multicenter, double-blind, placebo controlled randomised clinical trial (Liverhope)****Investigators**

Kath Starr, HSRU; European Clinical Research Infrastructure Network (ECRIN)

Source and amount of HSRU funding (total funding)

EU H2020 £22,161 (£22, 161)

Summary

This Horizon 2020 EU funded project seeks to evaluate simvastatin and rifaximin as new therapy for patients with decompensated cirrhosis. This European multi-centre project is clinically led by Institut D'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) and managed in conjunction with the European Clinical Research Network (ECRIN). CHaRT are working with UCL and the Royal Free Hospital, London on behalf of ECRIN to manage the study in the UK. The project has two phases, LIVERHOPE_safety and LIVERHOPE_efficay.

LIVERHOPE_SAFETY will aim to address the safety and tolerability of the combination of simvastatin plus rifaximin in patients with decompensated cirrhosis. It will recruited 45 patients throughout the EU over three months and will follow participants for three months.

LIVERHOPE_EFFICACY is a double-blind, placebo-controlled trial on the effect of simvastatin plus rifaximin in halting disease progression and the development of acute-on-chronic liver failure (ACLF) in patients with decompensated cirrhosis. It will recruit 240 participants over 12 months. Participants will receive study medication for one year and will be followed during this time and for three months post-treatment.

Current status

Ongoing

Publications and presentations

None

A.70

Secukinumab for treating moderate to severe plaque psoriasis

Investigators

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

The aim of this project, which was commissioned by NICE through the NIHR HTA Programme as part of the NICE's Single Technology Appraisal process, was to review the evidence for the clinical and cost-effectiveness of Secukinumab for treating moderate to severe plaque psoriasis. The clinical evidence submitted by the company (Novartis) responsible for manufacturing Secukinumab (Cosentyx) consisted of four phase III RCTs comparing Secukinumab with placebo and a dose-response trial. The Aberdeen HTA Group acted as the Evidence Review Group (ERG) for the project and provided an independent critique of the clinical and cost-effectiveness evidence submitted by the company.

After taking into consideration the company submission and the findings of the ERG's critique, NICE released clinical guidance (TA350, July 2015). Secukinumab is currently recommended as an option for treating people with plaque psoriasis if (i) the disease is severe, as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index of more than 10; (ii) the disease has failed to respond to standard systemic therapies, for example, ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation), or these treatments are contraindicated or the person cannot tolerate them; (iii) the company provides it with the discount agreed in the patient access scheme. Secukinumab treatment should be stopped in people whose psoriasis has not responded adequately at 12 weeks. <https://www.nice.org.uk/guidance/ta350>

Current status

Completed

Key publications

Cummins, E, Scott, N, Cruickshank, M, Fraser, C, Ormerod, A, Brazzelli, M. Secukinumab for treating moderate to severe plaque psoriasis. *Evidence Review Group report in support of the NICE STA Programme*. University of Aberdeen: Health Services Research Unit; 2015.

<https://www.nice.org.uk/guidance/ta350/documents/secukinumab-for-treating-moderate-to-severe-plaque-psoriasis-committee-papers2>

A.71**Sedation in ICU: Alpha-2 agonists for sedation of mechanically ventilated adults in intensive care units: a systematic review****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

Sedation of critically ill patients in the intensive care unit (ICU) often requires potentially invasive or uncomfortable procedures, such as mechanical ventilation. In the UK, the most commonly used sedatives are propofol, benzodiazepines (for example, midazolam and lorazepam) and α 2-agonists (dexmedetomidine and clonidine). The main difference between α 2-agonists and the other sedatives is that patients can readily be aroused, which is an important aspect of maintaining minimal levels of sedation.

This NIHR HTA-funded systematic review compared the clinical effectiveness of α 2-agonists (dexmedetomidine and clonidine) with propofol or benzodiazepines (midazolam and lorazepam) in mechanically ventilated patients in the ICU. Major electronic databases were searched for RCTs comparing dexmedetomidine with clonidine, or dexmedetomidine or clonidine with propofol or benzodiazepines. Methods recommended by the Centre for Reviews and Dissemination and Cochrane Handbook for Systematic Reviews of Interventions were used. The findings from 18 RCTs involving 2489 adult patients showed that length of ICU stay and time to extubation were significantly shorter for patients receiving dexmedetomidine. Dexmedetomidine was associated with a higher risk of bradycardia than propofol or benzodiazepines but not of overall mortality. Evidence on clonidine was very limited. Further research was recommended to assess the use of clonidine in this clinical context and identify subgroups of patients more likely to benefit from dexmedetomidine.

<https://www.journalslibrary.nihr.ac.uk/hta/hta20250>

Current status

Completed

Key publications

Cruickshank, M, Henderson, L, MacLennan, G, Fraser, C, Campbell, M, Blackwood, B, Gordon, A, Brazzelli, M
Alpha-2 agonists for sedation of mechanically ventilated adults in intensive care units: a systematic review.
Health Technol Assess 2016;20(25)

A.72

Single Centre Appendectomy RCT: Laparoscopic vs Endoscopic Single-port Surgery (SCARLESS)

Investigators

Kirsty McCormack, Joanne Coyle, HSRU; Dr Irfan Ahmed, Dr Zygmunt Krokowski, NHS Grampian

Source and amount of HSRU funding (total funding)

CSO £50,000 (£50,000)

Summary

Laparoscopic surgery is the preferred approach for many abdominal procedures because of the reduced postoperative pain, more rapid recovery and improved cosmesis. One of the recent innovations is Single Port/Incision Laparoscopic Surgery (SPILS). The SCARLESS study, funded by the Chief Scientist Office (CSO), aimed to compare the effectiveness of SPILS with standard standard 3-port laparoscopic surgery for appendicectomy. Feasibility measures were collected to assess the viability of a multicentre randomised controlled trial (RCT) to evaluate more complex single port techniques.

A single centre (Aberdeen, UK) RCT was conducted. Seventy nine participants were randomised to receive either SPILS or Standard 3-port laparoscopic surgery and followed-up for six weeks. The primary patient reported outcomes were body image and cosmetic scores at six weeks. The primary clinical outcome was severity of pain at 1 to 7 days.

The study reported at six weeks post operation, SPILS patients answered significantly more favourably to the items in the body image scale and the cosmetic scale compared with patients in the standard group. The duration of operation was shorter in the SPILS group. Patients also required less morphine when in immediate recovery. However, there were no statistically significant differences in other outcomes such as intraoperative and postoperative complications, postoperative analgesia use on ward, length of stay and return to normal activity. It was concluded that patient-reported body image and cosmesis outcomes were better, and surgical outcomes were similar following SPILS. However, the SPILS procedure is more technically demanding and may not be achievable or necessary in routine clinical care. Further assessment of the findings is needed through larger multicentre studies.

Current status

Completed

Key publications

SCARLESS Trial Group, [Duncan, A, MacLennan, G, McCormack, K Single port/incision laparoscopic surgery compared with standard 3 port laparoscopic surgery for appendicectomy - A randomised controlled trial. *Surg Endosc* 2015;29(1):77-85

A.73**Single-incision adjustable mini-slings versus standard tension-free mid-urethral slings in the management of stress urinary incontinence: a pragmatic multicentre non-inferiority randomised controlled-trial (SIMS)****Investigators**

Graeme MacLennan, Kirsty McCormack, HSRU; John Norrie, University of Edinburgh; Mr Mohamed Abdel-Fattah, Mr James N'Dow, Mary Kilonzo, University of Aberdeen; Mr Phil Assasa, Mid Yorkshire Hospitals NHS Trust; Judith Wardle, Continence Foundation

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £1,505,204 (£1,664,018)

Summary

SIMS is a multi-centre randomised controlled trial, funded by the NIHR HTA Programme, of surgical options for the management of female stress urinary incontinence (SUI). The aim of this trial is to evaluate the clinical and cost effectiveness of adjustable anchored Single Incision Mini-Slings (SIMS) compared to tension-free Standard Mid-urethral Slings (SMUS).

SIMS recruited 650 women. Trial participants will be followed-up for 36 months.

The primary outcome measure will be patient-reported success rate measured by the validated PGI-I (a 1-item questionnaire designed to assess the patient's impression of changes in her urinary symptoms) at 12-months.

SIMS is led by Mr Mohamed Abdel-Fattah based at the University of Aberdeen.

Current status

Ongoing

Key publications and presentations

Abdel-Fattah, M, MacLennan, G, Kilonzo, M, Assasa, P, McCormack, K, Davidson, T, McDonald, A, n'Dow, J, Wardle, J, Norrie, J. The SIMS trial: adjustable anchored single-incision mini-slings versus standard tension-free midurethral slings in the surgical management of female stress urinary incontinence. A study protocol for a pragmatic, multicentre, non-inferiority randomised controlled trial. *BMJ Open* 2017;7(8):e015111

Oral presentations

Davidson, T. Lessons learned in trial management - the HARD way. *International Clinical Trials Methodology Conference, Glasgow, 16-17 November 2015*

Davidson, T, McDonald, A, McPherson, G, Norrie, J, SIMS Trial Group. Evaluating the use of real-time data collection using SMS texts in the SIMS study. *International Clinical Trials Methodology Conference, Glasgow, 16-17 November 2015*

Constable, L, Davidson, T, McDonald, A, Foulkes, M, Norrie, J. What happens when a trial is interrupted? How to deal with suspension of randomisation and restart your trial. *Society for Clinical Trials, 37th Annual Meeting, Montreal, 25-18 May 2016*

A.74

Surveillance for Ocular Hypertension

Investigators

Jen Burr, Luke Vale, Joanne Coyle, HSRU; Prof Mandy Ryan, HERU; Dr John Deeks, University of Birmingham; David Garway-Heath, Moorfields Eye Hospital; Dr Augusto Azuara-Blanco, NHS Grampian; Richard Wormald, Moorfields Eye Hospital; Rodolfo Hernandez, HERU; Dr David Crabb, City University, London; Dr Rafael Perera, University of Oxford; Dr Aachal Kotecha, City University, London; Prof Paul Glasziou, University of Oxford

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £242,534 (£357,246)

Summary

The aim of the study was to determine the optimum frequency of monitoring patients identified as at risk of glaucoma due to raised intraocular pressure (IOP), a condition called ocular hypertension, and the extent this varied according to individual risk characteristics.

We used a discrete event simulation economic modelling evaluation to compare alternative monitoring pathways. Systematic reviews and individual patient data analysis were conducted and public preferences elicited in order to provide data to structure and populate the economic model. These included reviews of available risk prediction models and also of the agreement between tonometers. We used existing datasets to validate identified risk models and determine optimal monitoring criteria for measuring IOP and for tests to detect glaucoma. Public preferences for a monitoring scheme were elicited using a discrete choice experiment of the general population.

The study found the best available risk prediction model was the OHTS-EGPS means model. Study findings support the clinical importance of establishing a true baseline IOP prior to initiating monitoring or treatment and the same type of tonometer should be used to compare IOP measurements in an individual. Based on a small sample, findings suggest biennial IOP monitoring for untreated or stable treated OHT but the optimal frequency of clinical testing (perimetry or optic nerve evaluation) to detect glaucoma remains uncertain.

The economic evaluation findings suggested no clear benefit in intensive monitoring to detect glaucoma. It was clear from public preference data that any service reconfigurations should consider patient experiences, ensuring adequate time to explain the purpose of monitoring and avoid treatment side effects. If the NHS costs for repeat visits to monitor IOP response to treatment are minimised, biennial hospital-based monitoring appears optimal. The economic model may not have fully captured all data uncertainties. The feasibility of community care pathways should be explored. Further research is recommended to refine the glaucoma risk prediction model in a UK setting and determine the optimum type and frequency of serial glaucoma tests.

Current status

Completed

Key publications and presentations

Burr, JM, Botello, AP, Takwong, Y, Hernandez, R, Vazquez-Montes, M, Elders, A, Asoaka, R, Banister, K, van der Schoot, J, Fraser, C, King, A, Lemij, H, Sanders, R, Vernon, S, Tuulonen, A, Kotecha, A, Glasziou, P, Garway-Heath, D, Crabb, D, Vale, L, Azuara-Blanco, A, Perera, R, Ryan, M, Deeks, J, Cook, J Surveillance for ocular hypertension: an evidence synthesis and economic evaluation. *Health Technol Assess* 2012;16(29)

Cook, JA, Botello, AP, Elders, A, Alia, A, Azuara-Blanco, A, Fraser, C, McCormack, K, Burr, J, Surveillance of Ocular Hypertension Study Group Systematic review of the agreement of tonometers with Goldmann applanation tonometry. *Ophthalmology* 2012;119(8):1552-57

Hernandez, R, Burr, J, Vale, L, Azuara-Blanco, A, Cook, JA, Banister, K, Tuulonen, A, Ryan, M, Surveillance of Ocular Hypertension Study Group Monitoring ocular hypertension, how much and how often? A cost-effectiveness perspective. *Br J Ophthalmol* 2016;100(9):1263-68

Hernandez, R, Burr, J, Azuara-Blanco, A, Cook, JA, Banister, K, Tuulonen, A, Ryan, M Treatment or monitoring for people with ocular hypertension. *HERU Policy Briefing* May 2016.
https://www.abdn.ac.uk/heru/documents/Policy_Briefs/HERU_PB_May_2016.pdf

Oral presentations

Hernandez, R, Ryan, M, Vale, L, Botello, AP, Burr, JM. Incorporating discrete choice experiments into an economic evaluation: a case study of preferences for alternative monitoring services for individuals with ocular hypertension. *Health Economists Study Group Meeting, Oxford, June 2012*

A.75**SWATs and SWARs: Studies Within A Trial (SWAT) and Studies Within A Review (SWAR)****Investigators**

Shaun Treweek, HSRU; Mike Clarke, Queen's Belfast; Trudie Lang, Chris Bray, Ed Juszcak, Oxford; Peter Bower, Manchester; Declan Devane, School of Nursing, Ireland; Peter Davidson, Southampton; Lelia Duley, Nottingham

Source and amount of HSRU funding (total funding)

MRC £None (£12,233)

Summary

Studies Within A Trial (SWAT) and Studies Within A Review (SWAR). This MRC Network of Hubs for Trials Methodology Research funded study aims to promote the routine adoption of nested studies within clinical trials to test out different ways to aid the conduct and delivery of clinical trials. SWATs are short protocols describing an intervention that could be evaluated in a host trial, for example, interventions aimed at increasing recruitment, or linked to trial management. An example is at <http://onlinelibrary.wiley.com/doi/10.1111/jebm.12049/abstract;jsessionid=9B11769C61F70E780D056F7D584A5479.f02t04>.

The SWAT/SWAR project is led by Mike Clarke at the University of Belfast.

Current status

Ongoing

Publications and presentations

None

A.76**Systematic review and economic modelling of the relative clinical benefit and cost-effectiveness of laparoscopic surgery and robotic surgery for removal of the prostate in men with localised prostate cancer****Investigators**

Craig Ramsay, Graham Mowatt, HSRU; Dr Rob Pickard, Newcastle University; Nigel Armstrong, Newcastle University; Prof David Neal, University of Cambridge; Thomas Lam, NHS Gampian; Chris Eden, Royal Surrey County Hospital NHS Trust; Dr Mary Robinson, Newcastle upon Tyne Hospitals NHS Foundation Trust; Naeem Soomro, Ditto

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £158,729 (£232, 386)

Summary

This NIHR HTA funded project aimed to determine the relative clinical effectiveness and cost-effectiveness of robotic radical prostatectomy compared with laparoscopic radical prostatectomy in the treatment of localised prostate cancer. We undertook a systematic review with economic modelling of the effectiveness and safety of the two procedures in the longer term guided by advice from an international panel of experts.

This study demonstrated that robotic prostatectomy had lower perioperative morbidity and a reduced risk of a positive surgical margin compared with laparoscopic prostatectomy although there was considerable uncertainty. Our modelling showed that this excess cost can be reduced if capital costs of equipment are minimised and by maintaining a high case volume for each robotic system of at least 100–150 procedures per year. This finding was primarily driven by a difference in positive margin rate. There is a need for further research to establish how positive margin rates impact on long-term outcomes.

Current status

Completed

Key publications

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 and robotic surgery for removal of the prostate in men with localised prostate cancer. *Health Technol Assess* 2012;16(41):1-313

Close, A, Robertson, C, Rushton, S, Shirley, M, Vale, L, Ramsay, C, Pickard, R Comparative cost-effectiveness of robotic prostatectomy and laparoscopic prostatectomy as alternatives to open radical prostatectomy for the treatment of men with localized prostate cancer: a Health Technology Assessment from the perspective of the UK National Health Service. *Eur Urol* 2013;64(3):361-69

A.77**Systematic reviews of selected nutritional supplementation interventions****Investigators**

Alison Avenell, HSRU; David Noble, John Barr, Dominic Culligan, Andy Fraser, Tom Engelhardt, Emma Metcalfe, Xueli Jia, Geraldine McNeill, Aberdeen Royal Infirmary; Diane O'Connell, Cancer Epidemiology Research Unit, Sydney, Australia; Helen Handoll, University of Edinburgh; William Gillespie, Hull York Medical School; Lesley Gillespie, University of Otago; Angela Vivanti, Princess Alexandra Hospital, Woolloongabba, Australia; Audrey Stephen, Robert Gordon University; Jan Potter, South East Sydney and Illawarra Area Hospital, Sydney, Australia; Anne Milne, Ron Koretz, UCLA, USA; Tim Lipman, Veterans Affairs Medical Center; Washington, USA, Mark Crowther, Worcester Royal Hospital, UK

Source and amount of HSRU funding (total funding)

No external funding £None

Summary

A series of systematic reviews are being undertaken, including for the Cochrane Collaboration, on the effects of nutritional supplementation on people at risk of undernutrition and obesity. Topics include vitamin D supplementation and the prevention of osteoporotic fractures, protein and energy supplementation in older people including those with hip fracture, and fish oil supplementation in critical care.

Current status

Ongoing

Key publications

Koretz, RL, Avenell, A, Lipman, TO. Nutritional support for liver disease. *Cochrane Database of Systematic Reviews* 2012, Issue 5. DOI: 10.1002/14651858.CD008344.pub2

Palmer, AJ, Ho, C, Ajibola, O, Avenell, A The role of omega-3 fatty acid supplemented parenteral nutrition in critica illness in adults: a systematic review & meta-analysis. *Crit Care Med* 2013;41(1):307-16

Metcalfe, EL, Avenell, A, Fraser, A Branched chain amino acid supplementation in adults with cirrhosis and porto-systemic encephalopathy: systematic review. *Clin Nutr* 2014;33(6):958-65

Avenell, A, Mak, JCS, O'Connell, DL. Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. *Cochrane Database of Systematic Reviews* 2014, Issue 4. DOI: 10.1002/14651858.CD000227.pub4

Witham, M, Band, M, Littleford, R, Avenell, A, Soiza, RL, McMurdo, MET, Sumukadas, D, Ogston, S, Lamb, E, Hampson, G Does oral sodium bicarbonate therapy improve function and quality of life in older patients with chronic kidney disease and low-grade acidosis (the BiCARB trial)? Study protocol for a randomized controlled trial. *Trials* 2015;16:326

Avenell, A, Smith, TO, Curtain, JP, Mak, JCS, Myint, PK. Nutritional supplementation for hip fracture aftercare in older people. *Cochrane Database of Systematic Reviews* 2016, Issue 11. DOI: 10.1002/14651858.CD001880.pub6

Bolland, M, Avenell, A, Gamble, GD, Grey, A Systematic review and statistical analysis of the integrity of 33 randomized controlled trials. *Neurology* 2016;87(23):2391-402



Bolland, M, Avenell, A, Grey, A Should adults take vitamin D supplements to prevent disease? *BMJ* 2016;355:i6201 doi: 10.1136/bmj.i6201

Bolland, M, Avenell, A Do vitamin D supplements help prevent respiratory tract infections? *BMJ* 2017;356:j456 doi: 10.1136/bmj.j456

A.78**The clinical and cost effectiveness of surgical interventions for stones in the lower calyx of the kidney: The PUrE Randomised Controlled Trial****Investigators**

Graeme MacLennan, Kirsty Shearer, Graham Scotland, Ruth Thomas, HSRU; Sam McClinton, NHS Grampian, Thomas Boon Lam, Rodolfo Hernandez, University of Aberdeen; Oliver Wiseman Addenbrooke's NHS Trust, Daron Smith, University College London Hospital; Ken Anson, St George's Healthcare NHS Trust; Ben Turney, Oxford University Hospitals NHS Trust

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £1,877,149 (£1,839,269)

Summary

PUrE is a research study collecting information on the different ways of treating lower pole kidney stones. PUrE stands for the Percutaneous nephrolithotomy, flexible Ureterorenoscopy and Extracorporeal shockwave lithotripsy for lower pole kidney stone.

Currently within the NHS there are three treatment options for lower pole calyceal stones: extracorporeal shockwave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), and flexible ureterorenoscopy with laser lithotripsy (FURS). The aim of the PUrE study is to determine the clinical effectiveness and cost effectiveness of using FURS compared to ESWL or PCNL.

PUrE is a multi-centre randomised trial, funded by the NIHR HTA Programme. It will recruit 1044 participants over 34 months. Participants with stones <10mm will be eligible for RCT1 (ESWL vs FURS) and those with stones >10 mm to <25 mm for RCT (FURS vs PCNL) with 522 participants recruited to each RCT.

PUrE is led by Prof Sam McClinton of Aberdeen Royal Infirmary

Current status

Ongoing

Publications and presentations

None

A.79**The clinical and cost-effectiveness of Elucigene FH20 and LIPOchip for the diagnosis of familial hypercholesterolaemia: systematic review and economic evaluation****Investigators**

Craig Ramsay, Miriam Brazzelli, Marion Campbell, Graham Scotland, HSRU; Ewen Cummins, McMasters Development Consultants

Source and amount of HSRU funding (total funding)

NIHR £None – Please refer to A.8

Summary

This NIHR HTA-funded project aimed to determine i) the diagnostic accuracy, ii) the effect on patient outcomes and iii) the cost-effectiveness of Elucigene FH20 and LIPOchip as standalone tests or in combination with other tests for the diagnosis of familial hypercholesterolaemia (FH) in adults and children with a clinical diagnosis of definite or possible FH. The diagnostic accuracy of Elucigene FH20 and LIPOchip was compared with LDL-C concentration measurement against comprehensive genetic analysis (CGA) combined with clinical criteria. An economic model was constructed to assess the cost-effectiveness of alternative diagnostic strategies for the confirmation of clinically diagnosed FH in index cases and for the identification and subsequent testing of first-, second- and possibly third-degree biological relatives of the index case. Based on the results of this diagnostic assessment, NICE released diagnostics guidance in December 2011 (DG2) not recommending the use of Elucigene FH20 and LIPOchip for the diagnosis of FH and the cascade testing of relatives. The guidance was subsequently withdrawn as both diagnostic tests were no longer commercially available.

<https://www.nice.org.uk/guidance/dg2>

Current status

Completed

Key publications

Sharma, P, Boyers, D, Boachie, C, Stewart, F, Miedzybrodzka, Z, Simpson, W, McNamee, P, Mowatt, G. Elucigene FH20 and LIPOchip for the diagnosis of familial hypercholesterolaemia: a systematic review and economic evaluation. *Health Technol Assess* 2012;16(17)

Oral presentations

Boyers, D, Sharma, P, Kilonzo, M, Boachie, C, Stewart, F, Miedzybrodzka, Z, Simpson, W, Mowatt, G. Cost-effectiveness of diagnostic strategies for familial hypercholesterolaemia (FH). *Health Technology Assessment International (HTAi), Annual Meeting, Bilbao, 23-27 June 2012*

A.80**The Effectiveness and cost-effectiveness of Surgical Treatments for womEn with stRes urinary incontinence: an evidence synthesis (ESTER)****Investigators**

Graeme MacLennan, Miriam Brazzelli, Charis Glazener, HSRU; Dawn Craig, Eoin Moloney, Prof Eileen Kaner, Fiona Airey, Newcastle University; Dr Lucy Saraswat, NHS Grampian; Ash Monga, University Hospital Southampton NHS Foundation Trust

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £162,167 (£295,516)

Summary

This NIHR HTA-funded project will assess the current evidence for the clinical effectiveness, safety and cost-effectiveness of surgical treatments for stress and stress-predominant urinary incontinence in women. Current network meta-analysis methodology will be used to combine direct and indirect evidence in order to estimate treatment effects for surgical treatments where no direct head-to-head clinical trials have been conducted. This analysis will provide relative treatment effects for the surgical techniques under assessment. In addition, a model based economic evaluation will be conducted to estimate the cost-effectiveness of alternative surgical treatments and to undertake a value of information analysis. The results of this project will enable decision-makers to identify which type of surgery for stress urinary incontinence is most clinically effective, safest, and cost-effective for the NHS. The value of information analysis will be used to quantify the main uncertainties with regard to policy decision-making as well as quantify the value of undertaking further research.

<https://www.journalslibrary.nihr.ac.uk/programmes/hta/150906/#/>

Current status

Ongoing

Publications and presentations

None

A.81**The United Kingdom Rotator Cuff Trial (UKUFF)****Investigators**

Craig Ramsay, John Norrie, Marion Campbell, HSRU; Prof A Carr, Prof R Fitzpatrick, Prof A Gray, Dr J Dawson, University of Oxford

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £644,944 (£1,937,992)

Summary

The UKUFF trial (funded by the NIHR Health Technology Assessment Programme) is a multi-centre randomised controlled trial to measure the clinical and cost effectiveness of different types of management of rotator cuff repairs. The Nuffield Department of Orthopaedic Surgery (NDOS) at the University of Oxford co-ordinates the trial in collaboration with CHaRT.

The rotator cuff is a group of muscles that control movements within the shoulder. Tears of the rotator cuff are one of the most common causes of shoulder pain and dysfunction. The clinical evidence available regarding the natural history and the treatment of rotator cuff tears is limited and conflicting. The UKUFF trial (funded by the NIHR Health Technology Assessment Programme) was a multi-centre randomised controlled trial to measure the clinical and cost effectiveness of different types of management of rotator cuff repairs. In early 2010 the UKUFF trial was reconfigured to compare the effectiveness of arthroscopic repair (where the tear is repaired through key-hole surgery) against open repair of the rotator cuff (involving a longer skin incision to undertake the procedure under direct vision). The primary outcome was Oxford Shoulder Score (OSS), two years post-surgery.

The mean OSS improved in both groups. At two years, there was no statistically significant difference in OSS between the groups (difference -0.76; 95% confidence interval -2.75 to 1.22; $p=0.452$). Rates of re-tear were high in both groups; but there was no statistically significant difference between groups. Use and cost of resources were similar between arthroscopic and open management in the trial; as was quality of life. There was uncertainty about which strategy was most cost-effective.

Current status

Completed

Key publications

Carr, AJ, Cooper, CD, Campbell, MK, Rees, JL, Moser, J, Beard, DJ, Fitzpatrick, R, Gray, A, Dawson, J, Murphy, J, Bruhn, H, Cooper, D, Ramsay, C The clinical and cost-effectiveness of arthroscopic versus open surgical repair for tears of the rotator cuff (UKUFF trial). *Health Technol Assess* 2015;19:80

Murphy, J, Gray, A, Cooper, C, Cooper, D, Ramsay, C, Carr, A Costs, quality of life and cost-effectiveness of open and arthroscopic repair for rotator cuff tears: economic evaluation alongside the UKUFF trial. *Bone Joint J* 2016;98-B(12):1648-55

Carr, A, Cooper, CD, Campbell, M, Rees, J, Moser, J, Beard, D, Fitzpatrick, R, Gray, A, Dawson, J, Murphy, J, Bruhn, H, Cooper, D, Ramsay, C Effectiveness of open and arthroscopic rotator cuff repair (UKUFF): a randomized controlled trial. *J Bone Joint Surg* 2017;99-B(1):107-15

A.82**UK TAVI: The United Kingdom Transcatheter Aortic Valve Implantation Trial (UK TAVI)****Investigators**

Mark Forrest, Gladys McPherson, HSRU; Dr William Toff (University of Leicester), Prof Doug Altman & Prof Alastair Gray (Oxford)

Source and amount of HSRU funding (total funding)

NIHR HTA £125,582 (£2,691,954)

Summary

Aortic stenosis is a narrowing of the valve through which blood flows as it leaves the heart, and affects 13% of people over the age of 70 years. The only effective conventional treatment is surgical replacement of the valve, which involves open chest surgery and temporarily stopping the heart, with use of a heart-lung machine. Surgical results are generally excellent but the elderly often have other medical problems that may result in an increased risk of death and complications. Transcatheter Aortic Valve Implantation (TAVI) is a recently developed technique to implant an artificial aortic valve without major surgery, using a catheter to deliver the valve to the heart through the arteries, which are usually accessed by puncturing the skin in the groin.

UK TAVI is a multi-centre randomised controlled trial, funded by the NIHR HTA Programme. The UK TAVI trial will assess the clinical effectiveness and cost-utility of TAVI, compared with conventional surgical aortic valve replacement, in patients with severe symptomatic aortic stenosis, who are at intermediate or high operative risk.

UK TAVI will randomise 808 participants over 3 years.

The primary outcome is all cause mortality at 1 year.

The trial is led by Dr William Toff based at the University of Leicester.

Current status

Ongoing

Publications and presentations

None

A.83**Theophylline with inhaled corticosteroids (TWICS)****Investigators**

Graeme MacLennan, Sarah Cameron, HSRU; Graham Devereux, David Price, John Haughney, Amanda Lee, University of Aberdeen; Peter Barnes, Imperial College London, Andy Briggs, University of Glasgow; Chaudhuri Rekha, NHS Greater Glasgow and Clyde; Chrystyn Henry, University of Huddersfield; Lisa Davies, Aintree Hospitals NHS Trust; Anthony De Soyza, Newcastle University; Alyn Morice, University of Hull; Anita Sullivan, University Hospitals Birmingham NHS Foundation Trust; Andrew Wilson, University of East Anglia

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £1,819,363 (£2,248,495)

Summary

Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung disease characterised by progressive airflow limitation. It affects approximately 1 million people in the UK, is the fifth leading cause of death in the UK and costs the NHS approximately £1 billion annually. Exacerbations of COPD account for 60% of NHS COPD costs and are associated with accelerated rate of lung function decline, reduced physical activity, reduced quality of life, increased mortality and increased risk of comorbidities such as acute myocardial infarction and stroke. Current treatment includes inhaled corticosteroids, usually in combination with inhaled LABA to reduce exacerbation rates and improve lung function. However the COPD airway inflammation is relatively insensitive to the anti-inflammatory effects of ICS and even high doses fail to prevent exacerbations. It has been observed that the reduced HDAC2 activity of COPD can be reversed in a dose-dependent manner by theophylline at 'low' concentrations.

The TWICS trial, funded by the NIHR HTA programme, is a national, multi-centre randomised controlled trial which aims to determine the clinical effectiveness and cost-effectiveness of adding low dose theophylline (Uniphyllin MR 200mg od or bd [depending on smoking status and ideal body weight]) to inhaled corticosteroid therapy in patients with COPD and a history of exacerbations. 1424 participants will be recruited, half from primary care. Patients will be randomised to low-dose theophylline or placebo for one year. The primary clinical outcome is the number of participant reported COPD exacerbations necessitating a change in management (minimum change treatment with antibiotics and/or oral corticosteroids) during the one year treatment period.

Recruitment to the trial is now complete and follow-up is ongoing.

Current status

Ongoing

Key publications

Devereux, G, Cotton, S, Barnes, P, Briggs, A, Burns, G, Chaudhuri, R, Chrystyn, H, Davies, L, DeSoyza, A, Fielding, S, Gompertz, S, McCormack, K, McPherson, G, Morice, A, Norrie, J, Sullivan, A, Wilson, A, Price, D Use of low-dose oral theophylline as an adjunct to inhaled corticosteroids in preventing exacerbations of chronic obstructive pulmonary disease: study protocol for a randomised controlled trial. *Trials* 2015;16:267

A.84**Therapeutic Interventions for Stones of the Ureter (TISU)****Investigators**

Graeme MacLennan, Ruth Thomas, HSRU; Sam McClinton, NHS Grampian; James N'Dow, AUU, University of Aberdeen; Mary Kilonzo, HERU, University of Aberdeen; Frank Keeley, Southmead Hospital, Bristol; Ken Anson, St Georges NHS Trust, London; Rob Pickard, Newcastle University

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £1,469,618 (£1,489,056)

Summary

Urinary stone disease is very common with an estimated prevalence among the general population of 2–3% (1.8 million people in the UK) and is a major burden on the NHS. Urinary tract stones, and ureteric stones, in particular, are associated with severe pain as they pass through the urinary tract and can have a significant impact on patients' quality of life due to the detrimental effect on their ability to work and the need for hospitalisation. Between a fifth and a third of cases require an active intervention (stone removal) because of failure to pass the stone, continuing pain, infection or obstruction to urine drainage. The two standard active intervention options are extracorporeal shockwave lithotripsy (ESWL) and ureteroscopic stone retrieval

TISU is a multicentre randomised controlled trial, funded by the NIHR HTA Programme, of ESWL as first treatment option compared with direct progression to ureteroscopic treatment for ureteric stones. The clinical and cost-effectiveness of ESWL, as the first treatment option compared with ureteroscopic treatment will be determined with respect to the primary outcomes of:

1. clinical stone clearance, defined as no further intervention required to facilitate stone passage
2. incremental cost per quality adjusted life years (QALYs) and
3. disease or treatment-related harms up to 6 months after randomisation.

TISU recruited 613 participants.

Adults (≥ 16 years old), presenting with a unilateral ureteric stone within any segment of the ureter, confirmed by computed tomography scan of the kidneys, ureters, and bladder (CTKUB), are recruited into the trial and participants were randomised to one of the treatment options.

The TISU trial is led by Professor Sam McClinton based at the University of Aberdeen.

Current status

Ongoing

Key publications

Skea, Z, Treweek, S, Gillies, K "It's trying to manage the work": A qualitative evaluation of recruitment processes within a UK multi-centre trial. *BMJ Open* 2017;7(8): e016475

A.85**Total or Partial Knee Arthroplasty Trial (TOPKAT)****Investigators**

Marion Campbell, Joanne Coyle, HSRU; Dr David Beard, Prof David Murray, Dr Andrew Price, Prof Andrew Carr, Nuffield Department of Orthopaedic Surgery, University of Oxford; Dr Helen Doll, Dr Helen Campbell, Prof Ray Fitzpatrick, Department of Public Health, University of Oxford

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £397,813 (£397,813)

Summary

TOPKAT is a multicentre randomised controlled trial, funded by the NIHR HTA Programme. TOPKAT aims to compare the effectiveness and cost-effectiveness of total versus uni-compartmental knee replacement for the management of knee osteoarthritis. TOPKAT recruited 529 participants from 27 different UK orthopaedic units over a two year period. The study incorporates a standard randomised design for surgeons willing to randomise between the two interventions and an expertise-based design for surgeons who have an approach of choice.

The primary outcome is the Oxford Knee Score at five years post randomisation.

TOPKAT is led by Professor David Beard based at the University of Oxford.

Current status

Ongoing

Key publications and presentations

Beard, D, Price, A, Cook, J, Fitzpatrick, R, Carr, A, Campbell, M, Doll, H, Campbell, H, Arden, N, Cooper, C, Davies, L, Murray, D Total or Partial Knee Arthroplasty Trial - TOPKAT: study protocol for a randomised controlled trial. *Trials* 2013;14:292

Beard, D, Price, A, Davies, L, Cook, J, MacLennan, GS, Campbell, M, Carr, A, Fitzpatrick, R, Murray, D Early adverse events and complications following total and partial knee replacement: results from the TOPKAT randomised controlled trial. *Bone & Joint Journal* 2017 (submitted for publication)

Oral presentations

Beard, D, Price, A, Cook, J, Fitzpatrick, R, Carr, A, Campbell, H, Arden, N, Cooper, C, Davies, L, MacLennan, G, Murray, D. Is over recruitment to a single site problematic for surgical trials? *3rd International Clinical Trials Methodology Conference, Glasgow, 16-17 November 2015*

Beard, D, Price, A, Davies, L, Cook, J, MacLennan, G, Campbell, M, Carr, A, Fitzpatrick, R, Campbell, H, Arden, N, Doll, H. A multicentre randomised study comparing total or partial knee replacement – One year results of the TOPKAT trial. *British Association for Surgery of the Knee (BASK) Annual Spring Meeting 30-31 March 2016*

Beard, D, Price, A, Cook, J, Fitzpatrick, R, Carr, A, Campbell, M, Doll, H, Campbell, H, Arden, N, Cooper, C, Davies, L, MacLennan, G, Murray, D. Is over recruitment to a single site problematic for surgical trials? . *Society for Clinical Trials, 37th Annual Meeting Montreal, 15-18 May 2016*

Beard, D, Price, A, Cook, J, Fitzpatrick, R, Carr, A, Campbell, M, Doll, H, Campbell, H, Arden, N, Cooper, C, Davies, L, MacLennan, GM, Murray, D. What can we learn from experience? Impact of healthcare provider effects in the Total or Partial Knee Arthroplasty Trial (TOPKAT) *Society for Clinical Trials 37th Annual Meeting Montreal, 15-18 May 2016*

Beard, D, Price, A, Cook, J, MacLennan, G, Campbell, M, Davies, L, Murray, D. A multicentre randomised study comparing total or partial knee replacement - one year results of the TOPKAT trial. *17th European Society of Sports Traumatology, Knee Surgery & Arthroscopy Congress (ESSKA), Barcelona, 4-7 May 2016*

Beard, D, Price, A, Cook, J, MacLennan, G, Fitzpatrick, R, Carr, A, Campbell, M, Campbell, H, Arden, N, Cooper, C, Davies, L, Murray, D. Total or partial knee replacement: one year results from a large multicentre randomised controlled trial (TOPKAT) *European Federation of National Associations of Orthopaedics, 17th Congress, Geneva, 1-3 June 2016*

Beard, D, Price, A, Cook, J, Fitzpatrick, R, Carr, A, Campbell, M, MacLennan, G, Davies, L, Murray, D. Total or partial knee replacement for medial osteoarthritis? Early results from the TOPKAT Trial. . *International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine, 11th Congress, Shanghai, 4-8 June 2017*

A.86**Treatment of Advanced Glaucoma Study. A multicentre randomised controlled trial comparing primary medical treatment with primary augmented trabeculectomy for people with newly diagnosed advanced glaucoma (TAGS)****Investigators**

Graeme MacLennan, HSRU; Prof Anthony King, Nottingham Universities NHS Trust; Dr Jen Burr, University of St Andrews; Prof Luke Vale, Newcastle University; John Sparrow, University Hospitals Bristol NHS Foundation Trust; Keith Barton, Richard Wormald, Moorfields Eye Hospital NHS Foundation Trust; Peter Shah, Good Hope Hospital, Heart of England Foundation Trust; Ted Garway-Health, University College London, Moorfields

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £913,198 (£1,743,775)

Summary

A multi-centre randomised controlled trial, funded by the NIHR HTA Programme comparing primary medical treatment with primary augmented trabeculectomy (glaucoma surgery) for patients presenting with newly diagnosed advanced glaucoma.

The trial has a primary patient reported outcome, the vision specific health profile (NEI-VF Q25). The primary outcome will be evaluated at 24 months.

TAGS closed recruitment in May 2017 with 453 participants recruited.

TAGS is led by Professor Anthony King based at Nottingham University Hospital NHS Trust.

Current status

Ongoing

Key publications and presentations

King, A, Fernie, G, Azuara-Blanco, A, Burr, J, Garaway-Heath, D, Sparrow, J, Vale, L, Hudson, J, MacLennan, G, McDonald, A, Barton, K, Norrie, J Treatment of Advanced Glaucoma Study: a multicentre randomised controlled trial comparing primary medical treatment with primary trabeculectomy for people with newly diagnosed advanced glaucoma—study protocol. *Br J Ophthalmol* 2017;bjophthalmol-2017-310902; DOI: 10.1136/bjophthalmol-2017-02 (published ahead of print)

Oral presentations

Fernie, G. TAGS Tales: Treatment of Advanced Glaucoma Study (TAGS). *Scottish Ophthalmology Trainee Research Network Meeting, Edinburgh, 9 December 2015*

Fernie, G. Treatment of Advanced Glaucoma Study (TAGS) - the challenges of recruiting to an ophthalmic clinical trial in Scotland. *Scottish Ophthalmology Trainee Research Network Meeting, Gartnavel General Hospital, Glasgow, 23 November 2016*

A.87**Trial comparing stapled haemorrhoidopexy with traditional excisional surgery for haemorrhoidal disease (eTHoS)****Investigators**

Luke Vale, Jen Burr, Joanne Coyle, Laura Ternent, HSRU; Angus Watson, Malcom Loudon, NHS Highland; David Jayne, Leeds Teaching Hospitals NHS Trust; Andrew Maw, Glan Clwyd Hospital; Finlay Curran, Stepping Hill Hospital; Brian Buckley, National University of Ireland

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £1,312,473 (£1,341,217)

Summary

The aim of eTHoS is to establish the effectiveness and cost-effectiveness of stapled haemorrhoidopexy (SH) compared with traditional excisional haemorrhoidectomy (TH). At present there is no evidence that tells us which of these types of surgery is best for patients who have haemorrhoids that require surgery.

This multi-centre trial, funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme, will recruit 800 patients (400 to SH and 400 to TH). Patients who require surgical treatment to improve symptoms with circumferential haemorrhoids grade II, III and IV can take part.

The study will run over 72 months, with the primary outcome being patient reported overall health related quality of life over a period of two years.

Current status

Completed

Key publications

Watson, AJM, Bruhn, H, Macleod, K, McDonald, A, McPherson, G, Kilonzo, M, Norrie, J, Loudon, M, McCormack, K, Buckley, B, Brown, S, Curran, F, Jayne, D, Rajagopal, R, Burr, J, Cook, J, Group, eS A pragmatic multicentre randomised controlled trial comparing stapled haemorrhoidopexy to traditional excisional surgery for haemorrhoidal disease (eTHoS): study protocol for a randomised controlled trial. *Trials* 2014;15:439

Watson, A, Hudson, J, Wood, J, Kilonzo, M, Brown, S, McDonald, A, Norrie, J, Bruhn, H, Cook, JA Comparison of stapled haemorrhoidopexy with traditional excisional surgery for haemorrhoidal disease (eTHoS): a pragmatic, multicentre, randomised controlled trial. *Lancet* 2016;388(10058):2375-85

Kilonzo, M, Brown, S, Bruhn, H, Cook, J, Hudson, J, Watson, A, Wood, J Cost Effectiveness of Stapled Haemorrhoidopexy and Traditional Excisional Surgery for the Treatment of Haemorrhoidal Disease. *PharmacoEconomics Open* 2017 (25 August 2017)

A.88**Trial Forge: a systematic approach to making trials more efficient****Investigators**

Shaun Treweek, Moira Cruickshank, John Norrie, HSRU; Mike Clarke, Queen's Belfast; Athena Lane, Bristol; Prof of Biostatistics, Liverpool; Trudie Lang, Oxford

Source and amount of HSRU funding (total funding)

MRC £6,080 (£6,080)

Summary

Randomised trials, especially when brought together in systematic reviews, are regarded as the gold standard for evaluating the effects of healthcare treatments with thousands of trials and hundreds of systematic reviews reported every year. PubMed has indexed over 370,000 reports of randomised trials; the World Health Organisation's International Clinical Trials Registry Platform contains over 250,000 trial records, of which 71,000 are listed as recruiting; and the Cochrane Central Register of Controlled Trials contains more than 800,000 records. Tens of billions of dollars of public and private money are invested globally in trials every year (US\$25 billion in the US alone in 2010) and the average cost of recruiting a patient to a trial in the UK is estimated to be almost £8,500.

Much of these resources is wasted, often because results are not published, or are poorly reported. However, resources are also wasted because the research asks the wrong questions or is badly designed. Moreover, despite trials being a cornerstone of evidence-based healthcare, the methodology and infrastructure for conducting these complex studies is a largely evidence-free zone.

The Trial Forge initiative aims to make trials more efficient by looking for small gains across all trial processes, from research question through to reporting. It will encourage everyone connected with trials to be more sceptical of what we do by asking for the evidence behind all of our trial decisions. Where no evidence exists (as will often be the case), Trial Forge will provide a platform to highlight this gap and bring researchers and others (including funders) together so that they can fill the gap. Insights from disciplines not normally associated with trials, such as business and organisational change management, will be part of this efficiency drive.

Trial Forge is led by Shaun Treweek at the University of Aberdeen.

Daniel Shanahan of Biomed has written a blog on the first Trial Forge workshop, which is available at <http://blogs.biomedcentral.com/on-medicine/2014/07/15/wheres-the-evidence-for-how-we-run-clinical-trials/>.

Further details on Trial Forge are available at <http://www.trialforge.org>.

Current status

Ongoing

Key publications

Bower, P, Brueton, V, Treweek, S, Tudur Smith, C, Young, B, Williamson, P Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. *Trials* 2014;15:399

Treweek, S, Altman, D, Bower, P, Campbell, M, Chalmers, I, Cotton, S, Craig, P, Crosby, D, Davidson, P, Loudon, K, McDonald, A, Norrie, J, Ramsay, CR Making randomised trials more efficient: report of the first meeting to discuss the Trial Forge platform. *Trials* 2015;16:261

Gardner, H, Fraser, C, MacLennan, G, Treweek, S A protocol for a systematic review of non-randomised evaluations of strategies to improve participant recruitment to randomised controlled trials. *Syst Rev* 2016;5:131

Bandholm, T, Christensen, R, Thorborg, K, Treweek, S, Henriksen, M Preparing for what the reporting checklists will not tell you: the PREPARE Trial guide for planning clinical research to avoid research waste. *Br J Sports Med* 2017 (in press)

Houghton C, Dowling M, Meskell P, Hunter A, Gardner H, Conway A, Treweek S, Sutcliffe K, Noyes J, Devane D, Nicholas JR, Biesty LM. Factors that impact on recruitment to randomised trials in health care: a qualitative evidence synthesis (Protocol). *Cochrane Database of Systematic Reviews* 2017, Issue 5. Art. No.: MR000045. DOI: 10.1002/14651858.MR000045.

Conway A, Clarke MJ, Treweek S, Schünemann H, Santesso N, Morgan RL, Darragh M, Maguire LK, Devane D. Summary of findings tables for communicating key findings of systematic reviews. *Cochrane Database of Systematic Reviews* 2017, Issue 2. Art. No.: MR000044. DOI: 10.1002/14651858.MR000044.

A.89**Use of drug therapy in the management of symptomatic ureteric stones in hospitalised adults: a multicentre placebo controlled randomised trial of calcium channel blockers (nifedipine) and alpha blockers (tamsulosin) (SUSPEND)****Investigators**

Graeme MacLennan, Jen Burr, Ruth Thomas, Kirsty Shearer, HSRU; Sam McClinton, Urology, NHS Grampian; Prof James N'Dow, Urology, University of Aberdeen; Kathryn McMullan, Thomas Lam, NHS Grampian; Neil Burgess, Norfolk & Norwich UHT; Ken Anderson, St George's NHS Trust London; Prof Glenn Preminger, Duke University Medical Centre, USA; Rob Pickard, Newcastle University; Dr Uday Patel, The Princess Grace Hospital London

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £950,808 (£1,585,180)

Summary

Use of drug therapy in the management of symptomatic ureteric stones in hospitalised adults: a multicentre placebo controlled randomised trial of a calcium channel blocker (nifedipine) and an alpha-blocker (tamsulosin).

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. Given the pain experienced passing a ureteric stone and the high cost of having to remove them, any simple treatment that hastens or increases the chance of spontaneous stone passage would be welcomed by both patients and the NHS.

The aim of this trial was to determine the clinical and cost-effectiveness of the use of alpha blockers (tamsulosin) and calcium channel blockers (nifedipine) in the management of symptomatic urinary stones. The primary clinical outcome of the trial (measured at four weeks) was the spontaneous passage of the stone as measured by the need for further intervention in the treatment of the stone. To reflect the multidimensional nature of the possible effects the intervention may have there was also a primary health economic outcome of incremental cost per quality adjusted life years (QALYs) gained at 12.

This multi-centre trial, funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme, recruited 1200 participants over 24 months who were deemed suitable for conservative management (randomising 400 to each of the three treatment groups; alpha blockers, calcium channel blockers and placebo).

Current status

Completed

Key publications

McClinton, S, Starr, K, Thomas, R, MacLennan, G, McPherson, G, McDonald, A, Lam, T, N'Dow, J, Kilonzo, M, Pickard, R, Anson, K, Burr, J Use of drug therapy in the management of symptomatic ureteric stones in hospitalised adults (SUSPEND a multicentre, placebo controlled, randomised trial of a calcium channel blocker (nifedipine) and an alpha-blocker (tamsulosin). Study protocol for a randomised controlled trial. *Trials* 2014;15:238

Pickard, R, Starr, K, MacLennan, G, Kilonzo, M, Lam, T, Thomas, R, Burr, J, Norrie, J, McPherson, G, McDonald, A, Shearer, K, Gillies, K, Anson, K, Boachie, C, N'Dow, J, Burgess, N, Clark, T, Cameron, S, McClinton, S Use of drug therapy in the management of symptomatic ureteric stones in hospitalised adults: a multicentre, placebo-controlled, randomised controlled trial and cost-effectiveness analysis of a calcium channel blocker (nifedipine) and an alpha-blocker (tamsulosin) (the SUSPEND trial). *Health Technol Assess* 2015;19(63)

Pickard, R, Starr, K, MacLennan, G, Lam, T, Thomas, R, Burr, J, McPherson, G, McDonald, A, Anson, K, N'Dow, J, Burgess, N, Clark, T, Kilonzo, M, Gillies, K, Shearer, K, Boachie, C, Cameron, S, Norrie, J, McClinton, S Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. *Lancet* 2015;386(9991):341-49

Starr, K, McPherson, G, Forrest, M, Cotton, S SMS text pre-notification and delivery of reminder e-mails to increase response rates to postal questionnaires in the SUSPEND trial: a factorial design, randomised controlled trial. *Trials* 2015;16:295

A.90**Vault or Uterine prolapse surgery Evaluation (VUE)****Investigators**

Graeme MacLennan, Alison McDonald, Charis Glazener, Lynda Constable, Suzanne Breeman, HSRU; Mary Kilonzo, Anthony Smith, Central Manchester University Hospital; Christine Hemming, Kevin Cooper, NHS Grampian; Robert Freeman, NHS Plymouth, Suzanne Hagen, Andy Elders, Glasgow Caledonian University; Isobel Montgomery, Lay Representative

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £316,415, (£325,927)

Summary

Vault or Uterine prolapse surgery evaluation: Two parallel randomised controlled trials of surgical options for upper compartment (vault or uterine) pelvic organ prolapse (VUE).

Around one in ten women will need prolapse surgery at some point in their lives. Prolapse occurs when the pelvic organs (such as the bladder, the bowel or the 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. There are many different operations for prolapse and there is a high failure rate after surgery. There is not enough evidence to identify which operation is best for these two types of prolapse.

VUE is a multicentre randomised controlled trial, funded by the NIHR HTA programme.

The VUE trial aims to compare surgeries for uterine or vault prolapse to one of two trials:

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

VUE will randomise 910 women (630 in the Uterine Trial and 280 in the Vault trial) over 3 years.

The primary clinical outcome is women's prolapse symptoms measured using the Pelvic Organ Prolapse Symptom Scale (POP-SS), at one year after surgery.

The VUE trial is led by Dr Christine Hemming based at NHS Grampian and closed to recruitment in November 2016.

Current status

Ongoing

Key publications

Glazener, C, Constable, L, Hemming, C, Breeman, S, Elders, A, Cooper, K, Freeman, RF, Smith, A, Hagen, S, McDonald, A, McPherson, G, Montgomery, I, Kilonzo, M, Boyers, D, Goulao, B, Norrie, J Two parallel, pragmatic, UK multicentre, randomised controlled trials comparing surgical options for upper compartment (vault or uterine) pelvic organ prolapse (the VUE Study): study protocol for a randomised controlled trial *Trials* 2016;17:441

A.91**What is the best way to avoid recruitment and retention problems in trials?****Investigators****Adel El Feky, Shaun Treweek, Katie Gillies, HSRU****Source and amount of HSRU funding (total funding)**

No external funding £None

Summary**Background**

Many trials struggle to recruit and retain participants and recruitment and retention are the top two priorities for methodology research. There is still little evidence available to support the development of effective recruitment and retention strategies.

Feasibility and pilot work is common before a full-scale trial but there are rarely clear descriptions of recruitment and retention strategies, success/failure thresholds are often absent, nor are there clear assessments of the generalisability limits of feasibility and pilot studies for any future trial. The link between pilot work and successful recruitment and retention remains ambiguous.

The PhD proposal

The PhD proposal is divided into three phases:

1. **Phase 1:** Systematic review and meta-synthesis of qualitative research undertaken to improve retention and recruitment to trials at the feasibility stage. This will provide a framework for trialists regarding the ways qualitative research can help to ensure that recruitment and retention processes are efficient, more transferable to other trials, easier to adapt in light of ongoing recruitment and retention and generally improved.
2. **Phase 2:** Stakeholder involvement through surveys and in-depth interviews to explore their experiences of running feasibility studies, particularly with regard to recruitment and retention. Brief questionnaires and semi-structured interviews will be conducted to explore how teamwork influences recruitment and retention in trials. Participants will be purposefully selected to maximize variation in views and experiences, as well as trial setting, intervention type and disease.
3. **Phase 3:** Packaging the results of Phases 1 and 2 into a form that trialists and others can easily fit into their work. In particular, the specification of a new type of document, the recruitment and retention plan, equivalent in status to the statistical analysis plan. These information packages would be evaluated together with trialists and trial team members based at selected UK Trials Units.

Current status

Ongoing

Key publications

Brazzelli, M, Cruickshank, M, Tassie, E, McNamee, P, Robertson, C, Elders, A, Fraser, C, Hernandez, R, Lawrie, D, Ramsay, CR Collagenase clostridium histolyticum for the treatment of Dupuytren's contracture: systematic review and economic evaluation *Health Technol Assess* 2015;19(90)

A.92**What types of urethral catheter are more effective at reducing symptomatic urinary tract infections in hospitalised adults requiring short-term catheterisation (Catheter)****Investigators**

Adrian Grant, Charis Glazener, Luke Vale, John Norrie, HSRU; James N'Dow, Dept of Surgery, University of Aberdeen; Robert Pickard, University of Newcastle upon Tyne; Dr K Orr, Newcastle NHS Trust; Brian Buckley, National University of Ireland; Thomas Lam, NHS Grampian

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £282,969 (£1,582,036)

Summary

Approximately 25% of patients admitted to hospital will require urethral catheterisation at some stage during their stay. Catheter-associated symptomatic urinary tract infections (CAUTI) are the leading cause of hospital acquired infections, accounting for between 23% and 40% of all cases. Such infections result in additional morbidity and mortality and represent a considerable economic burden to the health care sector, patients and their carers.

The CATHETER Trial was a multicentre UK trial which aimed to establish the clinical benefits and cost-effectiveness of using antibiotic- (nitrofurazone) or antiseptic- (silver) impregnated urethral catheters over standard urethral catheters in hospitalised adults requiring short term (≤ 14 days) catheterisation. The trial recruited 7102 participants from 24 UK centres.

The study concluded that silver alloy-coated catheters are unlikely to be effective at reducing CAUTI. Nitrofurazone catheters were also ineffective against CAUTI, but did show some antimicrobial activity for secondary bacteriological outcomes. However, any benefit may be offset by increased discomfort from their use and concerns regarding indiscriminate antimicrobial use.

Current status

Completed

Publications and presentations

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. (2012). 'Antimicrobial catheters for reduction of symptomatic urinary tract infection in adults requiring short-term catheterisation in hospital: a multicentre randomised controlled trial'. *The lancet*, vol 380, no. 9857, pp. 1927-1935

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. (2012). '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 Technology Assessment*, vol 16, no. 47, pp. 1-197

APPENDIX 1

HSRU PROJECTS

IMPROVING EXPERIENCES OF CARE PROJECTS

B.1

A meta-ethnographic synthesis of studies reporting participant reasons for clinical drop-out

Investigators

Katie Gillies, HSRU

Source and amount of HSRU funding (total funding)

ISSF Women Returners Scheme/Wellcome Trust £18,016 (£18,016)

Summary

Background

Randomised controlled trials are integral for evidenced based clinical decision making. Within the context of clinical trials, the focus of much methodological research has been on issues relating to trial recruitment. Issues around retention (i.e. ensuring that trial participants remain in the trial to provide primary outcome data) have not received equal scrutiny in the literature despite being arguably just as important for trials in terms of ensuring that research questions are adequately answered.

The aim of this study was to undertake a meta-ethnographic synthesis of findings from primary qualitative studies that explored factors influencing non-retention within a clinical trial context.

Findings

We identified 8 qualitative studies (reporting data from 9 trials). Emergent from our synthesis was the significance of trial non-retainers' perceptions around the personal 'fit' of key aspects of the trial with their pre-existing beliefs or life circumstances. These beliefs or circumstances related to their own health state, preferences for how they wanted to receive care, their individual capabilities, beliefs about or experiences of side effects, and also considerations around the extent to which trial participation could be appropriately accommodated (or not) into their broader lives.

If trialists want to improve retention then they should focus on attempts to reduce trial burden, both in terms of the intervention itself and also the ways that follow up data is collected. Providing more detail on the nature of the trial interventions at the consenting stage would prove helpful in order to manage expectations and some early and meaningful patient/public involvement could be particularly important for ensuring that aspects of the trial are user-friendly and as compatible as possible with the target population's likely preferences and capabilities.

Current status

Completed

Key publications

Skea, Z, Newlands, R, Gillies, K What influences non-retention in clinical trials? A meta-ethnographic synthesis of studies reporting participant reasons for drop out. *PLoS Med* 2017 (submitted for publication)

B.2**Achieving Self-directed Integrated Cancer Aftercare (ASICA)****Investigators**

Graeme MacLennan, HSRU; Peter Murchie, Amanda Lee, Judith Mastoff, Julia Allen and Marie Johnston, University of Aberdeen

Source and amount of HSRU funding (total funding)

Cancer Research UK £322,352 (£747,337)

Summary

The ASICA (Achieving Self-directed Integrated Cancer Aftercare) digital intervention supports high quality total skin self-examination (TSSE) by people with cutaneous melanoma, and appropriate clinical responses when they raise a concern. It is rigorously developed, digitally-supported and theoretically-based app, using specified behaviour-change techniques to prompt users to perform regular TSSE. By enabling prompt recognition and treatment of recurrent and new primary melanomas, ASICA may enable earlier treatment and improved outcomes for patients and the NHS.

The ASICA study, funded by Cancer Research UK, is a two-arm, open multi-centre randomised controlled trial (RCT) comparing a digital intervention to increase TSSE by people treated for melanoma with usual follow-up in 240 participants.

The primary outcome is the impact of receiving ASICA on Melanoma Worry Scale, anxiety and depression (HADS) and quality of life (EQ-5D) up to 12 months following randomisation.

The ASICA study is led by Dr Peter Murchie based at the University of Aberdeen.

Current status

Ongoing

Publications and presentations

None

B.3

ActWELL

Investigators

Shaun Treweek, HSRU; Annie Anderson (CI), Angela Craigie, University of Dundee; Nanette Mutrie, University of Edinburgh; Ronan O'Carroll, Martien Stead, Stirling University; Jane Macaskill, Ninewells Hospital; Aileen Neilson, HERU; Chloe McAdam, University of Edinburgh; Naveed Sataar, University of Glasgow

Source and amount of HSRU funding (total funding)

Scottish Government £74,714 (£969,265)

Summary

Current evidence suggests that breast cancer risk can be decreased by about 30% through lifestyle choices <https://www.wcrf-uk.org/uk/preventing-cancer/cancer-types/breast-cancer>. The most important factors are managing body weight through decreasing calories from food and drink and being physically active. However, it can be difficult to make changes to everyday life and sometimes a little support is needed.

The ActWELL lifestyle programme was developed and pilot tested in Scotland. Now we need to test if the lifestyle programme can be effective in helping women achieve weight loss and increase physical activity.

During the trial period (starting in July 2017) all women attending routine NHS Breast Screening clinics in Grampian, Tayside, Lothian and Greater Glasgow and Clyde are being offered the chance to hear more about the ActWELL study. Women who sign up for the trial will be asked to attend an assessment visit for measurements, questionnaires and blood samples. Women will then be placed in either the intervention or control group at random.

Those randomised to the intervention group will receive the ActWELL programme. This comprises two face to face sessions with a lifestyle coach from the charity Breast Cancer Now and up to 9 support telephone contacts over a year. Women randomised to the control group will be provided with written guidance on weight loss, then offered a personalised session with a lifestyle coach after the 12 month measurements are completed.

At the end of the study women will be invited for another assessment visit in order to measure differences after the 12 month period.

The study is being carried out by the Universities of Dundee, Aberdeen, Glasgow, Edinburgh and Stirling and is funded by the Scottish Government.

Current status

Ongoing

Key publications

Anderson, AS, Macleod, N, Mutrie, N, Sugden, J, Dobson, H, Treweek, S, O'Carroll, R, Thomson, A, Kirk, A, Brennan, G, Wyke, S Breast cancer risk reduction - is it feasible to initiate a randomised control trial of a lifestyle intervention programme (ActWell) within a national breast screening programme? *Int J Behav Nutr Phys Act* 2014;11:156

B.4

Benefits of incentives for breastfeeding and smoking cessation in pregnancy (BIBS): A mixed methods study to inform trial design

Investigators

Marion Campbell, Pat Hoddinott, HSRU; Prof Anne Ludbrook, HERU, UoA; Prof Linda Bauld, Stirling University; Dr Falko Sniehotta, Newcastle University; Prof Fiona Dykes, University of Central Lancashire; Dr David Tappin, University of Glasgow

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £242,034 (£316,807)

Summary

The aim of this research is to try and find out which incentives (financial or non-financial), if any, are most likely to help women to stop smoking in pregnancy (and not restart) and to breastfeed their babies until 6 months, to benefit the health of both mothers and babies. There are three stages to BIBS:

Stage 1. We will synthesize the evidence for incentives delivered to women, families and NHS or non NHS providers and their associated theories of behaviour change, using focused research questions to inform the design of a trial. This will produce: i) evidence synthesis reports ii) a taxonomy of incentive characteristics, behaviour change theory, mechanisms of action and the barriers/facilitators to stopping smoking in pregnancy and breastfeeding iii) a short list of promising incentives.

Stage 2. For the incentive short-list we will investigate recipient, provider and public acceptability and any unintended effects. Mixed method data will refine the incentive characteristics, timing, quantity, delivery processes, recipient monitoring, organisational, environmental and contextual factors that are likely to increase effectiveness.

Stage 3. A Discrete Choice Experiment will refine the most promising intervention(s) to trial. The DCE will identify the relative probabilities of behaviour change for different types and level of incentive intervention and inform effect sizes. If probabilities vary across individuals with different characteristics, and affect outcomes, then a range of incentives may be more effective than a 'one-size-fits-all' approach. Combining all aspects of this study will enable us to define a trial intervention, recruitment and delivery strategies, provide a sample size calculation, model effect sizes and define outcome measurements. This will inform the design of a trial. For more information see: <http://www.nets.nihr.ac.uk/projects/hta/103102>

Current status

Completed

Key publications

Thomson, G, Dykes, F, Hurley, M, Hoddinott, P Incentives as connectors: perceptions of women and peer supporters participating in a breastfeeding incentive intervention in a disadvantaged area of North West England. *BMC Pregnancy Childbirth* 2012;12(22):29 March 2012

Hoddinott, P, Morgan, HM, MacLennan, GS, Sewel, K, Thomson, G, Bauld, L, Yi, D, Ludbrook, A, Campbell, MK Public acceptability of financial incentives for smoking cessation in pregnancy and breastfeeding. *BMJ Open* 2014;4(7):e005524

Thomson, G, Morgan, HM, Crossland, N, Bauld, L, Dykes, F, Hoddinott, P Unintended consequences of incentive provision for behaviour change and maintenance around childbirth. *PLoS One* 2014;9:10

Crossland, N, Thomson, G, Morgan, HM, Dombrowski, S, Hoddinott, P Incentives for breastfeeding and for smoking cessation in pregnancy: An exploration of types and meanings. *Soc Sci Med* 2015;128:10-17

Hoddinott, P, Thomson, G, Morgan, HM, Crossland, N, MacLennan, G, Dykes, F, Stewart, F, Bauld, L, Campbell, MK Perspectives on financial incentives to health service providers for increasing breastfeeding and smoking quit rates during pregnancy: a mixed methods study *BMJ Open* 2015;5(11):e008492

Moran, VH, Morgan, HM, Rothnie, K, MacLennan, G, Stewart, F, Thomson, G, Crossland, N, Tappin, D, Campbell, MK, Hoddinott, P Incentives to promote breastfeeding: a systematic review. *Pediatrics* 2015;135(3):e687-e702

Morgan, HM, Hoddinott, P, Thomson, G, Crossland, N, Farrar, S, Yi, D, Hislop, J, Hall Moran, V, MacLennan, G, Dombrowski, S, Rothnie, K, Stewart, F, Bauld, L, Ludbrook, A, Dykes, F, Sniehotta, F, Tappin, D, Campbell, M Benefits of incentives for breastfeeding and smoking cessation in pregnancy (BIBS): a mixed methods study to inform trial design. *Health Technol Assess* 2015;19(30)

Crossland, N, Thomson, G, Morgan, HM, MacLennan, G, Campbell, M, Dykes, F, Hoddinott, P Breast pumps as an incentive for breastfeeding: a mixed methods study of acceptability. *Matern Child Nutr* 2016;12(4):726-39

B.5**Cochrane Effective Practice and Organisation of Care (EPOC) Review Group****Investigators**

Craig Ramsay, Jemma Hudson, HSRU

Source and amount of HSRU funding (total funding)

£None

Summary

Systematic reviews of rigorous evaluations of implementation strategies provide the best evidence on effectiveness. The Cochrane EPOC group aim to prepare and update systematic reviews of rigorous research which examine interventions to improve professional practice and the delivery of health services.

The Unit is responsible for providing statistical support to the EPOC Group and includes development of guidance on the EPOC statistical methods, risk of bias assessment, and the teaching and training of the methodologies to review authors.

Current status

Ongoing

Key publications

Higgins, JPT, Ramsay, CR, Reeves, BC, Shea, B, Valentine, J, Tugwell, P, Wells, G Issues relating to study design and risk of bias when including non-randomized studies in systematic reviews on the effects of interventions. *Res Synth Methods* 2013;4(1):12-25

Reeves, BC, Higgins, JPT, Ramsay, CR, Shea, B, Tugwell, P, Wells, G An introduction to methodological issues when including non-randomized studies in systematic reviews on the effects of interventions. *Res Synth Methods* 2013;4(1):1-11

Taljaard, M, McKenzie, JE, Ramsay, C, Grimshaw, J The use of segmented regression in analysing interrupted time series studies: an example in pre-hospital ambulance care. *Implement Sci* 2014;9:77

Sterne, J, Hernan, M, Reeves, B, Savovic, J, Berkman, N, Viswanath, AK, Henry, DA, Altman, D, Ansari, M, Boutron, I, Carpenter, JR, Chan, AW, Churchill, R, Deeks, J, Juni, P, Loke, YK, Pigott, TD, Ramsay, CR, Regidor, D, Rothstein, HR, Sandhu, L, Santaguida, PL, Schunemann, HJ, Shea, B, Shrier, I, Tugwell, P, Turner, L, Valentine, JC, Waddington, H, Waters, E, Wells, GA, Whiting, P, Higgins, J ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions. *Br Med J* 2016;355:i4919

Davey, P, Marwick, CA, Scott, CL, Charani, E, McNeil, K, Brown, E, Gould, IM, Ramsay, CR, Michie, S. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Systematic Reviews* 2017, 2. Art. No.: CD003543 DOI: 10.1002/14651858.CD003543.pub4

B.6

Concept: SSM - conceptualising support for self-management

Investigators

Vikki Entwistle, Zoë Skea, HSRU; Prof Alan Cribb, Dr John Owens, Prof Sharon Gewirtz, King's College London; Prof Ian Watt, University of York; Dr Carl Counsell, University of Aberdeen

Source and amount of HSRU funding (total funding)

The Health Foundation £156,245 (£216,432)

Summary

The study aims to develop an account of professional support for self-management that can reflect and help promote meaningfully good practice in diverse health and social care contexts. It is an exercise in practical philosophy that draws on existing literature, incorporates primary research to investigate health professionals' perspectives on success and collaboration in their work with people with long-term conditions, and uses a series of knowledge exchange events to test and refine ways of thinking and talking about the purpose and processes of support for self-management.

During the course of the project, we have:

- drawn a distinction between support oriented to enable people to manage their long-term conditions well and support oriented to enable people to manage well with their long-term conditions.
- developed an explanation of why and how approaches to support for self-management that are narrowly oriented to educate and motivate people to adopt behaviours recommended for disease control can undermine the positive ambitions of the concept.
- developed an argument that support for people with long-term conditions should be oriented towards enabling them to live (and die) well with those conditions
- outlined some theoretical advantages of using a capabilities approach to thinking about living well.

In addition, we have recognised that the idea that support for self-management should be oriented to enable people to live well with their long-term conditions makes the purpose of professional practice more open-ended and contestable than is sometimes assumed.

Our (ongoing) analysis of the interviews is also highlighting the various uncertainties and tensions that health professionals have to navigate as they strive to work with people in less than ideal circumstances in pursuit of the multiple goods that living well can encompass. It suggests a need for professional education and continuing professional development initiatives to attend more explicitly to the balancing of values inherent to person-centred support.

Current status

Ongoing

Key publications and presentations

Morgan, HM, Entwistle, V, Cribb, A, Christmas, S, Owens, J, Skea, Z, Watt, I. We need to talk about purpose: a critical interpretive synthesis of health and social care professionals' approaches to self-management support for people with long-term conditions. *Health Expect* 2017;20(2):243-59

Owens, J, Entwistle, V, Cribb, A, Skea, Z, Christmas, S, Morgan, HM, Watt, I "Was that a success or not a success?": a qualitative study of health professionals' perspectives on support for people with long-term conditions. *BMC Fam Pract* 2017;18:39

Entwistle, V, Cribb, A, Owens, J Why health and social care support for people with long-term conditions should be oriented towards enabling people to live well *Health Care Anal* 2017:DOI 10.1007/s10728-016-0335-1 (published ahead of print)

Oral presentations

Entwistle, VA. 'Support for self-management': what might this mean in cancer contexts? *SIGOPAC (British Psychological Society Special Interest Group on Psychology and Cancer) meeting, Liverpool, 6 November 2014*

Entwistle, V. Conceptualising 'support for self-management'. *Sharpening the cutting edge of bioethics in the UK, Newcastle, 18 June 2015*

Entwistle, V. Re-visioning 'support for self management'. *VELiM conversation (Centre for Values, Ethics and Law in Medicine), Sydney, 23 July 2015*

Entwistle, V. Support for self-management in diabetes: is it helping people to live well? . *NHS Grampian Diabetes MCN professional meeting, Aberdeen 23 September 2015*

Entwistle, V. Support for self-management: refreshing the concept to enhance its practical potential. . *Seminar in practical philosophy, University of Gothenberg, 14 October 2015*

Entwistle, VA, Cribb, A, Watt, I, Owens, J, Skea, Z, Morgan, HM, Christmas, S. Support for patients' self-management of their long-term conditions: re-visioning purpose and re-valuing professional practice. *International Shared Decision-Making (ISDM) / International Society for Evidence Based Health Care (ISEHC) conference, Sydney, 19-22 July 2015*

Entwistle, V. Support for self-management: refreshing the concept to enhance its practical potential. . *Centre for Population Health, Cardiff University, 2 February 2016*

Skea, Z, Entwistle, V, Owens, J, Morgan, HM, Cribb, A, Watt, I, Christmas, S. Clinicians' Experiences Of Balancing Multiple Considerations When Supporting People To 'Self-Manage. . *14th International Conference on Communication in Healthcare, University Convention Centre, Heidelberg, 7-10 September 2016*

Entwistle, V. Support for self-management among people with long-term conditions: re-formulating the concept to reflect and promote good practice. *6th OCHER workshop on Clinical Communication Research. Oslo, Norway, 11-13 January 2017*

B.7

DECIDE - Developing and evaluating communication strategies to support informed decisions and practice based on evidence

Investigators

Shaun Treweek, HSRU; Andrew Oxman, Norwegian Knowledge Centre for the Health Services; Pablo Alonso, Research Institute of the Hospital of Santa Cruce and Sant Pau; Patrick Bosssuyt, Academisch Medisch Centrum Bij De Universitat van Amsterdam; Metin Gulmezoglu, World Health Organisation; Holger Schunemann, University Hospital Freiburg; Judith Thornton, National Institute for Health and Care Excellence; Duncan Service, Healthcare Improvement Scotland; Helena Liira, Kustannus Oy Duodecim; Marina Davoli, Azienda Sanitaria Locale Roma E; Peter Donnan, University of Dundee

Source and amount of HSRU funding (total funding)

EU (FP7) £65,436 (£65,436)

Summary

The EU-funded DECIDE project (<http://www.decide-collaboration.eu>) has worked on innovative ways to present research evidence in guidelines that is specifically tailored to meet the needs of different types of user: health professionals; policymakers and managers; patients and public, people making diagnostic decisions and people making decisions about health system interventions. DECIDE has some substantial outputs:

- A multi-layered approach to presenting guideline information to health professionals was developed.
- DECIDE has contributed to new international guidance on how to produce patient versions of guidelines through a collaboration with the Guideline International Network.
- Literature reviews of grading systems for diagnostic tests and the public's attitudes to, and awareness of, guidelines have been published.
- Evidence to Decision Frameworks have been developed to support guideline panels to explicitly consider research evidence in their judgements and were tested with the World Health Organisation guideline panels and others.
- A DECIDE tool to present interactive versions of evidence summaries called an interactive Summary of Findings (iSoF) table allows users to tailor a presentation to their own needs. An online randomised trial of the iSoF found that people want numbers in health information (rarely provided now) and that members of the public could not answer questions about benefits and harms with the current versions of patient information used in the trial.
- The GRADEpro Guideline Development Toolkit (GRADEproGDT, <http://gradepro.org>) has been developed by DECIDE and a key collaborator, the GRADE Working Group, to package much of DECIDE's work into a single tool and currently has over 11,000 users.

DECIDE has provided new information for guideline producers about how they can best meet the needs of the different users of their guidelines as well as how they can be more systematic about using research evidence when making their recommendations.

GRADEproGDT, and the link to the GRADE Working Group, means that guideline producers and others will benefit from DECIDE's results well beyond the end of the project.

Current status

Completed

Key publications

Schünemann, HJ, Wiercioch, W, Etzeandía, I, Falavigna, E, Santesso, N, Mustafa, R, Ventresca, M, Brignardello-Petersen, R, Laisaar, K-T, Kowalski, S, Baldeh, T, Zhang, Y, Raid, U, Neumann, I, Norris, SL, Thornton, J, Harbour, R, Treweek, S, Guyatt, G, Alonso-Coello, A, Rezapour, M, Brozek, J, Oxman, A, Akl, EA Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. *Can Med Assoc J* 2014;186(3):E123-E42

Loudon, K, Santesso, N, Callaghan, M, Thornton, J, Harbour, J, Graham, K, Harbour, R, Kunnamo, I, Liira, H, McFarlane, E, Ritchie, K, Treweek, S Patient and public attitudes to and awareness of clinical practice guidelines: a systematic review and thematic analysis. *BMC Health Serv Res* 2014;14:321

Kristiansen, A, Brandt, L, Alonso-Cuello, P, Agoritsas, T, Conboy, A, Elbarbary, M, Ferwana, M, Medani, W, Rigau, D, Rosenbaum, S, Spencer, AF, Treweek, S, Guyatt, G, Vandvik, PO Development of a novel, multilayered presentation format for clinical practice guidelines. *Chest* 2015;147(3):754-63

Liira, H, Saarelma, O, Callaghan, M, Harbour, R, Jousimaa, J, Loudon, K, McFarlane, E, Treweek, S Patients, health information and guidelines: a focus group study. *Scand J Prim Health Care* 2015;33(3):212-19

Alonso-Cuello, P, Oxman, A, Moberg, J, Brignardello-Petersen, R, Akl, A, Davoli, M, Treweek, S, Mustafa, MS, Vandik, O, Meerpohl, J, Guyatt, G, Schunemann, HJ GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines. *BMJ* 2016;353:i2089

Alonso-Cuello, P, Schunemann, HJ, Moberg, J, Brignardello-Petersen, R, Akl, A, Davoli, M, Treweek, S, Mustafa, MS, Rada, G, Rosenbaum, P, Morelli, A, Oxman, A GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. *BMJ* 2016;353:i2016

Fearn, N, Kelly, J, Callaghan, M, Graham, K, Loudon, K, Harbour, R, Santesso, N, McFarlane, E, Thornton, J, Treweek, S What do patients and the public know about clinical practice guidelines and what do they want from them? A qualitative study. *BMC Health Serv Res* 2016;16:74

Santesso, N, Carrasco-Labra, A, Langendam, M, Mustafa, MS, Heus, P, Lasserson, T, Opiyo, N, Kunnamo, I, Sinclair, D, Garner, P, Treweek, S, Tovey, D, Tugwell, P, Brozek, JL, Guyatt, G, Schunemann, HJ Improving GRADE Evidence Tables part 3: detailed guidance for explanatory footnotes supports creating and understanding GRADE certainty in the evidence judgements. *J Clin Epidemiol* 2016;74(6):28-39

Santesso, N, Morgano, G, Jack, S, Haynes, R, Hill, S, Treweek, S, Schunemann, HJ Dissemination of clinical practice guidelines: A content analysis of patient versions. *Med Decis Making* 2016;36(8):672-702

Hultcrantz, M, Rind, D, Akl, A, Treweek, S, Mustafa, R, Iorio, A, Alper, B, Meerpohl, J, Murad, H, Ansari, M, Katikreddi, V, Ostlund, P, Transeus, S The GRADE Working Group clarifies the construct of certainty of evidence. *J Clin Epidemiol* 2017;87:4-13

B.8

Decision Aids in Randomised Trials: The DART Study

Investigators

Katie Gillies, Marion Campbell, Craig Ramsay, Zoë Skea, HSRU; Glyn Elwyn, Cardiff University; Sara MacLennan, James N'Dow University of Aberdeen; Julia Wade, University of Bristol; Jamie Brehaut, University of Ottawa; Mary Politi, Washington University St Louis

Source and amount of HSRU funding (total funding)

CSO £165,975 (£165,975)

Summary

The use of decision-support interventions in the context of decisions about trial participation is an emergent field. There is a lack of evidence about what information is deemed important to support informed decisions about trial participation, whether different stakeholder groups agree on the relevance and importance of different types of information for inclusion and whether such tools are useful and acceptable for use in this context.

Informed by the wider trials and decision aid literature, a list of possible items which could be included in a trial participation aid was developed. There was consensus in the Delphi study across all stakeholder groups that the majority (60/66) of suggested items should be included in a trial participation decision aid. These included: information about trial participation and standard care; information on the likelihood of receiving different treatments; information to help patients' determine what matters most to them; ensuring the information is balanced; guidance on how to make a decision; disclosure of any conflicts of interest; using plain language in the tool and guidance on the decision support development process. However, some areas of divergence of opinion between stakeholder groups emerged (particularly around whether patient narratives should be included). The prototype decision aids were found to be generally well received by stakeholders, with most agreeing these were an improvement on existing patient information leaflets for trials and recognising their potential to improve decision making in this context.

This study has shown that there remains a paucity of research around the role of trial participation decision aids. We successfully identified a range of information features that multiple stakeholders agree should be central to any decision aid. However, the place of patient narratives is controversial and requires further research. This study has also shown that decision aids for trial participation are feasible to develop and broadly acceptable and useful to a wide range of stakeholders.

Current status

Completed

Key publications and presentations

Gillies, K, Skea, Z, MacLennan, S, Ramsay, C, Campbell, MK Determining information for inclusion in a decision support intervention for clinical trial participation: a modified Delphi approach. *Clin Trials* 2013;10(6):967-76

Gillies, K, Skea, Z, Campbell, M Decision aids for randomised controlled trials: a qualitative exploration of stakeholders' views. *BMJ Open* 2014;4(8):e005734

Gillies, K, Elwyn, G, Cook, J Making a decision about trial participation: the feasibility of measuring deliberation during the informed consent process for clinical trials. *Trials* 2014;15:307

Gillies, K, Huang, K, Skea, Z, Brehaut, J, Cotton, S Patient information leaflets (PILs) for UK randomised controlled trials: a feasibility study exploring whether they contain information to support decision making about trial participation. *Trials* 2014;15:62

Gillies, K, Cotton, S, Brehaut, J, Politi, M, Skea, Z. Decision aids for people considering taking part in clinical trials. *Cochrane Database of Systematic Reviews* 2015, 11. Art. No.: CD009736. DOI: 10.1002/14651858.CD009736.pub2

Oral presentations

Gillies, K. Patient Information Leaflets for RCT participation: do they conform to standards for good decision making? *National Research Ethics Service Training Day, London, 19 January 2012*

Gillies, K, Skea, Z, MacLennan, S, Ramsay, C, Campbell, MK. Determining information for inclusion in a decision support intervention for clinical trial participation: a modified Delphi approach. *2nd UK Clinical Trials Methodology Conference, Edinburgh, 18-19 November 2013*

Gillies, K, Elwyn, G, Cook, J. Making a decision about trial participation: the feasibility of measuring deliberation during the informed consent process for clinical trials. *Society for Clinical Trials, 35th Annual Meeting, Philadelphia, 18-21 May 2014*

B.9**Designing and providing information support materials for urological cancer patients****Investigators**

Zoë Skea, HSRU; Karolina A Kazimierczak, Sara J MacLennan, James N'Dow, Academic Urology Unit, University of Aberdeen

Source and amount of HSRU funding (total funding)

UCAN £None (UCAN funded research fellow salary)

Summary

The aim of this project was to provide wide-ranging practical recommendations for the design and provision of information packages for urological cancer patients.

The first phase of the project involved a critical interpretative synthesis of the relevant research literature. The aim of this synthesis was to provide a critical overview of the literature related to the design and provision of patient information, and to produce a theoretical framework, which could be used to inform the creation of a series of information guides for patients.

In the second phase of the project, participant observation of clinical consultations and semi-structured interviews with patients and health professionals was conducted, investigating the provision of information, use of existing information materials, and underlying communication practices.

Current status

Completed

Key publications

Kazimierczak, KA, Skea, Z, Dixon-Woods, M, Entwistle, VA, Feldman-Stewart, D, N'Dow, J, MacLennan, S
Provision of cancer information as a "support for navigating the knowledge landscape": findings from a critical interpretive literature synthesis. *Eur J Oncol Nurs* 2013;17(3):360-69

Skea, ZC, Entwistle, VA, MacLennan, SJ, N'Dow, J
Communicating good care: a qualitative study of what people with urological cancer value in interactions with clinicians. *Eur J Oncol Nurs* 2014;18(1):35-40

Kazimierczak, KA, Skea, ZC
'I've used the word cancer but it's actually good news': discursive performativity of cancer and the identity of urological cancer services. *Sociol Health Illn* 2015;37(3):340-54

B.10**Developing a Patient and public involvement Intervention to enhance Recruitment and Retention in Surgical Trials (PIRRIST)****Investigators**

Shaun Treweek, Louise Locoock, HSRU; Joanna Crocker (PI), Richard Bulbiulia, Jonathan Cook, Nicola Farrar, University of Oxford; Sian Rees, Oxford AHSN; Kerry Woolfall, Liverpool, Jennifer Bostock, Alan Chant, Lay partner

Source and amount of HSRU funding (total funding)

MRC Methodology £None (£41,523)

Summary

Clinical trials, including surgical trials, often struggle to recruit patient participants and keep them in the trial (retention). These difficulties can mean a trial takes longer, costs more money, or even fails completely. Involving patients in the design and management of trials has the potential to enhance recruitment and retention, but the evidence for this is weak at best.

This MRC-funded study aims to investigate these issues by developing and testing a patient and public involvement 'intervention' aimed at improving recruitment and/or retention in surgical. The project will consist of several phases including surveys, focus groups and a consensus workshop, involving surgical trial investigators, administrators, and patients and members of the public involved in surgical trials.

<https://www.phc.ox.ac.uk/research/health-experiences/research-projects/developing-a-patient-and-public-involvement-intervention-to-enhance-recruitment-and-retention-in-surgical-trials-pirrist>

Current status

Ongoing

Publications and presentations

None

B.11**Developing and evaluating interventions to reduce inappropriate prescribing of antibiotics in primary care: Comparison of paper-based and web-based modelling experiments****Investigators**

Shaun Treweek, HSRU; Prof Ian Ricketts, Dr Debbie Bonetti, Prof Nigel Pitts, Prof Frank Sullivan, University of Dundee; Prof Martin Eccles, Newcastle University

Source and amount of HSRU funding (total funding)

CSO £8,277 (£224,722)

Summary

Intervention modelling experiments (IMEs) allow complex interventions to be explored and refined prior to a full-scale trial by delivering key elements of the intervention in a simulation that approximates clinical practice. This project, funded by the CSO, builds on previous CSO-funded work by running a full, web-based IME (WIME) to advance the methodology of IMEs by directly comparing results with an earlier paper-based IME. The WIME targets inappropriate prescribing of antibiotics in primary care. First, we compare predictors of prescribing behaviour obtained from the WIME with those obtained in the paper-based IME. Second, we use a randomised design to compare the effects on simulated prescribing behaviour of a previously-developed intervention with a new intervention developed specifically for web-based delivery.

Current status

Completed

Key publications

Treweek, S, Bonetti, D, MacLennan, G, Barnett, K, Eccles, MP, Jones, C, Pitts, NB, Ricketts, I, Sullivan, F, Weal, M, Francis, JJ Paper-based and web-based Intervention Modelling Experiments identified the same predictors of general practitioner antibiotic prescribing behaviour: an evaluation of the Intervention Modelling Experiment methodology. *J Clin Epidemiol* 2014;67(3):296-304

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):793-97

McCleary, N, Francis, JJ, Campbell, MK, Ramsay, CR, Eccles, M, Treweek, S, Allan, J "Better" clinical decisions do not necessarily require more time to make. *J Clin Epidemiol* 2017;82:173-4

B.12**Development of core clinical outcome measures for glaucoma interventions****Investigators****Rehab Ismail, Craig Ramsay, Augusto Azuara-Blanco, HSRU****Source and amount of HSRU funding (total funding)**

No external funding £None

Summary

This PhD research utilised a mixed methods approach of qualitative and quantitative studies. Phase 1 identified the variation of reported clinical outcomes by conducting systematic reviews. Phase 2 refined and built on identified outcomes using a DELPHI study on glaucoma experts through respective glaucoma societies. Based on the findings of phase 1 and 2, Phase 3 identified how to measure the core clinical outcomes using COSMIN methodology.

Current status

Completed

Key publications

Ismail, R, Azuara-Blanco, A, Ramsay, C Variation of clinical outcomes used in glaucoma randomised controlled trials: a systematic review. *Br J Ophthalmol* 2014;98(4):464-68

Ismail, R, Azuara-Blanco, A, Ramsay, C Consensus on Outcome Measures for Glaucoma Effectiveness Trials: Results From a Delphi and Nominal Group Technique Approaches. *J Glaucoma* 2016;25(6):539-46

Ismail, R, Azuara-Blanco, A, Ramsay, C. Consensus on outcome measures for glaucoma effectiveness trials: A modified Delphi approach. *Association for Research in Vision and Ophthalmology Egypt, 13-14 November 2014*

Ismail, R, Azuara-Blanco, A, Ramsay, C. Consensus on outcome measures for glaucoma effectiveness trials: A modified Delphi approach. *COMET IV meeting, Rome, 19-20 November 2014*

Ismail, R, Azuara-Blanco, A, Ramsay, C. Consensus on outcome measures for glaucoma effectiveness trials: A modified Delphi approach. *European Glaucoma Society meeting, Nice, 7-11 June 2014*

Ismail, R, Azuara-Blanco, A, Ramsay, C Consensus on Outcome Measures for Glaucoma Effectiveness Trials: Results From a Delphi and Nominal Group Technique Approaches. *J Glaucoma* 2016;25(6):539-46

Ismail, R, Azuara-Blanco, A, Ramsay, C. Variation of clinical outcomes used in glaucoma randomised controlled trials: a systematic review. *Association for Research in Vision and Ophthalmology Egypt, 13-14 November 2014*

Ismail, R, Cornish, K, Kumarasamy, M. Glaucoma Follow-up Service in NHS Grampian: Closing the Loop. *Scottish Ophthalmological Club Autumn Meeting, Edinburgh 19 September 2014*

B.13**Development of core outcome set for symptomatic uncomplicated gallstone disease****Investigators**

Katie Gillies, Craig Ramsay, Miriam Brazzelli, Graeme MacLennan, Alison Avenell HSRU

Source and amount of HSRU funding (total funding)

Please refer to A.3

Summary

Gallstone disease (cholelithiasis) is one of the most common gastrointestinal disorders in industrialised countries. As yet there is no evidence on which treatment is the most clinical or cost-effective for the treatment of uncomplicated gallstone disease. Our team are currently running a randomised controlled trial comparing laparoscopic cholecystectomy (surgical management) with observation/conservative treatment (medical management) for preventing recurrent symptoms and complications in adults with uncomplicated symptomatic gallstones (The C-GALL Trial).

Many of the completed gallstone trials are not as helpful as they could be due to lack of standardisation across studies, outcome definition, collection and reporting. This heterogeneity of outcomes across studies also hampers useful synthesis of primary studies in meta-analyses and ultimately negatively impacts on decision making by all stakeholders. In addition to the heterogeneity of outcomes currently reported and the problems this causes, measuring the wrong outcomes (i.e. those that are not valued by clinicians or, more importantly, patients) could also be a real risk for many studies if stakeholders are not consulted during the trial design process. One way that these problems with heterogeneity and relevance to stakeholders can be addressed is through the development and use of core outcome sets.

The aim of this study is to develop a core outcome set for uncomplicated symptomatic gallstone disease effectiveness trials, which recommends what outcomes should be measured and reported as a minimum, and that reflects the interests of relevant stakeholders in order to facilitate decision making.

Current status

Ongoing

Publications and presentations

None

B.14**Early signs Monitoring to Prevent relapse in psychosis and promote Wellbeing, Engagement and Recovery (EMPOWER)****Investigators**

Graeme MacLennan, HSRU; Andrew Gumley (PI), Christopher Williams & Andrew Briggs (University of Glasgow), Simon Bradstreet, Scottish Recovery Network; Matthias Schwannauer, University of Edinburgh; Sandra Bucci, John Ainsworth, Alison Yung & Shon Lewis, University of Manchester; Max Birchwood, Swaran Singh & Andrew Thompson, University of Warwick; John Gleeson, Australian Catholic University; John Farhall, La Trobe University; Cathrine Mihalopoulos, Deakin University; Suresh Sundram, Susan Cotton, Revva Ledeman and Marion Alvarez-Jimenez, University of Melbourne; Alasdair Street, Jenna-Marie Lundy & Sally-Ann Cooper, University of Glasgow; Erica Packard, NHS Greater Glasgow & Clyde

Source and amount of HSRU funding (total funding)

NIHR HTA and Australia's National Health and Medical Research Council (NHMRC) £98,066 (£874.649)

Summary

Relapse in schizophrenia is a major cause of distress and disability amongst patients and their families. Relapse is predicted by changes in symptoms such as anxiety, depression and suspiciousness. These so-called early warning signs (EWS) can be used as the basis to promote timely interventions to prevent relapse and hospitalization. However, many individuals experience a fear of relapse, which can block accessing timely support. Our approach builds on helping individuals become more attuned to changes in their thoughts, feelings and experiences of psychosis in daily life to support improved awareness and self-management.

The EMPOWER team have developed a smartphone App (the EMPOWER App). The EMPOWER App prompts people on a daily basis to respond to a set of questions that relate to how they are feeling. Based on each individual's own personal baseline score, the EMPOWER App can then calculate changes in wellbeing to prompt self-management or to enable access to timely access to further support. For further more detailed information and blog updates on the EMPOWER system: <https://empowerstudy.net/>

The EMPOWER trial, funded by the NIHR HTA Programme and the Australian Government National Health and Medical Research Council, will evaluate the EMPOWER App against treatment as usual, using a multicentre, two arm, parallel group, cluster randomised controlled design involving eight purposively selected Community Mental Health Services (6 in Glasgow and 2 in Melbourne). Eligible patients are adults with a diagnosis of Schizophrenia-related disorder who have either been admitted to a psychiatric in-patient service at least once in the previous two years for relapse of psychosis or have received crisis intervention in the previous two years for a relapse of psychosis. The primary outcome is relapse over a 12 month follow-up period.

Current status

Ongoing

Publications and presentations

None

B.15**ECLS study: Early Cancer detection test - Lung cancer Scotland****Investigators**

Shaun Treweek, HSRU; Frank Sullivan, St Andrews University

Source and amount of HSRU funding (total funding)

Scottish Government & Oncimmune Ltd £None (£970,000)

Summary

Lung cancer is the most common cause of cancer related death worldwide. The majority of cases are detected at a late stage when prognosis is poor. The EarlyCDT[®]-Lung Test (ECLS) detects autoantibodies to abnormal cell surface proteins in the earliest stages of the disease which may allow tumour detection at an earlier stage thus altering prognosis.

The primary research question is: Does using the EarlyCDT[®]-Lung Test to identify those at high risk of lung cancer, followed by X-ray and computed tomography (CT) scanning, reduce the incidence of patients with late-stage lung cancer (III & IV) or unclassified presentation (U) at diagnosis, compared to standard practice?

ECLS is a randomised controlled trial of 10 000 participants recruited in Scotland from the most deprived quintile of the Scottish Index of Multiple Deprivation. Adults aged 50 to 75 who are at high risk of lung cancer are eligible to participate. The intervention is the EarlyCDT[®]-Lung Test followed by X-ray and CT in those with a positive result. The comparator is standard clinical practice. The primary outcome is the difference, after 24 months, between the rates of patients with stage III, IV or unclassified lung cancer at diagnosis. The secondary outcomes include: all-cause mortality; disease specific mortality; a range of morbidity outcomes; cost-effectiveness and measures examining the psychological and behavioural consequences of screening.

Participants with a positive test result but for whom the CT scan does not lead to a lung cancer diagnosis will be offered 6 monthly thoracic CTs for 24 months. An initial chest X-ray will be used to determine the speed and the need for contrast in the first screening CT. Participants who are found to have lung cancer will be followed-up to assess both time to diagnosis and stage of disease at diagnosis.

More details are available at <http://www.eclsstudy.org>.

Current status

Ongoing

Key publications

Sullivan, FM, Farmer, E, Mair, FS, Treweek, S, Kendrick, D, Jackson, C, Robertson, C, Briggs, A, McCowan, C, Bedford, L, Young, B Detection in blood of autoantibodies to tumour antigens as a case-finding method in lung cancer using the EarlyCDT[®]-Lung Test (ECLS): study protocol for a randomized controlled trial. *BMC Cancer* 2017;17:187

B.16**Effects of outpatient pharmacists' non-dispensing role on patient outcomes and healthcare professionals' prescribing patterns. A Cochrane Review update and application of the Behaviour Change Technique Taxonomy****Investigators**

Vikki Entwistle, HSRU; Christine Bond, C Matheson, Marijn de Bruin, Marie Johnston, University of Aberdeen

Source and amount of HSRU funding (total funding)

CSO £150,014 (£150,014)

Summary

Nationally and internationally, the pharmacist's role has changed substantially over recent years with a move away from the traditional function of medicine supply to a more patient-centred focus combined with collaborative working with other health professionals. To maximise the efficient use of resources, these changes should be guided by evidence. A growing number of randomised controlled trials (RCTs) have been conducted of pharmacist interventions, and there is now a need to synthesise this evidence and assess the value of different kinds of pharmacist interventions. This project will identify and combine the results of individual studies which have evaluated the contribution which pharmacists can make to (i) the use of medicines by patients and (ii) the prescribing behaviour of health professionals. These services often comprise a combination of different components or ingredients. It can be difficult to identify which ingredient or combinations of ingredients are most effective i.e. achieve the best results. We will examine and categorise the ingredients in each service and identify which ones are effective as well as ones which are not effective. The results of this project will be used to identify effective services which pharmacist can provide which directly benefit patient health and well-being. These results will be relevant to patient, health professionals and policy makers

Current status

Ongoing

Publications and presentations

None

B.17**Electronic Records in Ambulances (ERA)****Investigators**

Heather Morgan, HSRU, Zoë Morrison, University of Aberdeen; Alison Porter, Helen Snooks, Bridget Wells, Robert Harris-Mayes, Ronan Lyons, Swansea University; Henry Potts, UCL; Suzanne Mason, University of Sheffield; Jeremy Dale, University of Warwick; Robin Lawrenson, Scottish Ambulance Service; Niro Siriwardena; University of Lincoln; Sarah Black, South Western Ambulance Service; Richard Whitfield, Welsh Ambulance Service

Source and amount of HSRU funding (total funding)

NIHR HS&DR £19,584 (£380,317)

Summary

Increasingly, ambulance services have a role to play in keeping people out of hospital and technology can have a role in helping paramedics with all of these.

This research aims to find out how ambulance services can make the best use of information technology to support people with good quality care out of hospital. We will look at what happens day to day, when paramedics use technology in practice; at how the ambulance service as an organisation starts to use new technology and adapts to the changing landscape of care; and at what happens in between, as paramedics respond to this changing environment, learn new skills and change their role and practice.

We will talk to all the ambulance services in the UK to find out what they are doing in terms of introducing electronic records and other IT to support care delivery and decision making. We will then do a detailed study of four ambulance services - one service which has used electronic records for a few years, one which does not use them, and two which are part way through bringing them into use.

We will talk to paramedics, managers, and people running other relevant health services, read reports and documents and spend time on ambulances looking at how records and other technology are used. We will compare what has gone on across the four sites. We will look in detail at care for people with three particular conditions (falls, diabetic hypoglycaemia, mental health crisis) which have potential for increased non-conveyance, to see what difference electronic records in ambulances are making - or could make - to people with those conditions. We will then bring together all the ambulance services in the UK to talk about what we have found and discuss what they think will be the best way to make use of technology to help paramedics keep people out of hospital.

This project, funded by NIHR HS&DR programme, is being led from Swansea University:

<http://www.primecentre.wales/era.php>.

HSRU is supporting data collection and analysis across Scotland.

Current status

Ongoing

Publications and presentations

None

B.18**Ethical and policy issues in cluster randomised trials****Investigators**

Zoë Skea, HSRU; Judith Belle Brown, Schulich School of Medicine and Dentistry, Ontario; Jamie C Brehaut,, Shazia H Chaudhry, Jeremy M Grimshaw, Raphael Saginur, Monica Taljaard, University of Ottawa; Martin P Eccles, Newcastle University; Robert Boruch, University of Pennsylvania; Merrick Zwarenstein, Centre for Health Services Sciences, Toronto; Ariella Binik, Andrew McRae, Allan Donner, Charles Weijer, University of Western Ontario

Source and amount of HSRU funding (total funding)

Canadian Institute of Health Research £None (£237,086)

Summary

Cluster randomised trials are an increasingly important methodological tool in health research. In cluster randomized trials, intact social units or groups of individuals, such as medical practices, schools, or entire communities - rather than individual themselves - are randomly allocated to intervention or control conditions, while outcomes are then observed on individual cluster members. The substantial methodological differences between cluster randomized trials and conventional randomized trials pose serious challenges to the current conceptual framework for research ethics. The ethical implications of randomizing groups rather than individuals are not addressed in current research ethics guidelines, nor have they even been thoroughly explored. The main objectives of this research were to: (1) identify ethical issues arising in cluster trials and learn how they are currently being addressed; (2) understand how ethics reviews of cluster trials are carried out in different countries (Canada, the USA and the UK); (3) elicit the views and experiences of trial participants and cluster representatives; (4) develop well-grounded guidelines for the ethical conduct and review of cluster trials by conducting an extensive ethical analysis and organizing a consensus process; (5) disseminate the guidelines to researchers, research ethics boards (REBs), journal editors, and research funders.

Current status

Completed

Key publications

Chaudhry, SH, Brehaut, JC, Grimshaw, JM, Weijer, C, Boruch, R, Donner, A, Eccles, MP, McRae, AD, Saginur, R, Skea, ZC, Zwarenstein, M, Taljaard, M Challenges in the research ethics review of cluster randomized trials: international survey of investigators. *Clin Trials* 2013;10(2):257-68

McRae, A, Bennett, C, Skea, Z, Boruch, R, Brehaut, J, Donner, A, Eccles, M, Grimshaw, J, Weijer, C, Taljaard, M Reporting of patient consent in healthcare cluster randomised trials is associated with the type of study interventions and publication characteristics. *J Med Ethics* 2013;39(2):119-24

Rogers, W, Hutchison, K, Skea, Z, Campbell, MK Strengthening the ethical acceptability of placebo-controlled surgical trials: three proposals. *BMC Med Ethics* 2014;15:78

B.19

EuroFIT - Social innovation to improve physical activity and sedentary behaviour through elite European football

Investigators

Shaun Treweek, HSRU; University of Glasgow, PAL Technologies Ltd, European Healthy Stadia Network CIC, Stichting VU-VUMC, Stichting, Katholieke Universiteit, Norges Idrettshogskole, Universidade Tecnica de Lisboa - UTL, Pintail Ltd, University of Dundee, University of Edinburgh

Source and amount of HSRU funding (total funding)

EU (FP7) £27,763 (£5,063,584)

Summary

Football can change lives. Europeans have a deep attachment to football and to their top clubs. Each week, across Europe, around 20.2 million people attend matches in the top 50 leagues. They celebrate or despair as their club rises or falls through league tables; their allegiance to their team is often lifelong and cross-generational.

EuroFIT's **social innovation** is to *harness the personal connection, loyalty and attachment many men feel to football and their club to attract them to health-promoting lifestyle change programmes that they might otherwise dismiss.*

Our project has **six central features**. First, we use the allegiance that many men, including those of low socioeconomic status (SES), feel to their football clubs to attract them to healthy lifestyle programmes delivered within professional football club stadia. Second, we apply *state-of-the-art* theory and evidence on *motivating and maintaining behavioural change* in a technology-supported, culturally- and gender- sensitive, lifestyle programme to improve health. Third, we develop *low-cost, advanced sensors* that can simultaneously monitor both *activity and sedentary behaviour* to provide real-time feedback and enhanced motivation for change. Fourth, we use *social media*, games-based *social interaction*, *group- and family- support* and specific *behaviour change techniques* to enhance intrinsic motivation to support change *in the long-term*. Fifth, we use the randomised controlled trial to provide robust evidence of cost-effectiveness. Sixth, we deliver every aspect of the project with the aim of *widespread replication* – our aim is to make tangible changes to people's lives and health across Europe.

Current status

Ongoing

Key publications

van de Glind, I, Bunn, C, Gray, C, Hunt, K, Andersen, E, Jelsma, J, Morgan, HM, Pereira, O, Roberts, G The intervention process in the European Fans in Training (EuroFIT) trial: a mixed method protocol for evaluation. *Trials* 2017;18:356

(Treweek, S) et al, Study protocol of European Fans in Training (EuroFIT): a four-country randomised controlled trial of a lifestyle program for men delivered in elite football clubs. *BMC Public Health* 2016;16:598

B.20**Evidence-based Care of People with Dementia: Investigating Research Implementation Strategies (IRIS)****Investigators**

Jill Francis, HSRU; Sally Green, Colette Browning, Claire Harris, Joanne McKenzie, Duncan Mortimer, Kerry Murphy, Denise O'Connor, Daniel O'Connor, Neil Spike, Barbara Workman, Monash University; Martin Eccles, University of Newcastle; Leon Flicker, Simon French, University of Melbourne; Jeremy Grimshaw, University of Ottawa; Susan Michie, UCL

Source and amount of HSRU funding (total funding)

Australian NH MRC £None (£550,000)

Summary

Across the developed world, the number of people with dementia is increasing and so therefore is the frequency of people with dementia presenting to general practice. In Australia, there is a recent evidence based clinical practice guideline to inform the diagnosis and management of people with dementia and the support of their carers. Many of the recommendations from this guideline are relevant to general practitioners (GPs). Strategies to implement guidelines into practice are needed in all areas of health care, but changing clinical practice is complex and a body of research developing methods of identifying barriers to specific practice changes is emerging. This project aims to support GPs in improving the general practice based care of people with dementia. In addition it will contribute to the body of knowledge about how to bring about practice change and implement a clinical practice guideline. We will design an intervention for implementing this new guideline into practice, working with GPs to change their practice where needed. Using a randomised design we will test the effect of this intervention on the care of people with dementia, and on the quality of life of people with dementia and their carers.

Current status

Completed

Publications and presentations

None

B.21**Evidence-informed decision aids for clinical trial participation: a methodological investigation of core components and outcome measures****Investigators**

Katie Gillies, HSRU; Dr Hilary Bekker, University of Leeds; Prof Richard Thomson, Newcastle University; Prof Paula Williamson, University of Liverpool; Dr Hugh Davies, NRES

Source and amount of HSRU funding (total funding)

MRC £224,545 (£243,095)

Summary

The overall aim of this fellowship project is to generate and disseminate new methodological knowledge relating to innovations in decision support for trial participation. Following on from the Decision Aids in Randomised Trials (DART) project, this work aims to inform the design and assessment of trial participation decision aids by answering the following research questions:

1. What are the potential implications of including patient stories in trial decision aids?
2. What are effective methods for presenting probabilistic trial information within trial decision aids?
3. Which outcomes should be considered 'core' for the evaluation of trial decision aids?

Current status

Ongoing

Key publications

Gillies, K, Entwistle, VA, Treweek, S, Fraser, C, Williamson, P, Campbell, MK. Evaluation of Interventions for informed Consent for randomised controlled Trials (ELICIT): protocol for a systematic review of the literature and identification of a core outcome set using a Delphi survey. *Trials* 2015;16(484)

Gillies, K, Duthie, A, Campbell, MK. A systematic review of measures of informed consent for randomised controlled trials. *PLoS One* 2017 (submitted for publication)

Oral presentations

Gillies, K. Supporting decisions about trial participation – lessons from information leaflets. *National Research Ethics Service Training Day, London, 19 January 2012*

Gillies, K, Entwistle, VA, Treweek, S, Fraser, C, Williamson, P, Campbell, MK. Evaluation of Interventions for informed Consent for randomised controlled Trials (ELICIT): protocol for a systematic review of the literature and identification of a core outcome set using a Delphi survey. *Society for Clinical Trials, 36th Annual Meeting, Arlington, 18-21 May 2015*

Gillies, K, Entwistle, VA, Treweek, S, Fraser, C, Williamson, P, Campbell, MK. Evaluation of Interventions for informed Consent for randomised controlled Trials (ELICIT): protocol for a systematic review of the literature and identification of a core outcome set using a Delphi survey. *International Clinical Trials Methodology Conference, Glasgow, 16-17 November 2015*

B.22**Feasibility of a multi-site RCT exploring the effectiveness of mindfulness-based cognitive therapy to improve emotional wellbeing and glycaemic control among adults with type 1 diabetes****Investigators**

Andy Keen, HSRU; Stewart Mercer, University of Glasgow; Ann Gold, NHS Grampian; Margaret Maxwell, University of Stirling; Marijn De Bruin University of Aberdeen

Source and amount of HSRU funding (total funding)

CSO £107,247 (£218,262)

Summary

Diabetes is a challenging condition to manage. Anxiety and depression are common among this group and are associated with poorer diabetes control. This study aims to ascertain the feasibility of conducting a trial of a psychological intervention designed to alleviate significant levels of anxiety and/or depression and improve glycaemic control among those with diabetes who have significant difficulties in these areas.

Eligible patients from NHS Grampian and NHS Greater Glasgow and Clyde will be randomly allocated to intervention or wait-list control groups. The intervention group will receive a course of mindfulness-based cognitive therapy (MBCT) comprising eight weekly sessions of 2-hours with trained mindfulness facilitators, and half an hour of mindfulness practice each day between sessions using pre-recorded audio files. Measures of anxiety/depression (HADS), diabetes control (HbA1c), and a range of other indicators of diabetes control, quality of life and emotional wellbeing will be taken at baseline, immediately post-intervention and at 3-months follow up. Use of health services in the 6-months prior to the intervention and during the 3-months follow-up period will also be assessed. Wait-list controls will complete the measures at the same time points for comparison and will be invited to receive the MBCT course after the 3-month follow-up period.

Current status

Completed

Publications and presentations

None

B.23**Feasibility study for a weight loss intervention for women treated for breast cancer****Investigators**

Pat Hoddinott, Rumana Newlands, HSRU; Steve Heys, Geraldine McNeill, Leone Craig and Julia Clark, University of Aberdeen

Source and amount of HSRU funding (total funding)

CRANES Breast Cancer Charity and the University of Aberdeen Development Trust £None (£78,000)

Summary

This project was funded jointly by a breast cancer charity (CRANES) and the University of Aberdeen Development Trust. Evidence suggests that weight loss can improve breast cancer outcomes. A mixed method approach informed the design of an acceptable and feasible weight loss intervention. The study included focus groups, semi-structured interviews and a survey of breast cancer patients attending local charity support groups and a hospital clinic.

Current status

Completed

Oral presentations

Newlands, R. Development and testing of a Lifestyle Weight Loss Intervention in Women Treated for Breast Cancer. *Rowett Seminar for Cancer Study Donors/Charity Organisations, 3rd March 2017*

B.24**Feedback matters: How should trial results be reported back to participants?****Investigators****Katie Gillies HSRU****Source and amount of HSRU funding (total funding)**

Academy of Medical Sciences £99,940 (£99,940)

Summary

A core tenet of clinical trials is the timely and effective return of trial results to participants; however, the routine sharing of research results with trial participants is rare. When information is fed back it is often very poorly done. Practice is highly variable and has been known in some cases to cause harm. There are often hundreds of thousands of participants waiting to hear about the results of the trials they took part in. Yet the routine sharing of results with trial participants is uncommon, despite the evidence that feeding back results improves participants' experience and encourages future participation. There is an urgent need to address this poor practice. Yet the details of the "what", "how", "by whom" and "when" of results feedback, has not been evidenced appropriately with trial stakeholders (specifically participants but also research ethics committees, industry, funders, etc). Existing studies have called for 'clear guidelines' and 'ethical frameworks' generated from empirical data as an appropriate way to inform sharing results meaningfully with trial participants. This project aims to generate participant-centred, evidence-based recommendations for trialists to implement the dissemination of results to trial participants. The specific objectives are:

1. Explore and evaluate the range of methods for feeding back results to trial participants that are currently used, appraising the advantages and disadvantages of each.
2. Determine consensus amongst trial stakeholders (participants, trialists, industry representatives, regulators) surrounding key content of trial feedback.
3. Explore trial stakeholders' views and perceptions about how trial feedback is delivered.
4. Develop practice recommendations for feeding back results to trial participants.

Identifying current practice and determining what should be delivered and how (in ways that are individually appropriate and responsive) would be a demonstrable step forward in realising and fulfilling the ethical and regulatory requirements. There is significant potential for the results of this research to improve trial participants' experience and encourage participation in future trials.

Current status

Ongoing

Publications and presentations

None

B.25**From policy to practice: An international comparison of approaches to systemic quality and safety****Investigators**

Lorna McKee, HSRU; Prof Patrick Flood, Dublin City University; Aoife McDermott, Cardiff University

Source and amount of HSRU funding (total funding)

Irish Health Research Board £7,100 (£143,500)

Summary

This research funded by the Irish Health Research Board studied and benchmarked (1) the policy and supporting structures that aim to promote quality and safety in the Irish and Scottish healthcare systems as a whole and (2) explored the enablers and barriers to implementing such policy in Irish and Scottish hospitals. Overall using qualitative and quantitative method, the research will evaluate how system *and* organisational structures and processes affect quality and safety. Specifically, it explored policy and institutional support for quality and safety at system-level, and the enactment of policy at organisation level. Hence the research considered health system and policy design as well as the organisation of structures, systems and staff to deliver quality and safety within hospitals. The approach adopted was grounded in the increasing recognition that quality is a systems property that requires attention to the policy, organisational and managerial, as well as clinical, aspects of care. From this perspective concerns shifts away from individual errors and incidents and towards the overarching system *and* organisational enablers and barriers to quality and safety. Hence, integrating a system and organisational level focus highlights where support is needed - at system or organisational level - to ensure that policies are effective on-the-ground.

Current status

Completed

Oral presentations

Hamel, LM, McDermott, A, McKee, L, Flood, PC. Comparison of influence strategies utilised by institutions responsible for supporting quality and safety in hospitals in Ireland and Scotland. *International Conference on Communication in Health Care, University of St Andrews, 4-7 September 2012*

McDermott, A, McKee, L, Hamel, LM, Flood, PC. A review of Scottish and Irish healthcare policy: understanding the development and exactment of the quality and safety agenda through international benchmarking. *International Organisational Behaviour in Healthcare Conference, Trinity College, Dublin, 15-17 April 2012*

McDermott, A, McKee, L, Hamel, LM, Flood, PC. A review of Scottish and Irish healthcare policy: understanding the development and exactment of the quality and safety agenda through international benchmarking. *HORNET Research Workshop, Heriot-Watt University, 2 December 2012*

B.26**Geospacial evaluation of systems of trauma care for Scotland****Investigators**

Jan Jansen, Marion Campbell (HSRU); Jonny Morrison, Glasgow Royal Infirmary; Robin Lawrenson and Gerry Egan, Scottish Ambulance Service; Shan He and Handing Wang, University of Birmingham

Source and amount of HSRU funding (total funding)

NHS Research Scotland & North of Scotland Planning Group £None (£97,447)

Summary

The GEOS study aimed to determine the optimal configuration of trauma system for Scotland. Phase 1 comprised a prospective notional triage of all trauma patients attended by the Scottish Ambulance Service, for one year. Phase 2 involved the calculation of drive-times and flight-times from every incident location to every hospital in Scotland which could become a trauma centre. Phase 3 comprised the mathematical modelling of every possible configuration of trauma system, based on triage categories and access times. Phase 4 involved the selection of geospatially optimised solutions, using multi-objective optimisation methodology.

Current status

Completed

Key publications

Jansen, JO, Campbell, M, GEOS Investigators The GEOS study: Designing a geospatially optimised trauma system for Scotland. *The Surgeon* 2014;12(2):61-63

Jansen, JO, Morrison, JJ, Wang, H, Lawrenson, R, Egan, G, He, S, Campbell, MK Optimizing Trauma System Design: The GEOS (Geospatial Evaluation of Systems of Trauma Care) Approach. *J Trauma Acute Care Surg* 2014;76(4):1035-40

Jansen, JO, Morrison, JJ, Wang, H, He, S, Lawrenson, R, Hutchison, JD, Campbell, MK Access to specialist care: Optimizing the geographic configuration of trauma systems. *J Trauma Acute Care Surg* 2015;79(5):756-65

Jansen, JO, Morrison, JJ, Yeung, D, Walshaw, T, Ross, NP, Mekhail, P, Samarage, M, Wang, H, He, S, Lawrenson, R, Campbell, MK Population-Based Evaluation of the Implementation and Performance of the ACS/CDC Field Triage Decision Scheme in Preparation for Establishing a Trauma System. *J Trauma Acute Care Surg* 2017 (submitted for publication)

Jansen, JO, Moore, G, Wang, H, Morrison, J, Hutchinson, J, Campbell, MK A.Quality Improvement of Trauma System Configurations: Analysis of the Colorado Trauma System. *J Trauma Acute Care Surg* 2017 (submitted for publication)

B.27**Health literacy, communication and the quality of health care****Investigators**

Vikki Entwistle, HSRU; Phyllis Easton, NHS Tayside; Cathy Charles (deceased; formerly McMaster University)

Source and amount of HSRU funding (total funding)

No external funding £None

Summary

Two doctoral research projects, one based at the University of Dundee, and one at McMaster University, Canada.

The first (Phyllis Easton's PhD) confirmed that a hidden population of adults with low literacy has a worse average health status than can be accounted for by other demographic or socio-economic variables. It then showed how the social stigma attached to low literacy can impede effective communication with health professionals and contribute, both directly and indirectly, to poor health.

The second (Leslie Malloy-Weir's PhD) critiqued the various definitions of health literacy that have been used in academic literature and highlighted the diverse ways in which aspects of health literacy can support and be supported by shared decision-making processes in health care.

Current status

Completed

Key publications and presentations

Easton, PM, Entwistle, VA, Williams, B How the stigma of low literacy can impair spoken patient-professional interactions and affect health: insights from a qualitative investigation. *BMC Health Serv Res* 2013;13:319

Malloy-Weir, L, Charles, C, Gafni, A, Entwistle, VA Empirical relationships between health literacy and treatment decision-making: a scoping review of the literature. *Patient Educ Couns* 2015;98(3):296-309

Malloy-Weir, L, Charles, CA, Gafni, A, Entwistle, VA A Review of Health Literacy: Definitions, interpretations, and implications for policy initiatives
J Public Health Policy 2016;37(3):334-52

Oral presentations

Entwistle, VA. Health literacy and shared decision-making: thinking in terms of capabilities. *Health literacy and shared decision-making, Newcastle University, 13 May 2013*

B.28**Improving access, efficiency and equity through family-centred goal setting: Good Goals intervention****Investigators**

Niina Kolehmainen, Jill Francis, Graeme MacLennan, Eilidh Duncan, Craig Ramsay, Lorna McKee, HSRU; Edward Duncan, University of Stirling; Elaine Cargill, NHS Tayside; Joanne Thomas, NHS Grampian

Source and amount of HSRU funding (total funding)

CSO £195,665 (£197,761)

Summary

Community allied health services are striving toward better quality service provision (including access, family-centredness, equity, and efficiency). One way to achieve this may be by changing individual clinicians' practices related to assessment, treatment provision and discharging (here referred to as 'caseload management actions').

The completed research undertaken were:

1. Generate an evidence base of therapists' caseload management actions: (i) a systematic review, (ii) an interview study with occupational therapists, (iii) an interview study with parents, and (iv) analysis of children's case notes.
2. Build a theoretical model of therapists' caseload management actions: a synthesis of the above evidence and existing theory and evidence in behaviour change.
3. Design an evidence- and theory-based intervention to change therapists' caseload management: a collaborative study with therapists and experts in behaviour change (i.e. health psychologists).
4. Investigate the feasibility of using the intervention in practice: three mixed-methods case studies of children's occupational therapy services (n=46 therapists).

The intervention, titled *Good Goals*, aims to increase clinicians' implementation of three actions: identifying good quality goals; agreeing these goals with clients; and evaluating the client's progress toward the agreed goal. These are the actions which the evidence from step 1 indicated as fundamental for good quality service provision.

Good Goals consists of four clusters of clearly specified behaviour change techniques. The pathways through which these techniques are hypothesised to cause changes in the outcome are explicitly specified.

Good Goals is delivered over 25 weeks and through face-to-face training sessions, DVDs, practical group tasks, and therapist-led team meetings. Some aspects are delivered by a trained facilitator whilst others are self-administered by the therapists. The delivery follows an explicit manual.

A formal evaluation is required to investigate the effectiveness and cost-effectiveness of *Good Goals*.

Current status

Completed

Key publications and presentations

Kolehmainen, N, MacLennan, G, Tement, 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. *Implement Sci* 2012;7(76):16 August

Kolehmainen, N, Francis, JJ Specifying content and mechanisms of change in interventions to change professionals' practice: an illustration from the Good Goals study in occupational therapy. *Implement Sci* 2012;7(100):18 October

Kolehmainen, N, Duncan, EAS, Francis, J Clinicians' actions associated with the successful patient care process: A content analysis of interviews with paediatric occupational therapists. *Disabil Rehabil* 2013;35(5):388-96

Oral presentations

Gorter, JW, Gentis, M, Kolehmainen, N, Camden, C. The F-words in childhood disability. *NeuroDevNet Conference, Vancouver, May 2013*

Kolehmainen, N. Mixed methods implementation research in health services for children and families: the Good Goals project. *The Center for Mental Health Implementation and Dissemination Science in States (IDEAS) New York University Child Study Center, New York, September 2012*

Kolehmainen, N. Developing multifaceted interventions in rehabilitation: illustrations from caseload management and physical activity. *McGill University, Montreal, February 2012.*

Kolehmainen, N. Managing caseloads efficiently, equitably and with focus on the family. *Chedoke Grand Rounds, McMaster Children's Hospital, Hamilton, Canada, April 2012*

Kolehmainen, N. Improving rehabilitation interventions and services: sharing challenges and solutions. *Ottawa Hospitals Research Institute, Ottawa, May 2013*

Kolehmainen, N. Outcome measurement in rehabilitation: the importance and issues. *NHS Fife Child Health AHP Outcomes Day, Dunfermline May 2013*

Kolehmainen, N, McAnuff, J. Feeling guilty, worried and inadequate: clinicians' negative emotions about practice? *Allied Health Professions in Children & Young People's Health Services (AHP CYP) Network Annual Meeting, Edinburgh, October 2012*

McAnuff, J, Boyes, C, Kolehmainen, N. Family-centred interactions in childhood rehabilitation: an explorative study in occupational therapy. *British Academy of Childhood Disability, Derby, March 2012*

Kolehmainen, N, MacLennan, G, Ternent, L, Duncan, EAS, Duncan, EM, Ryan, S, McKee,. Multi-level case studies in development of complex interventions: an example of the good goals intervention. *2nd UK Clinical Trials Methodology Conference, Edinburgh, 18-19 November 2013*

B.29**Improving NHS quality using internet ratings and experience (INQUIRE)****Investigators**

Louise Locock (PI) HSRU; John Powell, Sue Ziebland, Sue Dopson, Ray Fitzpatrick, Trish Greenhalgh, Crispin Jenkinson, Elizabeth Gibbons, University of Oxford; Neil Churchill, NHS England; Sian Rees, Oxford AHSN; Jennifer Bostock, Lay partner; Melanie Gager, Royal Berkshire Hospitals NHS Foundation Trust; Chris Graham, Jenny King, Picker Institute

Source and amount of HSRU funding (total funding)

NIHR HS &DR £TBA (£786,867)

Summary

This NIHR Health Services and Delivery Research programme study investigates how the NHS should best interpret and act on patient experiences as online patient feedback to improve the quality of NHS services. The research includes interviews with people who have given online feedback as well as ethnographic case studies in four NHS sites in England to examine how in practice they engage with online feedback. A toolkit for the NHS on using online patient experience feedback data will be produced.

<https://www.phc.ox.ac.uk/research/health-experiences/research-projects/improving-nhs-quality-using-internet-ratings-and-experiences-inquire>

Current status

Ongoing

Publications and presentations

None

B.30**Improving Quality in Healthcare: A Case Study in Dental Primary Care in Scotland****Investigators**

Craig Ramsay, Lorna McKee, Shaun Treweek, HSRU; Heather Cassie, Jan Clarkson, University of Dundee

Source and amount of HSRU funding (total funding)

CSO £None (£110,783)

Summary

The aim of this PhD study was to explore, using a mixed-method approach, which aspects of a healthcare organisation influence the translation of guidance into practice. Understanding of the role of organisational factors will enable better targeting of knowledge and guidance. This study contributed to a framework for the translation of national recommendations into routine clinical practice (the Translation Research in a Dental Setting Programme), thus improving patient outcomes and quality in healthcare.

Current status

Completed

Publications and presentations

None

B.31**Improving the Quality of Dentistry: A randomised controlled trial comparing oral hygiene advice and periodontal instrumentation for the prevention and management of periodontal disease in dentate adults attending dental primary care (IQuaD)****Investigators**

Craig Ramsay, HSRU; Dr Jan Clarkson, University of Dundee; Prof Helen Worthington, University of Manchester; Prof Peter Heasman, Newcastle University; Margaret Ross, University of Edinburgh; Dr Debbie Bonetti, University of Dundee

Source and amount of HSRU funding (total funding)

NIHR HTA Programme £142,807 (£55,543)

Summary

Periodontal disease is the most common oral disease affecting adults. Effective self-care (tooth brushing and interdental aids) for plaque control and removal of risk factors such as calculus, by periodontal instrumentation (PI), commonly known as a "scale and polish", are considered necessary to prevent and treat periodontal disease. Despite evidence of an association between sustained good oral hygiene and a low incidence of periodontal disease there is a lack of reliable evidence to inform clinicians of the relative effectiveness of different types of Oral Hygiene Advice (OHA).

This multi-centre trial, funded by the NIHR HTA Programme, aims to compare the effectiveness and cost effectiveness of theoretically based, personalised OHA or PI at different time intervals (no PI, 6 monthly PI or 12 monthly PI) or their combination to routine OHA, for improving periodontal health in dentate adults attending general dental practice.

Participating dentists will be cluster randomised to provide routine (current practice) or theory-based personalised (to the needs of the patient) OHA. A total of 1860 individual eligible patients will be randomised to no PI, 6 monthly PI or 12 monthly PI (310 to each group within each cluster of routine or personalised OHA randomised dentists). Clinical outcomes will be measured at baseline and at 3 years follow-up by trained outcome assessors and participants will also be followed-up by postal questionnaires sent annually.

The primary clinical outcome is gingival inflammation/bleeding on probing at the gingival margin measured by the Gingival Index of Loe.

The IQuaD trial is led by Professor Jan Clarkson based in the University of Dundee.

IQuaD closed to recruitment in August 2013 with 1877 participants recruited.

Current status

Ongoing

Key publications and presentations

Clarkson, JE, Ramsay, CR, Averely, P, Bonetti, D, Boyers, D, Campbell, L, Chadwick, GR, Duncan, A, Elders, A, Gouick, J, Hall, AF, Heasman, L, Heasman, PA, Hodge, PJ, Jones, C, Laird, M, Lamont, TJ, Madden, I, McCombes, W, McCracken, GI, McDonald, AM, McPherson, G, Macpherson, LE, Mitchell, FE, Norrie, JD, Pitts, NB, van der Pol, M, Ricketts, DN, Ross, MK, Steele, JG, Swan, M, Tickle, M, Watt, PD, Worthington, HV, Young, L IQaD dental trial; improving the quality of dentistry: a multicentre randomised controlled trial comparing oral hygiene advice and periodontal instrumentation for the prevention and management of periodontal disease in dentate adults attending dental primary care [protocol]. *BMC Oral Health* 2013;13:58

Ramsay, C, Clarkson, JE, Duncan, A, Lamont, T, Heasman, L, Boyers, D, Goulao, B, Bonetti, D, Bruce, R, Gouick, J, Heasman, L, McDonald, A, McLaren-Neil, F, Mitchell, FE, Norrie, J, van der Pol, M, Steele, JG, Sharp, A, Watt, G, Worthington, HV, Young, L Improving the Quality of Dentistry (IQaD): A cluster factorial randomised controlled trial comparing the effectiveness and cost benefit of oral hygiene advice and/or periodontal instrumentation to routine care for the prevention and management of periodontal disease in dentate adults attending dental primary care. *Health Technol Assess* 2017 (accepted for publication)

Oral presentations

Duncan, A, Ramsay, CR, Clarkson, JE, Bonetti, D. Improving trial questionnaire response rates using behaviour change theory. *SPCRN Scientific Meeting, Surgeon's Hall, Edinburgh, 23 March 2015*

Boyer, M, van der Pol, M, Watson, M. Using DCEs to estimate willingness to pay for dental care. *European Conference in Health Economics, Hamburg, July 2016*

Clarkson, JE, Ramsay, C. Start skipping the dentist. Cabaret of dangerous ideas. *Edinburgh International Festival, 8 Aug 2017*

B.32**InS:PIRE – Intensive care Syndrome: Promoting Independence and Return to Employment****Investigators**

Marion Campbell, HSRU; John Norrie, University of Edinburgh; Joanne McPeake, NHS Greater Glasgow & Clyde; ICU Patient and Family Advisory Council (Glasgow Royal Infirmary), University of Glasgow; NHS Healthcare Improvement Scotland; Scottish Government Health and Social Care Quality Unit; Scottish Intensive Care Society

Source and amount of HSRU funding (total funding)

The Health Foundation £99,272 (£499,984)

Summary

Background: Many patients have poor quality of life following an intensive care admission. Glasgow Royal Infirmary has successfully prototyped a rehabilitation intervention for intensive care unit survivors: InS:PIRE (Intensive Care Syndrome: Promoting Independence and Return to Employment). This unique five-week recovery programme for patients and carers focuses on patient education, peer support and facilitating self-management. It aimed to increase how in control they feel about their health and wellbeing.

Aim: Led by NHS Greater Glasgow and Clyde Health Board, in partnership with University of Glasgow Higher Educational Institute, NHS Healthcare Improvement Scotland, Scottish Government Health and Social Care Quality Unit, and Scottish Intensive Care Society, the team is now implementing the InS:PIRE rehabilitation programme in five centres across four health boards in Scotland.

Evaluation: Led from the Health Services Research Unit, University of Aberdeen, the InS:PIRE project will comprise a systematic evaluation. Rigorous and evolving evaluation is essential to ensure the improvement project is implemented successfully (avoiding predictable mistakes and reducing latencies) and to show the final findings are robust and credible. The main evaluation purposes are therefore to: (a) conduct an initial Evaluability Assessment; (b) continue to evaluate all aspects of the improvement implementation using a formative approach; and (c) deliver a final independent evaluation (summative approach), with appropriate focus on what didn't go according to plan and what the remaining challenges are for a nationwide adoption.

Current status

Ongoing

Publications and presentations

None

B.33**'It's trying to manage the work': a qualitative evaluation of recruitment processes within a UK multicentre trial (TISUQual)****Investigators**

Katie Gillies, Zoë Skea, HSRU

Source and amount of HSRU funding (total funding)

Please refer to A.84

Summary

Objectives To explore trial site staff's perceptions regarding barriers and facilitators to local recruitment.

Design Qualitative semi-structured interviews with a range of trial site staff from four trial sites in the UK. Interviews were analysed thematically to identify common themes across sites, barriers that could be addressed and facilitators that could be shared with other sites.

Participants 11 members of staff from four trial sites: clinical grant Co-applicant (n=1); Principal Investigators (n=3); Consultant Urologist (n=1); Research Nurses (n=5); Research Assistant (n=1).

Setting Embedded within an ongoing randomised controlled trial (the TISU trial). TISU is a UK multicentre trial comparing therapeutic interventions for ureteric stones.

Results Our study draws attention to the initial and ongoing burden of trial work that is involved throughout the duration of a clinical trial. In terms of building and sustaining a research culture, trial staff described the ongoing work of engagement that was required to ensure that clinical staff were both educated and motivated to help with the process of identifying and screening potential participants. Having adequate and sufficient organisational and staffing resources was highlighted as being a necessary prerequisite to successful recruitment both in terms of accessing potentially eligible patients and being able to maximise recruitment after patient identification. The nature of the research study design can also potentially generate challenging communicative work for recruiting staff which can prove particularly problematic.

Conclusions Our paper adds to existing research highlighting the importance of the hidden and complex work that is involved in clinical trial recruitment. Those designing and supporting the operationalisation of clinical trials must recognise and support the mitigation of this 'work'. While much of the work is likely to be contextually sensitive at the level of local sites and for individual trials, some aspects are ubiquitous issues for delivery of trials more generally.

Current status

Completed

Key publications

Skea, Z, Treweek, S, Gillies, K "It's trying to manage the work": A qualitative evaluation of recruitment processes within a UK multi-centre trial. *BMJ Open* 2017;7(8): e016475

B.34**Lessening the impact of fatigue in inflammatory rheumatic diseases: a randomised clinical trial (LIFT)****Investigators**

Graeme MacLennan, Alison McDonald, HSRU; Neil Basu (CI), Paul McNamee, Richard Emsley, Stuart Gray, Katherine Martin, Sarah Hewlett, Alison Wearden, Gary MacFarlane, Stefan Siebert, Peter White, University of Aberdeen; Richard Emsley, Karina Lovell, University of Manchester; Lorna Paul, University of Glasgow; Emma Dures, University of West of England

Source and amount of HSRU funding (total funding)

Arthritis Research UK (ARUK) £667,041 (£735,536)

Summary

Fatigue is pervasive, disabling and challenging to manage across all inflammatory rheumatic diseases (IRDs).

The LIFT trial, funded by Arthritis Research UK, is a multi-centre, three-arm randomised controlled trial testing usual care alone versus usual care with additional adapted cognitive behavioural approach (CBA) or personalised exercise programme (PEP) therapies.

Approximately 375 participants will be randomly assigned to either a course of usual care and CBA or PEP or usual care alone. Those in the CBA and PEP groups will receive a course of treatment involving 7 sessions delivered by telephone/ internet-based audio/video call. A booster session will be conducted 22 weeks after the start date of treatment. The interventions will be delivered centrally, by either telephone or Skype. Follow-up data will be collected from all participants at 10 weeks, 26 weeks and 54 weeks after randomisation.

The primary outcome measures are fatigue severity and impact. Secondary outcome measures include quality of life, pain, psychological distress and work ability.

The trial is led by Dr Neil Basu based at the University of Aberdeen.

Current status

Ongoing

Publications and presentations

None

B.35**Making clinical trials more efficient: consolidating, communicating and improving knowledge of patient recruitment interventions****Investigators**

Heidi Gardner, Shaun Treweek, Katie Gillies, HSRU

Source and amount of HSRU funding (total funding)

University of Aberdeen Development Trust £3,000 (£3,000)

Summary

Randomised controlled trials are at the core of evidence-based healthcare; they guard against selection bias and therefore offer the fairest way of evaluating healthcare interventions. What is so surprising however, is the lack of evidence and high level of inefficiency that riddles the design and execution of trial processes.

This project will begin to tackle the problem of trial inefficiency by getting to grips with how participants are recruited into trials, ultimately aiming to improve recruitment methods in order to alleviate recruitment problems in trials on a global scale.

Study phases and objectives:

Phase 1: To consolidate existing information on participant recruitment into clinical trials.

This will involve completion of a systematic review of non-randomised evaluations of strategies to improve participant recruitment to RCTs, involvement in updating the existing Cochrane review on randomised evaluations of strategies to improve participant recruitment to RCTs, and involvement with a new Cochrane review led by NUI Galway which will look at the factors that impact participants' decisions regarding trial participation using a qualitative evidence synthesis.

Phase 2: To investigate how best to present and distribute this information for the consumption of clinical trial teams.

This phase will comprise of a semi-structured interview study with trial 'recruiters' and 'designers', generation of multiple methods of presenting recruitment evidence, and user-testing of these methods.

Phase 3: To improve the current knowledge base through facilitation of work designed to fill gaps in evidence

Supervision: Professor Shaun Treweek and Dr Katie Gillies

Current status

Phase 1: Ongoing

Phase 2: Ongoing

Publications and presentations

None

B.36**Methods for strengthening evaluation and implementation: specifying components of behaviour change interventions****Investigators**

Jill Francis, HSRU; Susan Michie, UCL; Prof Marie Johnston, IAHS/Psychology, University of Aberdeen

Source and amount of HSRU funding (total funding)

MRC £13,562 (£456,847)

Summary

The importance of behaviour change to improving health is demonstrated by increasing investment by funding bodies in developing and evaluating complex interventions to change population, patient and practitioner behaviours. The development of effective interventions is hampered by the absence of a nomenclature to specify and report their content. This limits the possibility of replicating effective interventions, synthesising evidence, and understanding the causal mechanisms underlying behaviour change. In contrast, biomedical interventions are precisely specified, e.g. the pharmacological "ingredients" of prescribed drugs, their dose and frequency of administration. For most complex interventions, the precise "ingredients" are unknown; descriptions e.g. "behavioural counselling" can mean different things to different researchers or implementers. The lack of a method for specifying complex interventions undermines the precision of syntheses of evidence of effectiveness, posing a problem for secondary, as well as primary, research. This project will develop a reliable method of specifying intervention components ("techniques") aimed at changing behaviour. This will strengthen the scientific basis for developing, evaluating and reporting complex interventions. The research builds on extensive pilot work, an identified multidisciplinary need for such a method and a large team of collaborators keen to participate in its development. Dissemination throughout the project will be by stakeholder meetings, targeted multidisciplinary workshops, conference presentations, journal publication and an interactive web-based platform.

Current status

Completed

Publications and presentations

None

B.37**Mobile Bone Density Scanning Services in the UK: an implementation and outcome evaluation****Investigators**

Rosemary Hollick, Lorna McKee, HSRU; Dr Alison Black, NHS Grampian, Professor David Reid, University of Aberdeen

Source and amount of HSRU funding (total funding)

No external funding £None

Summary

Many healthcare service delivery improvements are unsuccessful, yet there is an incomplete understanding of why many improvement initiatives fail. Despite a complex healthcare context, traditional biomedical paradigm approaches to improve healthcare persist; focusing on if interventions work rather than how and why. The influence of patients on the adoption, implementation and assimilation process is also often neglected. This thesis is based on introduction of a new mobile service, delivering osteoporosis services to remote, rural and island communities in Scotland. Similar services had been introduced elsewhere in the UK with variable success.

This study aimed to develop an empirical 'real time' integrated study of this complex, emerging cross boundary service to understand if, how and why mobile bone density scanning services work. A comparative case study design examined the adoption, implementation and assimilation of mobile DXA services across diverse contexts in the UK; three 'real-time' and three retrospective cases studies. An individual programme 'theory' was developed and tested, and evidence used to inform ongoing service development in 'real-time' cases. Mixed quantitative and qualitative methods were employed, alongside an action research informed dual implementer/evaluator role in real-time cases.

Findings suggest mobile DXA services offer an effective service delivery model. A complex interplay of contextual factors at multiple levels determined success adoption, implementation and assimilation of services. Place mattered; the 'right kind of rurality', policy and organisational context. People and effort mattered in terms of leadership, networks, individual and team capabilities and learning relationships and impact of improvement on professional working practices. A complex interplay between clinician and patient 'mindlines' contributed to a collective, iteratively developed 'knowledge in practice.' Patients were not simply passive recipients of services, but instead they made informed decisions based on their own set of 'mindlines.'

Findings have also affirmed and extended existing conceptual frameworks and theory on service implementation as well as conceptualisations of the role of context in healthcare service delivery. It has also revealed the value of upskilling clinicians in health services research methodology.

Impact: Results from this study have been used to support mobile DXA service sustainability longer term within Scotland and work is ongoing to apply contemporaneous 'real-time' evaluation of healthcare service development to a range of other complex, common services.

Current status

Completed

Publications and presentations

None

B.38**Monitoring Long Term Conditions in Primary Care****Investigators**

Louise Locock, HSRU; Rafael Perera (PI), Richard Hobbs, Richard Stevens, Jeffrey Aronson, Andrew Farmer, Carl Heneghan, Christopher O'Callaghan, Annette Pluddemann, Clare Bankhead, University of Oxford; Brian Shine, Oxford University Hospitals NHS Foundation Trust; Dan Lasserson, Birmingham; Paul Glasziou, Bond University Australia; Sula Wiltshire, Oxford Health NHS Foundation Trust

Source and amount of HSRU funding (total funding)

NIHR PGfAR £None (£1,988,812)

Summary

This NIHR programme grant involves a series of workpackages investigating the most effective ways to monitor people with chronic kidney disease and heart failure in primary care. Work includes systematic reviews, cohort studies, and qualitative interviews with patients.

<https://www.phc.ox.ac.uk/research/medical-statistics/projects/monitoring-chronic-kidney-disease-in-primary-care>

Current status

Ongoing

Key publications

Simmonds, R, Evans, J, Feder, G, Blakeman, T, Lasserson, D, Murray, E, Locock, L, Horwood, J Understanding tensions and identifying clinician agreement on improvements to early-stage chronic kidney disease monitoring in primary care: a qualitative study. *BMJ Open* 2016;6(3):e010337

Stevens, R, Evans, J, Oke, J, Smart, B, Hobbs, R, Holloway, E, Judd, M, Locock, L, McLellan, J, Perera, R Kidney age, not kidney disease. *CMAJ* 2017 (accepted for publication)

B.39**Normalization Process Theory****Investigators**

Shaun Treweek, HSRU; Tracy L Finch, Melissa Girling, Elaine McColl, Nicholas Steen, Tim Rapley, University of Newcastle; Carl R May, University of Southampton; Frances S Mair, University of Glasgow; Elizabeth Murray, University College London

Source and amount of HSRU funding (total funding)

ESCR £None (£439,350)

Summary

Innovation promises better ways of organising and delivering treatment, improvements in the clinical and cost-effectiveness of services, and reductions in the burdens of illness - especially chronic illness. Identifying and adopting an innovative health technology, or a new way of organizing professional work, is the beginning of the story, not the end. Down the line, policy-makers, managers, professionals, and patients all face two important problems as they try to get innovations into practice:

- **Process problems:** about the *implementation* of new ways of thinking, acting and organizing in health care
- **Structural problems:** about the *integration* of new systems of practice into existing organizational and professional settings.

These are important problems for researchers and evaluators too. To understand implementation and integration, we need focus on the dynamic processes that lead to innovations becoming embedded in everyday work. Normalization Process Theory is an explanatory model that helps managers, clinicians, and researchers understand these processes.

Normalization Process Theory work is led by Carl May at the University of Southampton.

The Normalization A useful paper on using Normalisation Process Theory is available at

<http://www.biomedcentral.com/1741-7015/8/63>.

Further details are available at <http://www.normalizationprocess.org>.

Current status

Completed

Key publications

Finch, TL, Rapley, T, Girling, M, Mair, FS, Murray, E, Treweek, S, McColl, E, Steen, IN, May, CR Improving the Normalisation of Complex Interventions: Measure Development based on Normalization Process Theory (NoMAD): study protocol. *Implement Sci* 2013;8:43

B.40**Participation in Physical Play in children with motor impairments****Investigators**

Niina Kolehmainen, Jill Francis, Craig Ramsay, Lorna McKee, HSRU; Christine Owen, NHS Lothian; Prof Peter Rosenbaum, McMaster University, Canada; Prof Stuart Logan, Peninsula Medical School; Dr Marjolijn Ketelaar, Utrecht, Dept of Neurology & Neurosurgery, Netherlands

Source and amount of HSRU funding (total funding)

MRC £217,409 (£217,409)

Summary

Motor impairments (e.g. difficulties with motor control, muscle tone) affect between 6-9% of children. These children are often diagnosed with conditions such as developmental coordination disorder or cerebral palsy. They experience significant difficulties in participating in everyday life and are at high risk of long-term health and social problems. Despite this high burden of disease, interventions to manage these problems have been subject to little systematic research.

This project consisted of the following five steps, and studies within them:

1. **Identify biomedical, personal and environmental factors proposed to predict children's participation in leisure pursuits and play:** (i) a systematic review of parents' views about children's participation in life at home, school and in the community; (ii) a survey of children with motor impairments regarding their participation in physical play and leisure; (iii) a survey of parents' beliefs about the same children's participation in physical play and leisure; (iv) a survey of clinicians about their views of the same children's difficulties (e.g. impairments and activity limitations); and (v) an interview study with a sub-sample of the children.
2. **Build a theoretical model of the key predictors of participation in physical play in children with motor impairments:** a synthesis of the above evidence and existing theory and evidence.
3. **Select therapeutic and behaviour change strategies to target the proposed predictors:** (i) a systematic review of the 'active ingredients' and mechanisms of change in occupational therapy and physiotherapy interventions for children with motor impairments; and (ii) use of the behaviour change matrix to select behaviour change techniques.
4. **Operationalise the strategies in a feasible and acceptable intervention:** a collaborative study with children, families and service providers.
5. **Investigate the feasibility of using the intervention in practice, and model the intervention processes and outcomes:** three mixed-methods interrupted-time-series single-case studies with children with motor impairments and with their families.

The project provided an exemplar for the development of further rehabilitation interventions.

Current status

Ongoing

Key publications and presentations

Shikako-Thomas, K, Kolehmainen, N, Ketelaar, M, Bult, M, Law, M Promoting leisure participation as part of health and well-being in children and youth with cerebral palsy. *J Child Neurol* 2014;29(8):1125-33

Kolehmainen, N, Ramsay, C, McKee, L, Missiuna, C, Owen, C, Francis, J Participation in Physical Play and Leisure in Children With Motor Impairments: Mixed-Methods Study to Generate Evidence for Developing an Intervention. *Phys Ther* 2015;95(10):1374-86

Powrie, B, Kolehmainen, N, Turpin, M, Ziviani, J, Copley, J The meaning of leisure for children and young people with physical disabilities: a systematic evidence synthesis. *Dev Med Child Neurol* 2015;57(11):993-1010

Oral presentations

McAnuff, J, Boyes, C, Kolehmainen, N. Family-centred interactions in childhood rehabilitation: a study of relational and participatory approaches. *American Academy of Cerebral Palsy and Developmental Medicine, Toronto, September 2012*

Kolehmainen, N. Goals, therapy support and education in the context of children with disabilities: sharing research and thoughts. *School of Education, University of Aberdeen, March 2013*

Kolehmainen, N. Improving rehabilitation interventions and services: sharing challenges and solutions. *Ottawa Hospitals Research Institute, Ottawa, May 2013*

Kolehmainen, N. Outcome measurement in rehabilitation: the importance and issues. *NHS Fife Child Health AHP Outcomes Day, Dunfermline May 2013*

Kolehmainen, N. Rehabilitation research through the MRC complex interventions framework: illustrations from two projects in the UK. *Hochschule für Gesundheit, Bochum, Germany, January 2013*

Kolehmainen, N. Using the MRC complex interventions framework and behavioural science to advance AHP interventions research. *Institute of Health and Society, Newcastle University, Newcastle March 2013*

B.41**Patient-centred trials (PACT): developing measures to improve the experience of people taking part in clinical trials****Investigators**

Katie Gillies, HSRU; Peter Bower, University of Manchester; Caroline Sanders, Katrina Turner, Bridget Young, Ailsa Donnelly, PPI

Source and amount of HSRU funding (total funding)

NIHR RFPB £6,722 (£149,827)

Summary

Significant effort is being expended to improve people's experience in trials, much of it through ensuring patient and public involvement (PPI) is built into trial development and delivery. However, the focus of much PPI work is on the process of patient and public *input* to trials, and less on assessing the *output* of such efforts in terms of how people experience the actual delivery of a trial. It has become clear through discussions with public contributors that failing to pay attention to how people experience trials is not acceptable. It is important that people feel valued when they take part in a trial, and that taking part is not a burden. If people have a good experience, this should encourage further participation in trials and high quality research. This will make it easier to do trials and make sure research informs clinical practice.

To improve people's experience in trials, we first need to be able to measure that experience. The aim of this study is to develop a measure of experience in trials that is reliable and valid from a scientific perspective, that is acceptable to people, and useful for those running trials.

In order to achieve this aim, this study will address the following objectives:

1. Developing the experience measure (testing questions, response options and instructions, using cognitive interviewing techniques to explore how people interpret and respond).
2. Piloting the measure – testing the measure in a number of ongoing randomised trials, across multiple sites, to assess its performance.
3. Developing guidance and materials to assist trials units, investigators and other stakeholders (e.g. CRN and HRA) to respond to feedback from the measure to improve trial delivery.

The resulting measure would be made available for use across the trials portfolio. The developed measure would not be viewed as 'necessary and sufficient' for better trials, but use of the measure alongside other 'inputs' to trial design (such as good PPI and detailed qualitative work) will add significant value and bring trialists closer to our goal of 'patient-centred' trials.

Current status

Ongoing

Publications and presentations

None

B.42**Person-centred care: conceptual understandings and practical implications****Investigators**

Vikki Entwistle, HSRU; Ian Watt, University of York; Phyllis Butow, University of Sydney

Source and amount of HSRU funding (total funding)

No external funding £None

Summary

Philosophical reflections and analyses relating to the notion of person-centred care. These draw on insights from a range of empirical projects and literatures.

Current status

Ongoing

Key publications

Entwistle, VA, Watt, IS Treating patients as persons: a capabilities approach to support delivery of person centered care. *Am J Bioeth* 2013;13(8):29-39

Entwistle, VA, Brown, RCH, Morgan, HM, Skea, ZC Involving patients in their care. *Curr Breast Cancer Rep* 2014;6(3):211-18

Lidsaar-Powell, R, Butow, PN, Charles, C, Gafu, A, Entwistle, V, Epstein, R The TRIO Framework: Conceptual insights into family caregiver involvement and influence throughout cancer treatment decision-making. *Patient Educ Couns* 2017;100(11):2035-46

Burton, C, Entwistle, V, Elliot, A, Krucien, N, Porteous, T, Ryan, M The value of different aspects of person-centred care: a series of discrete choice experiments in people with long-term conditions. *BMJOpen* 2017;7(4):e015689

Entwistle, V, Watt, IS. Patients' involvement in decision-making about their care: broadening concepts for real world contexts. In: Edwards, A, Elwyn, G and Thompson, R L *Shared Decision Making in Health Care* Oxford: Oxford University Press; 2016.

B.43**PRECIS-2. Pragmatic explanatory continuum indicator summaries****Investigators**

Shaun Treweek, HSRU; Merrick Zwarenstein, Sunnybrook Research Institute, Canada; Kirsty Loudon, Frank Sullivan and Peter Donnan, University of Dundee

Source and amount of HSRU funding (total funding)

CSO £16,467 (£36,185)

Summary

If you want to know which of two or more healthcare interventions is most effective, the randomised controlled trial is the design of choice. Randomisation, however, does not itself promote the applicability of the results to situations other than the one in which the trial was done. A tool published in 2009, PRECIS -PRagmatic Explanatory Continuum Indicator Summaries ([http://www.jclinepi.com/article/S0895-4356\(09\)00048-1/abstract](http://www.jclinepi.com/article/S0895-4356(09)00048-1/abstract)) – aimed to help trialists design trials that produced results matched to the aim of the trial, be that supporting clinical decision-making, or increasing knowledge of how an intervention works. Though generally positive, groups evaluating the tool have also found weaknesses, mainly that its inter-rater reliability is not clear, that it needs a scoring system and that some new domains might be needed.

The PRECIS-2 improved and validated a new version of PRECIS through three phases. Phase 1: brainstorming and a 2-round Delphi survey of authors who cited PRECIS, followed by user-testing of candidates for PRECIS-2. Phase 2 evaluated the validity and reliability of the most promising PRECIS-2 candidate using experienced trialists and methodologists and a selection of protocols. Phase 3 aimed to use PRECIS-2 to compare the internal validity and effect estimates a set of matched explanatory and pragmatic trials. Further details are available at www.precis-2.org.

Current status

Completed

Key publications

Loudon, K, Zwarenstein, M, Sullivan, F, Donnan, P, Treweek, S Making clinical trials more relevant: improving and validating the PRECIS tool for matching trial design decisions to trial purpose. *Trials* 2013;14:115

Loudon, K, Treweek, S, Sullivan, P, Thorpe, K, Zwarenstein, M The PRECIS-2 tool: Designing trials that are fit for purpose. *BMJ* 2015;350:h2147

Loudon, K, Zwarenstein, M, Sullivan, F, Donnan, P, Gagyor, I, Hobbelen, H, Alhabe, F, Krishnan, JA, Treweek, S The PRECIS - 2 tool has good inter - rater reliability and reasonable discriminant validity. *J Clin Epidemiol* 2017;88:113-21

Forbes, G, Loudon, K, Treweek, S, Taylor, SJ, Eldridge, S Understanding the applicability of results from primary care trials: lessons learned from applying PRECIS-2. *J Clin Epidemiol* 2017;90:119-26

Zwarenstein, M, Treweek, S, Loudon, K PRECIS-2 helps researchers design more applicable RCTs while CONSORT Extension for Pragmatic Trials helps knowledge users decide whether to apply them. *J Clin Epidemiol* 2017;84:27-29

B.44**Quality and Safety in the NHS: Evaluating Progress, Problems and Promise****Investigators**

Lorna McKee, HSRU, Micheal West, Jeremy Dawson, Aston University; Richard Lilford, University of Birmingham, Mary Dixon-Woods, Graham Martin, Madeleine Murtah, Richard Baker, University of Leicester; Patricia Wilkie, National Association for Patient Participation

Source and amount of HSRU funding (total funding)

Dept of Health Policy Research Programme £85,078 (£1,445,166)

Summary

A Department of Health commissioned project to evaluate the extent to which cultural and behavioural change is occurring in the NHS in England. The study follows on from the government's High Quality Care for All (HQCfA) agenda, which stressed the need for improved support of frontline NHS staff to provide the highest standard of care for patients.

This collaborative project between the Universities of Aberdeen, Aston, Leicester and Birmingham and the National Association for Patient Participation, led by Prof Michael West, monitored how the NHS is responding to HQCfA and made recommendations as to how higher quality of care can be achieved. It also set out detailed action plans to support implementation of these recommendations.

Current status

Completed

Oral presentations

McKee, L. Leading for quality: what makes a difference? *Quality and Safety in Health, University of Aberdeen*, 21 May 2012

B.45**Research into the Prevalence and Causes of Prescribing Errors Made by Junior Doctors****Investigators**

Jill Francis, HSRU; Prof Christine Bond, Prof Amanda Lee, Primary Care, Dr Sarah Ross, Mr James McLay, Dr Mary Joan Macleod, Prof Marie Johnston, University of Aberdeen; Prof Peter Davey, Dr Jean Ker, University of Dundee; Dr Simon Maxwell, Prof David Webb, University of Edinburgh; Dr Gerard Mackay, NHS Great Glasgow & Clyde/University of Glasgow

Source and amount of HSRU funding (total funding)

CSO £14,725 (£216,843)

Summary

The CSO funded PROTECT study investigated prescribing errors among Foundation Year doctors in Scotland. Two studies were conducted comprising: a national (Scottish) prospective observational study of prescribing errors made by hospital doctors, and interviews and questionnaires investigating F1/F2 doctors' knowledge, attitudes and experiences of prescribing errors whilst working in Scotland.

Current status

Completed

Key publications

Duncan, EM, Francis, JJ, Johnston, M, Davey, P, Maxwell, S, McKay, GA, McLay, J, Ross, S, Ryan, C, Webb, D, Bond, C, PROTECT Study Group Learning curves, taking instructions, and patient safety: using a theoretical domains framework in an interview study to investigate prescribing errors among trainee doctors. *Implement Sci* 2012;7(86):11 September 2012

Ryan, C, Ross, S, Davey, P, Duncan, EM, Fielding, S, Francis, JJ, Johnston, M, Ker, J, Lee, AJ, Macleod, MJ, Maxwell, S, McKay, G, McLay, J, Webb, DJ, Bond, C Junior doctors' perceptions of their self-efficacy in prescribing, their prescribing errors and the possible causes of errors. *Br J Clin Pharmacol* 2013;76(6):980-87

Ross, S, Ryan, C, Duncan, EM, Francis, JJ, Johnston, M, Davey, P, Fielding, S, Ker, J, Lee, AJ, Macleod, MJ, Maxwell, S, McKay, G, McLay, J, Webb, DJ, Bond, C Perceived causes of prescribing errors by junior doctors in hospital inpatients: a study from the PROTECT programme. *BMJ Qual Saf* 2013;22(2):97-102

Ryan, C, Ross, S, Davey, P, Duncan, E, Francis, JJ, Fielding, S, Johnston, M, Ker, J, Lee, AJ, Macleod, MJ, Maxwell, S, McKay, GA, McLay, JS, Webb, DJ, Bond, C Prevalence and causes of prescribing errors: The PRescribing Outcomes for Trainee Doctors Engaged in Clinical Training (PROTECT) Study. *PLoS One* 2014;9(1):e79802

B.46**SCOOP - Development of an intervention to increase physiotherapy adherence among young children with cystic fibrosis: A Medical Research Council complex intervention framework development and feasibility study****Investigators**

Shaun Treweek, HSRU; Dr Emma France, Dr Gaylor Hoskins, Prof Brian Williams, NMAHP, University of Stirling; Dr John McGhee, University of New South Wales; Prof Suzanne Hagen, NMAHP, Glasgow Caledonian University; Elain Dhouieb, NHS Lothian

Source and amount of HSRU funding (total funding)

CSO £2,898 (£169,067)

Summary

Cystic fibrosis (CF) is an inherited, life-threatening disorder of the lungs and digestive system affecting approximately 1 in 2,500 children. Chest physiotherapy is a major component in the respiratory management of CF to help prevent lung damage. Adherence in young children is important because damage occurs rapidly and can be irreversible. However, only 50% of parents and young children adhere to their recommended regimen. Interventions to address this significant problem are lacking.

SCOOP will develop and test the feasibility of a theoretically- and empirically-informed, multi-professional intervention for parents/carers to increase physiotherapy adherence among 0-8 year olds comprising of two components: 1) An audio-visual support resource to enhance parental intentions to adhere to physiotherapy; 2) A family-specific adherence plan to facilitate the translation of intentions into behavioural change. This will likely lead to a trial that should impact on patient outcomes such as decreasing the likelihood of lung damage thus potentially extending life.

SCOOP is led by Emma France at the University of Stirling.

Current status

Ongoing

Publications and presentations

None

B.47**Screening and overdiagnosis: communication and ethics****Investigators**

Vikki Entwistle, HSRU; Stacy Carter, University of Sydney; Wendy Rogers, Macquarie University

Source and amount of HSRU funding (total funding)

No external funding £None

Summary

An ongoing cluster of empirical and philosophical projects undertaken mainly in collaboration with colleagues at the University of Sydney and Macquarie University in Australia.

Current status

Ongoing

Key publications

Rychetnick, L, Carter, SM, Aberlson, J, Thornton, H, Barratt, A, Entwistle, VA, Mackenzie, G, Salkeld, G, Glasziou, P Enhancing citizen engagement in cancer screening through deliberative democracy. *J Natl Cancer Inst* 2013;105(6):380-86

Forbes, L, Ramirez, AJ, Expert group on Information about Breast Screening, [Entwistle VA] Offering informed choice about breast screening. *J Med Screen* 2014;21(4):194-200

Pickles, K, Carter, S, Rychetnick, L, Entwistle, V Doctors' perspectives on PSA testing illuminate key differences in prostate cancer screening rates between Australia and the United Kingdom: a qualitative study. *BMJ Open* 2016;6:e011932

Pickles, K, Carter, S, Rychetnick, L, McCaffery, K, Entwistle, V General Practitioners' Experiences of, and Responses to, Uncertainty in Prostate Cancer Screening: Insights from a Qualitative Study. *PLoS One* 2016: <http://dx.doi.org/10.1371/journal.pone.0153299>

Rogers, W, Craig, W, Entwistle, V Ethical issues raised by thyroid cancer overdiagnosis: a matter for public health? *Bioethics* 2017;31(8):590-98

Pickles, D, Entwistle, V Primary goals, information-giving and men's understanding: a qualitative study of Australian and UK doctors' varied communication about PSA screening. *BMJ Open* 2017 (accepted for publication)

B.48**Selective Decontamination of the Digestive tract in critically ill patients treated in Intensive Care Unit (SuDDICU)****Investigators**

Marion Campbell, Jill Francis, HSRU; Prof Brian Cuthbertson, Fiona Webster, Sunnybrook Health Sciences Centre, Canada; Karen Burns and John Marchall, St Michael's Hospital, Toronto; Deborah Cook, McMaster University; Peter Dodek, University of British Columbia; Jeremy Grimshaw, Lauralyn McIntyre, and Salman Kanji, Ottawa Hospital Research Institute; Richard Hall and Lynn Johnston, Dalhousie University, Nova Scotia; John Muscedere, Queen's University Ontario; Charles Weijer, University of Western Ontario

Source and amount of HSRU funding (total funding)

CIHR £None (Canadian \$299,050)

Summary

Hospital acquired infections are a major cause of morbidity and mortality. Critically ill patients in Intensive Care Units (ICUs) are particularly susceptible to these infections. One intervention that has gained much interest in the medical literature for reducing infection rates and deaths from hospital acquired infections is selective decontamination of the digestive tract (SDD). SDD involves the application of antibiotic pastes to the mouth, throat and stomach and a short course of antibiotics into a vein.

Previous research undertaken in HSRU (funded by NIHR) showed that there was considerable ongoing uncertainty about possible benefits and harms of SDD and that further large-scale effectiveness trials of SDD in ICUs would be required to address these uncertainties, especially the effect of SDD on antimicrobial resistance. Funding has now been received in Australia & New Zealand (from the Australian National Health and Medical Research Council) and Canada (from the Canadian Institutes of Health Research) to run international trials to a shared protocol (with a cluster-crossover design focusing on the effects of SDD on mortality and antimicrobial resistance). Patients are also being recruited from the UK. HSRU researchers are engaged in the international oversight of these trials, and also directly as co-applicants in the design, conduct and implementation of SuDDICU Canada - which is also seeking funding to undertake a parallel process evaluation.

Current status

Completed

Key publications

Cuthbertson, B, Campbell, MK, MacLennan, G, Duncan, EM, Marshall, AP, Wells, EC, Prior, ME, Todd, L, Rose, L, Seppelt, I, Bellingan, G, Francis, JJ, SuDDICU International Study Group Clinical stakeholders' opinions on the use of selective decontamination of the digestive tract in critically ill patients in intensive care units: an international Delphi study. *Crit Care* 2013;17(6):R266

Dombrowski, S, Prior, M, Duncan, EM, Cuthbertson, B, Bellingan, G, Campbell, MK, Rose, L, Binning, AR, Gordon, AC, Wilson, P, Shulman, R, Francis, J, SuDDICU Study Groups Clinical components and associated behavioural aspects of a complex healthcare intervention: Multi-methods study of selective decontamination of the digestive tract in critical care. *Aust Crit Care* 2013;26(4):173-79

Francis, JJ, Duncan, EM, Prior, ME, MacLennan, GS, Dombrowski, SU, Bellingan, G, Campbell, MK, Eccles, MP, Rose, L, Rowan, KM, Shulman, R, Wilson, APR, Cuthbertson, BH Selective decontamination of the digestive tract in critically ill patients treated in Intensive Care Units: a mixed-methods feasibility study (the SuDDICU study). *Health Technol Assess* 2014;18:25