YORK TRIALS UNIT

CELEBRATING 21 YEARS

1996 - 2017

REFLECTIONS ON THE PAST,
AND PROJECTIONS FOR THE FUTURE

This unit receives National Institute for Health Research CTU Support Funding. This funding has been awarded to support the unit in developing and supporting NIHR trials.
Welcome to our 21st Anniversary celebrations. Professor Ian Russell founded the Trials Unit in 1996 and echoing our earliest studies we continue to undertake large, national, complex trials that have a major impact on clinical practice. One of the ‘foundation’ trials included UK BEAM, which was a large, highly complex factorial trial of different treatments for low back pain. With over 1300 participants it remains, one of the largest RCTs of treatments for back pain ever completed with major impact on clinical practice across the world. We have continued to build our portfolio in this area, leading and supporting other high profile trials in back pain and other musculoskeletal conditions. Another, early, trial that helped establish our reputation and interests in the field of addiction and mental health was the UKATT trial of a behavioural intervention for the treatment of alcohol problems. A constant feature of our trials is methodological innovation, for example, YTU was one of the first trial units to introduce ‘distance’ randomisation (in 1998) to avoid the problem of subversion bias as used in the Vein Graft Surveillance trial. When the Trials Unit was founded there was no medical school consequently we have had to seek clinical and other collaborators more nationally, which is still reflected in our current portfolio of work.
Today

With over 60 current members of staff delivering 40 ongoing studies we are a UK Clinical Research Collaboration registered trials unit. We are also one of only seven Royal College of Surgeons registered trials unit and consequently one of our largest programmes of work is around orthopaedic and trauma trials. We have a programme of non-health care trials, particularly in education and criminal justice, and we have hosted for 12 years the Annual Conference of RCTs in the Social Sciences. We maintain the use of innovative or unusual designs including: cluster (shoulder pain, education), split plot (education, shoulder pain), partial split plot (mental health), Zelen’s method (lung cancer screening), randomised cohort (back pain and falls prevention), factorial (education, back pain), preference (most trials), unequal allocation (shoulder surgery), database (compression after surgery), adaptive (criminal justice), placebo (osteoarthritis), multi armed (neck pain trial), stepped wedge (probation office and prison trials), cross-over (rheumatoid arthritis), as well as the ‘standard’ two-armed pragmatic trial. Our main source of trial funding is from the National Institute of Health Research (NiHR), which also supports us with an infrastructure award and other sources representing the diverse nature of our work including: the Medical Research Council, Charities, Educational Endowment Foundation, Department of Health, the EU, and the Home Office. Our partnerships with colleagues in the NHS, public health, social care and the social sciences have been central to our success. Our ground breaking trials would not be possible without the expertise and commitment of our staff.
Roles: The Software Development team offer essential support to each trial managed by the York Trials Unit through the design, creation and maintenance of our web-based data management systems. These systems allow users to: randomise and manage participants; record and review data collection and participant contact; manage trial sites; and export data.

Responsibilities: These systems allow users to: randomise and manage participants; record and review data collection and participant contact; manage trial sites; and export data.

Data Management

Roles:
- Lead Data Manager
- Data Managers
- Assistant Data Manager
- Research Data Administrators
- Data Administrators
- Data Assistants

Responsibilities: The Data Management team provide a range of vital services within the York Trials Unit such as: offering data related advice on all phases of data collection; designing data collection tools; and coordinating large-scale mail-outs of trial documentation. Data returned to the Unit are entered into a bespoke database through either scanning - using a data capture system - or manual entry. Entered data are checked for accuracy, and any anomalies generate a query resolution process. This team also ensure data are stored according to current legislation and best practice.

Senior Management Team

Roles:
- Director
- Deputy Director
- Senior Research Fellows
- Unit Manager
- Group Administrator

Responsibilities: The Senior Management Team are responsible for the overall running, management and strategic planning of the York Trials Unit. This team also actively foster crucial links with other research groups, institutions and organisations.

Statistics and Health Economics

Roles:
- Deputy Director
- Senior Statisticians
- Statisticians
- Trainee Statisticians
- Health Economists

Responsibilities: Statisticians and Health Economists have a range of important responsibilities including: contributing to the design and analysis of trials in funding applications; developing statistical and economic analysis plans; reviewing and approving data collection forms; preparing reports for Trial Steering Committee and Data Monitoring Committee meetings; undertaking final analysis; and contributing to the writing up of research for publication. Prior to final analysis, collected data undergo a cleaning process to detect and correct or remove any invalid, contradicting or infeasible records to ensure the data accurately reflect the information provided by participants and are suitable for analysis.

Trial Management and Coordination

Roles:
- Trial Managers
- Trial Coordinators
- Trial Support Officers

Responsibilities: A Trial Management and Coordination team is assigned to each trial managed by York Trials Unit. This team works collaboratively with internal and external colleagues to: design the trial; write grant applications, the trial protocol, and any other trial-specific documentation; prepare data collection tools; gain ethical and other necessary regulatory approvals; plan and manage day-to-day coordination of the trial; undertake monitoring of trial sites; and contribute to writing up and disseminating research findings.

Software Development

Roles:
- Lead Software Developer
- Software Developer

Responsibilities: The Software Development team offer essential support to each trial managed by the York Trials Unit through the design, creation and maintenance of our web-based data management systems. These systems allow users to: randomise and manage participants; record and review data collection and participant contact; manage trial sites; and export data.

Group Administration

Roles:
- Group Administrator
- Assistant Group Administrator

Responsibilities: The Group Administration team provide valuable administrative support to the York Trials Unit Senior Management Team and all York Trials Unit trials, organise the Unit’s courses and conferences, and provide administrative support to the National Institute for Health Research (NIHR) Research Design Service Yorkshire and the Humber (RDS YH) and the British Orthopaedic Association (BOA).

Presented at the YTU 21st Anniversary Event, University of York.

Acknowledgements: Thank you to YTU staff, past and present for all the hard work and dedication that goes into every aspect of producing the high quality trials the unit is known for. Here’s to the next 21 years.
21 Trials at 21 Years
York Trials Unit Highlights

Prepared by Matt Northgraves, Thrimon Moe Byrne, Alison Booth and David Torgerson, York Trials Unit, Department of Health Sciences, University of York

Selected YTU ‘Studies Within A Trial’

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<td>VenUS II: a randomised controlled trial of two types of bandage for treating venous leg ulcers</td>
<td>Mitchell et al 2012; 21 Trials at 21 Years</td>
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Selected YTU ‘Social Science Trials’

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<td>Intervention</td>
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<td>Every child counts</td>
<td>Torgerson C et al, 2014</td>
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<td>Citizenship for probation officers</td>
<td>Pearson et al 2011</td>
</tr>
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<td>Improving writing quality</td>
<td>Torgerson C et al, 2014</td>
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Five most highly cited methodological publications (ranked by citations adjusted since publication)

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<th>Citations</th>
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<td>Torgerson D, Torgerson C. 2008</td>
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Congratulations and thank you to everyone involved in the work of YTU over the last 21 years.

Presented at the YTU 21st Anniversary Event, University of York.
Surgical Wounds Healing By Secondary Intention (SWHSI)

**Aims/Objectives:** To better understand surgical wounds healing by secondary intention (SWHSI), effective treatments and the value and nature of further research.

**Methods:** York Trials Unit delivered the inception cohort and pilot, feasibility randomised controlled trial for this programme. Patients with a SWHSI were recruited for both, with patients randomised 1:1 to Negative Pressure Wound Therapy (NPWT) or Usual care in the pilot, feasibility study.

A cross sectional survey, qualitative interviews and cost effectiveness analyses were also completed for this programme.

**Outcomes:**
- Cohort study - Wound healing occurred at a median of 86 days (95% CI: 75 to 103). Baseline wound area (p<0.01), surgical contamination (p=0.04) and infection at any time (p<0.01) were found to predict prolonged healing.
- Pilot, feasibility RCT - 248 patients screened for eligibility and 40 participants recruited and randomised to receive NPWT or Usual Care (no NPWT). It is feasible to complete a full RCT for the effectiveness of NPWT as a treatment for SWHSI.

**Outputs:** Pilot, feasibility protocol published (Trials: 2016;17:535). Cited in 1 article.

**Impact:** Application submitted for further funding to complete a large RCT, building on the results of the pilot, feasibility study.

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Aspirin for venous leg ulcers – The AVURT Randomised Controlled Trial

**Aims/Objectives:** To examine whether aspirin, additional to standard care, is effective for venous leg ulcer healing, is safe to use in patients with leg ulcers and whether recruitment to a larger study is possible.

**Methods:** A phase II, double-blind, parallel group, placebo controlled randomised controlled trial. Participants were randomised 1:1 to receive either 300mg of aspirin once daily or placebo in addition to standard care (compression therapy).

**Outcomes:** A total of 27 patients (target 100 patients) were recruited from 10 centres across the UK. There was no evidence of a difference in time to healing of the reference ulcer following adjustment for ulcer area and duration (hazard ratio 0.58, 95% CI: 0.18 to 1.85; p=0.357). One expected, serious adverse event, related to aspirin, was recorded.

**Outputs:** Protocol paper published (Trials: 2015, 16:513). Cited in 1 article.

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Venous Leg Ulcer Randomised Controlled Trials

**VenUS II**

**Aims/Objectives:** To compare the effectiveness of larval therapy with standard debridement for the healing of venous leg ulcers.

**Methods:** A pragmatic, 3-arm, randomised controlled trial. Participants were randomised to receive loose larvae, bagged larvae, or hydrogel.

**Outcomes:** A total of 267 participants were recruited and randomised. Time to healing did not differ between groups, even when prognostic and stratification factors were adjusted for.

There was no statistically significant difference in patient quality of life or QALYS. Considerable uncertainty was observed in relation to incremental cost effectiveness ratios.

**Outputs:** Results published (British Medical Journal 2009, doi.org/10.1136/bmj.b773). Cited in 177 articles.

**VenUS III**

**Aims/Objectives:** To compare the effectiveness of low dose ultrasound, additional to standard care, for the treatment of hard to heal venous leg ulcers.

**Methods:** A multi-centre, pragmatic, 2-arm, randomised controlled trial. Participants were randomised to receive low dose ultrasound plus standard care, or standard care alone.

**Outcomes:** A total of 337 participants were recruited and randomised. Time to healing did not differ between groups, even when prognostic factors were adjusted for.

Ultrasound therapy was found to be more costly and did not provide any benefit over standard care.

**Outputs:** Results published (British Medical Journal 2011, doi.org/10.1136/bmj.d1092). Cited in 42 articles.

**Economic results** published (British Medical Journal, 2011, 98(8), 1099-1106. Cited in 10 articles.

York Trials Unit have also completed the Venus I and Venus IV trials (British Journal of Surgery 2004, 91 (10), 1292-9; The Lancet 2014, 383 (9920), 871-9).

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**Acknowledgements:** AVURT – Funded by the NIHR HTA Programme (13/87/08); SWHSI – Funded by the NIHR R&D Programme (RP-PG0609-10)71); VenUS II – Funded by the NIHR HTA Programme (01/41/04); VenUS III – NIHR HTA Programme (02/37/03)


Presented at the YTU 21st Anniversary Event, University of York.
Overview
York Trials Unit has a long history of successfully completing randomised controlled trials in the area of musculoskeletal medicine. The discipline of musculoskeletal medicine employs a wide range of interventions which is reflected in the suite of trials currently ongoing or previously completed within the team, working with a range of clinical, charitable and academic partners.

Pharmacological interventions
Working with the charity sector
Optimising therapeutic agents in the NHS

HERO
Hydroxychloroquine Effectiveness in Reducing symptoms of hand Osteoarthritis trial (HERO)
(Protocol paper: Kingsbury et al, 2013, Trials, Vol 14 Issue 64)

PROMOTE
Pain Reduction with Oral Methotrexate in knee osteoarthritis, a pragmatic phase III trial of Treatment Effectiveness (PROMOTE)
(Protocol paper: Kingsbury et al, 2015, Trials, Vol 16 Issue 77)

Screening programmes
A pragmatic randomised controlled trial of the effectiveness and cost-effectiveness of screening older women for the prevention of fractures (SCOOP)
(Study website: http://www.scoopstudy.ac.uk)

Falls prevention
Interventions to enhance the lives of patients and professionals

Does Slip Resistant Footwear Reduce Slips Among Healthcare Workers? A Randomised Controlled Trial (SSHEW) (On-going trial)

Occupational Therapist Intervention Study (OTIS): Does Occupational Therapist led home environmental assessment and modification reduce falls among high risk older people?
(On-going trial. Study summary: on HRA Research Summaries website)

Bandage and support
Innovations to improve function

A Randomised Controlled Trial of the Effect of a Two-layer Compression Bandage System on Knee Function Following Total Knee Arthroplasty (KREBS)
(On-going trial. Study website: https://krebsnhs.weebly.com/)

Orthotics for Knee Instability
Orthotic management of instability of the knee related to neuromuscular and central nervous system disorders: systematic review, qualitative study, survey and costing analysis (OKIS)
(Study report: O’Connor et al, 2016, HTA Report Vol 20 Issue 55. Project blog:
https://kneearthotics.blogspot.co.uk/)

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Presented at the YTU 21st Anniversary Event, University of York.
Surgical Trials at York Trials Unit

Prepared by Stephen Brealey and Catriona McDaid, York Trials Unit, Department of Health Sciences, University of York

Lead Collaborating Institutions: South Tees Hospitals NHS Foundation Trust; University Hospitals of Leicester NHS Trust; Hull and East Yorkshire Hospitals NHS Trust; Barts Health NHS Trust; Northumbria Healthcare Foundation Trust; and Oxford University Hospitals NHS Foundation Trust.

Does surgery work better than non-surgical treatment?

**DISC**
RCT comparing injections of collagenase with surgical correction in the treatment of patients with moderate Dupuytren's contracture.

**PRESTO**
RCT of the feasibility of undertaking surgery compared with non-operative management for patients with stable thoracolumbar fractures.

**PROFHER**
RCT comparing surgical (usually nails and plates) with non-surgical treatment (sling immobilisation) in adult patients with displaced fractures of the proximal humerus (upper arm bone).

**SWIFFT**
RCT comparing plaster cast with surgical fixation in adult patients with a fracture across the waist of the scaphoid bone in the wrist.

Which surgery works best?

**ACTIVE**
RCT comparing internal plate fixation with external frame for patients with an ankle fracture that involves the joint.

**UK FROST**
RCT comparing two types of surgical procedures (manipulation under anaesthesia vs key hole surgery) with physiotherapy and steroid injection in patients with a frozen shoulder.

Three-armed trials

**PROFHER 2**
RCT comparing two types of surgery (reverse shoulder arthroplasty vs hemiarthroplasty) with non-surgical care in patients with complex fractures of the proximal humerus.

How do you improve pathways for surgical patients?

**KREBS**
RCT comparing standard wool with two layer compression bandage for patients having a total knee replacement.

**OPAL**
Development and testing of an occupation advice intervention for patients undergoing hip and knee replacements.

Introducing some of the staff working on surgical trials at YTU:

**Trial design/Methodologists**
Catriona McDaid, David Torgerson

**Trial Management and Co-ordination**
(Top left: Puvan Tharmanan, Stephen Brealey, Liz Cook, Catherine Arundel, Matt Northgraves, Adwoa Parker, Michelle Watson)

**Statistics/Health Economics**
Catherine Hewitt, Ada Keding, Belen Corbacho

Presented at the YTU 21st Anniversary Event, University of York.
What is a SWAT?

- A Study Within A Trial (SWAT) is a methodological study which aims to generate new knowledge to improve the design and delivery of future trials.
- In a SWAT, an intervention to improve the conduct of a trial is tested in the context of an ongoing trial. This forms the most rigorous evaluation of such interventions.
- SWATs can be randomised trials themselves (i.e. trial within a trial) or non-randomised evaluations, such as comparing electronic data collection methods alongside existing paper based data collection.

About YTU’s programme of SWATs

Our programme of SWATs aims to add to the evidence base for trial methodology, particularly the conduct and delivery of trials through the successful recruitment and retention of trial participants.

To date we have undertaken more than 20 SWATs focusing on recruitment, retention and data collection methods.

- Successful recruitment is critical for trials, yet 50% of all trials fail, leading to research waste and delays in generating evidence.
- Poor retention in trials makes it difficult to draw meaningful conclusions.

Recruitment interventions

Our programme of work aims to develop and test interventions to enhance participant recruitment into trials. We have published 5 SWATs focused on testing common interventions for recruiting participants using:

1. Post-it® notes
2. Advertising patient and public involvement in trials
3. Optimised participant information leaflets
4. Envelope colour (brown vs. white)
5. A pre-notification leaflet

All these SWATs found that these interventions DID NOT increase participant recruitment rates into trials, meaning trial teams can STOP USING THEM.

We have 3 ongoing SWATs which are testing recruitment interventions focused on a redesigned participant information sheet; using pens as an incentive; and remove versus on site initiation visit.

Retention interventions

One of the common problems that researchers face is losing participants in trials, either from loss to follow up or from participants withdrawing. We have published four SWATs of trial retention interventions and currently have four other SWATs ongoing.

We have found the following interventions are effective for increasing retention in trials:

1. Electronic prompts
2. Pens enclosed in questionnaires
3. Prior notification using a newsletter

Improving data collection methods

We have published 2 SWATs focused on improving data collection methods and are currently undertaking two more SWATs.

Our published SWATs have found that automated text messaging services offer a feasible and acceptable way of collecting trial data and monitoring depression in trials.
Health Outcomes

YTU have been involved in a number of RCTs which have investigated the effectiveness of a range of interventions which aim to improve health outcomes but are delivered in community settings, such as schools and mosques. Here are a few examples:

- **MCLASS**: Muslim Communities Learning About Second-hand Smoke (Shah et al 2015)
- **BRIGHT Trial**: Brushing Reminder 4 Good oral HealTh: The clinical and cost-effectiveness of a Short Messaging Service behaviour change programme to improve the oral health of young people living in deprived areas (Barber et al 2015)
- **Preschoolers in the Playground**: a pilot cluster randomised controlled trial of a physical activity intervention for children aged 18 months to 4 years (Barber et al 2015)

Policing/Crime and Justice

A randomised controlled trial of a mental health training package for frontline police officers, co-produced with North Yorkshire Police

Educational Interventions and/or Educational Outcomes

The last 10 years have seen rapid growth in educational interventions being evaluated using the RCT method in the UK. The York Trials Unit have been at the forefront in this field; conducting over 20 RCTs of educational interventions. Here are just some!

- **Independent Evaluation of Every Child Counts**. Three RCTs investigated the effect of Numbers Count delivered on a one to one basis and delivered in small groups, which showed moderate short term impacts on the maths attainment of children aged 6 to 7 (Torgerson et al 2013).

- **Efficacy trial among Year 6/7 pupils, of a self-regulated strategy development (SRSD) instruction intervention combined with ‘memorable’ experiences which showed a large improvement on writing (effect size 0.75) (Torgerson et al 2014).**

- **Ongoing effectiveness trial evaluating the impact of ReflectED (whole school intervention focussing on metacognition skills) on maths attainment in Key Stage 2 and Key Stage 1.**

- **YTU are now conducting two scaled up effectiveness trials to evaluate the impact of the intervention when rolled out at scale.**

- **Ongoing trial evaluating Online Maths Tuition intervention on maths attainment of Year 6 pupils.**

- **With thanks to the wide variety of academic and education based partners we have worked with and funders including NIHR, EEF and MRC.**

Presented at the YTU 21st Anniversary Event, University of York.

References


Carole J. Torgerson, Andy Wiggins, David J. Torgerson , Hannah Ainsworth ,Catherine Hewitt & on behalf of the Every Child Counts independent evaluation team (2013). The effectiveness of an intense individual tutoring programme (Numbers Count) delivered individually or to small groups of children: a randomised controlled trial, Effective Education, DOI:10.1080/19415532.2013.778591

**Mental Health and Addiction in the UK**

It is estimated that 23% of the UK population is directly affected by mental health problems at some point each year; however, research in this area (including research on substance misuse and addiction) receives only 5.5% of the total UK health research spend.¹

The total annual cost to society of alcohol-related harm is estimated to be £21bn and the NHS incurs £3.5bn a year in costs related to alcohol.² Modelling has shown that over the next five years, alcohol will be accountable for £17 billion in costs to the NHS (including £685 million in cancer treatment costs), 63,000 deaths and 4.2 million hospital admissions.³

In 2016, 15.5% of adults aged 18+ in England were found to be current smokers, down from 19.9% in 2010.⁴ However, there were estimated to be around 474,000 hospital admissions attributable to smoking in 2015/16 (an increase of 4% from 2005/06) and just under 11% of mothers were recorded as being smokers at the time of their baby’s delivery.⁵

**York Trials Unit’s contribution to the research in these areas**

Over the years, York Trials Unit has been involved in a large number of trials into treatments for mental health conditions, substance misuse and addiction, collaborating with a wide range of institutions and organisations. These trials have covered a range of age groups, acknowledging the wide ranging impact and scale of the se problems. Detailed below is just a small selection of those, including some currently ongoing.

**How can we help women quit smoking during Pregnancy?**

- MiQuit 3 (text messages)
- CPIT III (financial incentives)

**Ten percent of Children and Young People aged 5-16 suffer from a clinically significant mental health illness, with the most common problems being conduct disorders, attention deficit hyperactivity disorder, anxiety, depression and autism spectrum disorders.⁶⁷**

- cCBT (depression)
- ASSIST (autism)
- Y-SBNT (substance misuse)
- E-PlaYS (social communication impairment)

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**References**


Presented at the YTU 21st Anniversary Event, University of York.
**Yoga for Chronic Low Back Pain**

**Aims/Objectives:** To compare the effectiveness of yoga and usual care for chronic or recurrent low back pain.

**Methods:** A two-armed randomised controlled trial. Participants were randomised to receive a 12-class progressive yoga programme, delivered by 12 teachers over 3 months or usual care.

**Outcomes:** A total of 313 participants were randomised. The yoga group had better back function compared to the control group as measured on the RMDQ at 3 (-2.17 (-3.31 to -0.3) P value <0.001), 6 (-1.48 (-2.62 to -0.33) p value 0.011) and 12 (-1.57 (-2.71 to -0.42) p value 0.007) months. The differences were statistically significantly and in the range of clinical importance.


**Related publications:** Pilot trial, protocol, compliance effects and cost-effectiveness results *Spine*. 2012;37(18):1593-1601. Citations: 37

**Impact:** NICE guideline 59 2016

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**Acupuncture for IBS**

**Aims/Objectives:** To compare the effectiveness and cost-effectiveness of acupuncture for irritable bowel syndrome (IBS).

**Methods:** A two-armed pragmatic randomised controlled trial. Participants were randomised to receive 10 weekly individualised acupuncture sessions plus usual care or usual care.

**Outcomes:** A total of 233 patients had IBS for an average duration of 13 years. The acupuncture group had a reduction in IBS symptoms as measured on the IBS Symptom Severity Score at 3 months -27.43 (95%CI: -48.66 to -21, p=0.012). This benefit persisted at 6, 9 and 12 months. NNT for successful treatment (≥50 point reduction in the IBS SSS) was 6 (95% CI: 3 to 17).

**Output:** Clinical results MacPherson et al, 2012 *BMC Gastroenterology* 12:150

**Related publications:** Protocol MacPherson et al, 2010 *BMC Gastroenterology* 10:63

**Citations:** 13 Cost effectiveness results Stamuli et al 2012 *BMC Gastroenterology* 12:150

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**United Kingdom back pain exercise and manipulation trial (UKBEAM)**

**Aims/Objectives:** To estimate the effect of adding exercise classes, spinal manipulation delivered in NHS or private premises, or manipulation followed by exercise to “best care” in general practice.

**Methods:** Three by two factorial randomised controlled trial. Chiropractors, osteopaths, and physiotherapists provided manipulation for back pain.

**Outcomes:** A total of 1334 patients were randomised. Relative to “best care” in general practice, manipulation followed by exercise achieved a moderate benefit at 3 months and a small benefit at 12 months. Exercise achieved a small benefit at three months.


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**Acupuncture and Alexander Technique for neck pain (ATLAS)**

**Aims/Objectives:** To compare the effectiveness and cost-effectiveness of Alexander Technique lessons or acupuncture vs usual care for chronic, non-specific neck pain.

**Methods:** A three-armed randomised controlled trial. Participants were randomised to receive 12 acupuncture sessions, or 20 one-to-one AT lessons (both 600 minutes total) plus usual care or usual care.

**Outcomes:** A total of 517 patients had median duration of neck pain of 6 years. Between-group reductions in NPSQ score at 12 months versus usual care were 3.92 percentage points for acupuncture (95% CI, 0.97 to 6.87 %points, p=0.009) and 3.79 %points for AT (CI, 0.91 to 6.66 %points, p=0.010). Acupuncture and AT both led to significant reductions in neck pain.


**Citations:** 23 Related publications: Protocol and cost-effectiveness results (accepted for publication)

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**Acupuncture and counselling for depression in Primary Care (AcuDep)**

**Aims/Objectives:** To compare the effectiveness acupuncture and counselling for patients who continue to experience depression.

**Methods:** A three-armed trial. Participants were randomised to receive 12 weekly sessions of acupuncture or 12 weekly sessions of one-to-one counselling or usual care.

**Outcomes:** A total of 755 patients were randomised. Compared to usual care there was a statistically significant reduction in mean PHQ-9 depression scores at 3 months for acupuncture (-2.46, 95% CI -3.72 to 1.21) and counselling (-1.73, 95% CI 3.00 to -0.45) and at 12 months. Differences between acupuncture and counselling were not significant.


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*Presented at the YTU 21st Anniversary Event, University of York.*
The PROFHER story

Surgical vs Nonsurgical Treatment of Adults with Displaced Fractures of the Proximal Humerus

Produced by Stephen Brealey, York Trials Unit, Department of Health Sciences, University of York

Background to PROFHER

- Proximal humeral fractures (upper arm bone) account for 5% to 6% of all adult fractures.
- A Cochrane review found insufficient evidence from RCTs to conclude whether surgery (such as plates and screws) produces better outcomes than nonsurgical treatment (immobilisation with a sling) for the management of these fractures.
- In response to a Researcher led call, PROFHER commenced in 2008 with funding from the NIHR Health Technology Assessment Programme to address this uncertainty.
- 250 patients (mean age, 66 years) and presenting within 3 weeks of their fracture at one of 32 UK NHS hospitals were randomised between September 2008 and April 2011.
- Patients were followed up for 2 years (up to April 2013) with 231 included in the primary analyses using the Oxford Shoulder Score.

Main findings of the PROFHER Trial

During the 2-year period:

- surgery did not produce better outcomes than non-surgical treatment using a patient-reported measure (the Oxford Shoulder Score)\(^1\)
- surgery cost more on average (£1758) per patient when compared with non-surgical treatment\(^2\)

Study within the PROFHER Trial

- “Away Days” are well established to encourage engagement with site personnel.
- We found no evidence that an Away Day for PROFHER improved the number of patients screened or recruited at participating sites.\(^3\)
- This is important for informing the future design and conduct of Away Days.

Impact of PROFHER Trial

- High impact publication in JAMA (March 10, 2015)\(^1\)
- Long term follow-up funded that found the findings at two years were unchanged at five years\(^4\)
- Informed NICE guidelines on “Non-complex fractures” (NG38: February 2016)
- Responses from a survey of 265 surgeons who treated these type of patients found that around half (137) had changed practice to various extents because of PROFHER\(^5\)

PROFHER 2

- PROFHER found that the majority of displaced fractures of the proximal humerus can be treated without surgery.
- However, there is still uncertainty about the management of patients with the most complex fractures; especially with the increasing use of a new surgical method: reverse shoulder arthroplasty.
- PROFHER 2 is funded by the NIHR HTA programme to investigate: does either of two methods of shoulder replacement produce better outcomes?; and does either surgery work better than not operating?

References:

Acknowledgements: We are grateful for the funding of this project by the NIHR Health Technology Assessment programme (project number 06/404/502) and the Sponsor of the project, Teesside University.

Disclaimer: The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Ethics approval: York Research Ethics Committee (reference 08/H1311/12).
Co-production of Policing Evidence, Research and Training: Focus Mental Health

Poster produced by Arabella Scantlebury and Alison Booth, York Trials Unit, Department of Health Sciences, University of York

CO-PRODUCTION OF EVIDENCE

The Co-production of policing evidence, research and training: focus mental health (the Connect project) was a collaboration between North Yorkshire Police and researchers from across the University of York.

Together, the Connect team co-produced evidence to help improve outcomes for victims, suspects, witnesses or others who come into contact with the Police and who have a mental vulnerability.

CONNECT PROJECT WORKSTREAMS

<table>
<thead>
<tr>
<th>Workstream</th>
<th>Aim:</th>
<th>Department</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic and Scoping reviews</td>
<td>A series of systematic and scoping reviews on mental health and policing</td>
<td>York Trials Unit</td>
</tr>
<tr>
<td>Randomised Controlled Trial</td>
<td>A randomised controlled trial to assess the effectiveness of a new face-to-face mental health training intervention compared with a ‘business as usual’ control group of police officers.</td>
<td>York Trials Unit, Department of Social Policy and Social Work</td>
</tr>
<tr>
<td>Understanding partnerships</td>
<td>Gather data to build up an understanding of the current policing practices and their institutional relationships with other agencies in the delivery of mental health services.</td>
<td>Department of Politics, York Management School</td>
</tr>
<tr>
<td>Research methods training</td>
<td>Provide a one-day course in introductory research methods to managers and senior managers within North Yorkshire Police with the aim of building sustained capability among NYP officers and staff to understand, critique and use research.</td>
<td>Department of Social Policy and Social Work, Institute for Effective Education, Department of Health Sciences</td>
</tr>
</tbody>
</table>

Impact:

Findings from the Connect project are being widely disseminated to relevant audiences using a range of outputs tailored to the needs and understanding of the audience. Outputs include academics papers; evidence briefings; final report to funders; website summaries; oral and poster presentations; stakeholder events; advisory group discussions.

“We are now planning to expand the training across the force to all our frontline staff, from offices on the beat to our Force Control Room.” It is anticipated that the training will also inform the next review of national guidance for training police officers in their approach to individuals who may have mental health problems.

Deputy Chief Constable Lisa Winward, of North Yorkshire Police

Core aims of the Connect project

- Enable frontline staff to better identify need and demand in relation to victims and offenders who would benefit from accessing mental health services
- Develop proper internal processes and multi-agency agreements which make it simple for staff to support victims/offenders to access the correct mental health services
- To support appropriate diversion from the criminal justice system
- Reduce mental health related repeat incidence
- Reduce the use of section 136 (taking people to a place of safety)
- Better use of data, particularly North Yorkshire police data, to better understand demand and to determine the commission of local NHS provision
- To change the culture in relation to dealing with mental health issues on the ground

YORK TRIALS UNIT WORKSTREAMS:

Systematic and scoping reviews

YTU and NYP undertook reviews on mental health and policing related to:

- Training programmes: What evidence is there evaluating the effectiveness of a mental health training packages for non-mental health professionals whose work brings them in contact with people with mental health problems.
- Inter-agency collaboration: What evidence is there evaluating and describing inter-agency collaboration between the police and other organisations for people who appear to be suffering from mental health disorder.

Randomised Controlled Trial

YTU conducted a pragmatic, cluster randomised controlled trial to evaluate the effectiveness of a bespoke mental health training package for frontline police officers, relative to routine training. The training package was developed by colleagues in the Department of Social Policy and Social Work and was informed by our systematic review of mental health training.

The trial found that a specialised mental health training program did not reduce the number of reported incidents after six months, but may positively affect how police officers record incidents involving mental health and their knowledge, attitudes and confidence in responding to mental health incidents.

www.connectebp.org
@connectebp

The Connect project is funded by the Higher Education Funding Council for England (HEFCE) and the Home Office through the College of Policing

Presented at the YTU 21st Anniversary Event, University of York.
Methodological Studies at York Trials Unit
Prepared by Liz Cook and David Torgerson,
York Trials Unit, Department of Health Sciences,
University of York

Presented at the YTU 21st Anniversary Event, University of York.

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TRIAL DESIGN

Designing trials in health, education and the social sciences: An Introduction (Torgerson D, Torgerson C, 2008)
This book focuses on the design of rigorous trials, exemplifying their use in health, education and criminal justice research. It also includes a detailed description of randomisation procedures and different trial designs alongside their application to different social science settings.

Evidence For Risk Of Bias In Cluster Randomised Trials (Puffer et al, 2003)
Retrospective review of cluster randomised trials that had been published in 3 major journals. Cluster trials are vulnerable to the risk of bias. Careful planning and execution of such trials can avoid these biases.

Methodological Bias In Cluster Randomised Trials (Hahn et al, 2005)
Cluster randomised trials were sampled from a recent review and from a systematic review of hip protectors. Suggestions for mitigating biases associated with the use of cluster designs proposed.

Systematic review of stepped wedge cluster randomized trials shows that design is particularly used to evaluate interventions during routine implementation (Mdege et al, 2011)
Systematic review describing the application of the stepped wedge cluster randomized controlled trial (CRCT) design. For most of the included studies, there was a belief or empirical evidence suggesting that the intervention would do more good than harm. There was variation in data analysis methods and insufficient quality of reporting.

RECRUITMENT

Increasing recruitment to randomised trials: a review of randomised controlled trials (Watson & Torgerson, 2006)
This systematic review of controlled trials on recruitment methods was undertaken in order to identify strategies that are effective. Effective interventions included: telephone reminders; questionnaire inclusion; monetary incentives; using an ‘open’ rather than placebo design; and making trial materials culturally sensitive

Bias In Identifying And Recruiting Participants In Cluster Randomised Trials: What Can Be Done? (Eldridge et al, 2009)
Methods paper describing how bias may occur when individual participants are identified or recruited in cluster randomised trials and how it can be avoided.

The following ‘Studies Within a Trial’ have been conducted to address the some of the findings:

A randomized, embedded trial of pre-notification of trial participation did not increase recruitment rates to a falls prevention trial (Arundel et al, 2016)

Using short information leaflets as recruitment tools did not improve recruitment: A randomized controlled trial (Brierley et al, 2012)

ATTRITION

Reporting attrition in randomised controlled trials (Hewitt et al, 2010)
Meta-analyses using the mean difference at baseline between the trial arms were carried out using individual patient data from a convenience sample of 10 trials to evaluate whether the level of baseline imbalance was associated with the level of attrition. Although, in theory, attrition can introduce selection bias in randomised trials, the authors did not find sufficient evidence to support this claim in the sample of trials.

Attrition in randomised trials (Dumville et al, 2006)
Methods paper discusses the effect of loss to follow up on trial findings. The authors make a case for being explicit about loss to follow up in reporting.

The following ‘Studies Within a Trial’ have been conducted to address the some of the findings:

Electronic prompts significantly increase response rates to postal questionnaires: a randomized trial within a randomized trial and meta-analysis (Clark et al, 2015)

Randomized trial within a trial of yellow ‘post-it notes’ did not improve questionnaire response rates among participants in a trial of treatments for neck pain (Tilbrook et al, 2014)
Leishmania Vaccination (LEISH 1, LEISH 2a/2b)

**Objective:** To assess the safety and immunogenicity of a new Leishmania vaccine candidate (ChAd63-KH)

**Methods:**
- Phase I: A open label, single arm, two stage design, with 20 healthy volunteers in UK.
- Phase Ila: A open label, single arm, three stage design, with 24 patients with persistent PKDL (Post-kala-azar dermal leishmaniasis) in Sudan.
- Phase IIb: A randomised, three arm trial to evaluate the efficacy of ChAd63-KH and ChAd63-KH and low dose AmBisome in 90 patients with persistent PKDL in Sudan.

**Primary Outcomes:**
- Phase I and IIb: Safety (Adverse events)
- Phase Ila: Efficacy (Cure and severity of PKDL)

**Secondary Outcomes:** Immunogenicity (markers of humoral and cell-mediated immunity); reversion of Visceral Leishmaniasis; severity of PKDL.

**Study Status:**
- Phase Ila: Currently open to recruitment
- Phase IIb: To commence following Phase Ila results.

Tobacco Cessation within TB Programmes

**Objective:** To assess the effectiveness and cost effectiveness of Cytisine for smoking cessation in patients with tuberculosis who smoke tobacco on a daily basis.

**Methods:** A double blind, randomised, parallel group, placebo controlled trial. Eligible participants with pulmonary TB will be randomised to receive Cytisine or Placebo for 25 days. The study will recruit 2,388 participants in Bangladesh and Pakistan over a 10 month recruitment period.

**Primary Outcome:** Biochemically verified, continuous abstinence from tobacco at six months, using Russell Standard Criteria. Where smokeless tobacco is used, verification will also be completed using cotinine dip stick tests.

**Secondary Outcomes:** Continuous abstinence at 12 months, lapse and relapses; Clinical TB outcomes; Nicotine dependency and withdrawal; Adverse events

**Study Status:** The TB and Tobacco Trial is currently open to recruitment. Up to 14th November 2017, 1,168 of 2,388 participants have been recruited.

STRATEGIC – A cluster randomised trial of strategies to increase uptake amongst young women invited for their first cervical screen

**Objective:** To assess the feasibility and effectiveness of interventions to increase cervical screening uptake in young women.

**Methods:** A phase two phase, cluster randomised trial.
- Phase 1: UK Women, due for initial invitation to cervical screening, in practices randomized to intervention received a pre-invitation leaflet. The sub group women were also randomised to access to an online booking system.
- Phase 2: Non-attenders were randomized to receive: vaginal self-sample kits; timed appointments; nurse navigator; or a choice between nurse navigator or self-sample kits.

**Outcomes:**
- In Phase 1, 20, 879 women were randomised. The pre-invitation leaflet did not increase uptake (18.8% vs 19.2%) nor did access to online booking (17.8% vs 17.2%).
- In Phase 2, 10, 126 women were randomised. Sending self sample kits and timed appointments increased uptake at 12 months (OR 1.51, 95% CI 1.20 to 1.91, p = 0.001; OR 1.41, 95% CI 1.14 to 1.74, p = 0.001)


Yorkshire Lung Screening Trial (YLST)

**Objective:** To assess participation rates of a community-based lung cancer screening programme.

**Methods:** A two arm, single consent, Zelen’s randomised controlled trial in 62,980 current or ex-smokers aged 55-80 years and registered with a GP in Leeds. The intervention is invitation to telephone-based risk-assessment for a lung health check and the control receive no invitation. Telephone responders at high risk will be offered LDCT screening for lung cancer in the community on a mobile van.

**Primary Outcomes:** Participation rates; Performance of risk criteria for identifying population for lung screening; Effectiveness of intervention for reducing incidence of late stage lung cancer.

**Secondary outcomes:** Health economic outcomes; Screening programme performance indicators; Smoking cessation rates

**Study Status:** In set up, ethical approval being sought. Expected to recruit from June 2018.
Forthcoming Events

• Second International Conference on Stepped Wedge Trial Design - 19 - 20 March 2018
• 13th Annual Randomised Controlled Trials in the Social Sciences – 5 – 7 September 2018

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