Clinical Research Network
West Midlands

NHS
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Summary of Study Results for Primary Care

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Introduction

Over the past decade, more than 200 practices within the area covered by the CRN West Midlands South, i.e. Coventry, Warwickshire, Worcestershire and Herefordshire, have been active in recruiting to at least one research study taking place within a primary care setting. To date there have been more than 13,000 local patients included in research studies, a magnificent achievement.

The topics covered by these studies includes:

- Management of lower back pain
- Smoking cessation initiatives
- Blood pressure control
- Self-monitoring in diabetes control
- Targeted identification and treatment of COPD
- Diagnosis and treatment of UTIs in children

This research generated a number of high profile publications, and has contributed to important changes in the way patients are treated in primary care.

As part of our commitment to research, and to thank all the practices and CCGs who have assisted us, we are pleased to provide a short digest of publications resulting from some studies that involved local patients. We hope you may find it of interest.

Contents

Study Results

1. PRIMIT

Aim: The PRIMIT study examined the effectiveness of a web-based programme, aiming to reduce the transmission of respiratory infections by encouraging more frequent hand-washing.

Method: Across three winters from January 2011 to March 2013, in the midst of the season for flu and other respiratory infections, 20,066 adult patients aged 18 years and older took part from 344 general practices across the UK. Volunteers were randomly assigned access to the PRIMT website or no intervention. Participants were followed for 16 weeks and questionnaires were used to measure episodes of respiratory infections, duration of symptoms, and to check whether other household members had a similar illness.
The programme consisted of four weekly sessions which encourage users to plan and learn how to use simple techniques to avoid catching and passing on viruses, monitor handwashing behaviour and provide tailored feedback.

Results/conclusion: At 16 weeks, 4,242 individuals (51%) in the PRIMIT group reported at least one respiratory infection compared with 5,135 individuals (59%) in the control group, equivalent to a 14% reduction in risk. There was a similar reduction in transmission of viruses to family members.

The risk of catching a flu-like illness was about 20% lower in the PRIMIT group compared to the control group, as was the risk of getting a gastrointestinal infection (diarrhoea, or diarrhoea and vomiting). The need for primary care consultations and antibiotic prescriptions were also reduced by 10-15%.

Importance: The first worldwide study to show that handwashing can reduce respiratory infections within the home – not only for the person who washes their hands but also for the other family members.

In non-pandemic years this effective web-based programme could have an important effect in reduction of infection transmission and is likely to help during a pandemic.

Publication: The Lancet Volume 386, No. 10004, p1631-1639, 24 October 2015

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2. Morning versus Afternoon Flu Vaccination

Aim: To examine whether diurnal variations in immune responses might extend to the antibody response to vaccination.

Method: 24 general practices in the West Midlands, UK, were analysed between 2011 and 2013 in a cluster-randomised trial during the annual UK influenza vaccination programme.

276 adults aged over 65 were vaccinated against three strains of influenza, either in morning surgeries (09:00 - 11:00) or afternoon surgeries (15:00 - 17:00).

Results/conclusion: In two of the three given influenza virus strains, those in the morning cohort saw a significantly larger increase in antibody concentration one month following vaccination, when compared with those in the afternoon cohort. In the third strain, there was no significant difference between morning and afternoon vaccination.

Importance: Administering vaccinations in the morning, rather than the afternoon, could induce greater, and thus more protective, antibody responses. Thus by 'shifting the time of those vaccinations to the morning we can improve their efficiency with no extra cost to the health service'.

Publication: "Morning vaccination enhances antibody response over afternoon vaccination: a cluster-randomised trial," by Joanna E Long, Mark T Drayson, Angela E Taylor, Kai M Toellner, Janet M Lord, and Anna C Phillips*, online in Vaccine on 26 April 2016, published by Elsevier, with the DOI:10.1016/j.vaccine.2016.04.032

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3. STarT Back

Aim: To test the main hypothesis that a stratified approach to primary care management for low back pain results in clinical and economic benefits compared with current best practice.

Method: 1573 adults (aged ≥18 years) with back pain (with or without radiculopathy) consultations at ten general practices in England responded to invitations to attend an assessment clinic. Eligible participants were randomly assigned by use of computer-generated stratified blocks with a 2:1 ratio to intervention or control group. Primary outcome was the effect of treatment on the Roland Morris Disability Questionnaire (RMDQ) score at 12 months.

Results/conclusion: 851 patients were assigned to the intervention (n=568) and control groups (n=283). Overall, adjusted mean changes in RMDQ scores were significantly higher in the intervention group than in the control group at 4 months and at 12 months. At 12 months, stratified care was associated with a mean increase in generic health benefit (0·039 additional QALYs) and cost savings (£240·01 vs £274·40) compared with the control group.

Importance: The STarT Back approach uses a simple tool to match patients to treatment packages appropriate to them. This has been shown to significantly decrease disability from back pain; reduce time off work and save money by making better use of health resources**.** The IMPaCT study showed that this approach can be successfully embedded into normal primary care.

Publication: The Lancet Volume 378, No. 9802, p1560–1571, 29 October 2011

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4. COPERS

Aim: A pragmatic RCT to establish the effectiveness and cost-effectiveness of a new self-management (COPERS) course for those with chronic MSK pain, versus usual care plus a CD recording of simple relaxation exercises

Method: Nationally 700 patients (388 from West Midlands South) from primary, intermediate and secondary care services in NE London and Coventry & Warwickshire.

Intervention*:* Used psychological approaches shown to promote behaviour change e.g. pain education, attention control, relaxation and visualisation techniques, social interaction and new activity unrelated to pain. Learning was facilitated through group discussion, an educational DVD, role play, attention and distraction techniques and 'good' posture.
The course lasted 15 hours over 3 days, with a 2 hour follow-up session 2 weeks later. It was delivered by trained facilitators- a healthcare professional (physiotherapist, osteopath, chiropractor, occupational health practitioner or psychologist) and a lay person with experience of living with chronic pain.

Control*:* An audio CD of breathing and relaxation sequences to practise at least 1/day for 3 weeks (same duration as intervention) and as often as they liked thereafter and a booklet, 'The Pain Toolkit'.

Results/conclusion: After 6 months those who attended the COPERS course were coping with their pain better, had more self-confidence, were less depressed and anxious and more socially integrated than those who did not. At 1 year post-receiving intervention, they were still less depressed and more socially engaged than those who had not. The COPERS course did not make any difference to 'function despite pain' or health care utilisation.

Importance: Using the group based COPERS course enabled people to discuss their conditions and learn non-drug pain management techniques which helped psychological wellbeing. The study team hope that the course will be introduced into the NHS as they also found that it was cost-effective.

Publication: Study Protocol published BMJ Open 2013; 3:e002492
Final results due to be published with JAMA)

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5. TASMIN-SR

Aim: To determine the effect of self-monitoring with self-titration of antihypertensive medication versus usual care on SBP among patients with CVS disease, diabetes, or CKD.

Method: 540 patients (57 patients recruited from West Midlands South) aged > 35 years with a history of stroke, coronary heart disease, diabetes, or CKD baseline BP > 130/80 mm Hg treated at 59 practices between March 2011 and January 2013.

Intervention - Self-management*:* Patients were trained to self-monitor BP using a validated monitor, with self-titration of medication following a predetermined plan. BP was taken twice/morning for the first week of each month using simple colour-coded instructions. ≥ 4 BP readings recorded above target during the measurement week for 2 consecutive months led to a change in medication according to the algorithm.

For very high or very low readings (BP>180/100 mm Hg or <100 mm Hg systolic), patients were told to contact their practice. GPs were informed of any medication change.

Control - Usual care: Patients booked a routine BP check and medication review with their GP.BP measurement, BP targets, or adjustment of medication for these patients were at the discretion of GP.

Results/conclusion: Primary outcome was the BP at the 12-month visit. Data was available on 450 patients (81%). Baseline characteristics were well-matched. The mean baseline BP was 143.1 / 80.5mmHg in the intervention group and 143.6 / 79.5mmHg in the control group.

At 12 months, mean BP was less in the intervention group (Intervention group: 128.2 / 73.8mmHg and control group: 137.8 / 76.3mmHg) with a difference of 9.2 mmHg (95%CI, 5.7-12.7) in systolic and 3.4 mmHg (95%CI, 1.8-5.0) in diastolic following correction for baseline BP.

In both groups the numbers and doses of medications were increased, but significantly more in intervention group although there was no significant difference in adverse effects between the groups. The main changes were in prescription of calcium channel blocker and thiazides.
In conclusion clinically significant reductions in SBP and DBP without any increase in adverse events were achieved and the results were sustained over the 12 month trial.

Importance: Self-monitoring and self-titrating antihypertensive medication in patients with hypertension at high risk of CVD is feasible. Patients at high risk of CVD whose BP is not optimally controlled should be considered for self- management.

Publication: JAMA August 27, 2014, Vol 312, No. 8

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6. BP-ETH

Aim: To investigate whether ethnicity influences BP measured in clinic and by ambulatory BP monitoring (ABPM) in individuals with and without a diagnosis of hypertension.

Method: A primary care observational study (2010-12) of 28 practices involving 770 patients (White British, South Asian, African Caribbean) from Central England.

Results/conclusion: BP differences between ethnic groups where BP is carefully measured on multiple occasions are small and unlikely to alter clinical management. When BP is measured casually on a single occasion or in routine care, differences appear that could approach clinical relevance and affect clinical management.

Importance: The study emphasizes the importance of careful BP measurement irrespective of ethnic group and suggests that where this is not undertaken, erroneous difference may occur which could impact clinical decisions.

Publication: Martin et al Am J Hypertension 2014; DOI:10.1093/ajh/hpu 211
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7. OPERA – Older Peoples Exercise in Residential Accommodation

Aim: To test whether moderate intensity exercise reduces depressive symptoms in residents of care homes

Method: A cluster randomised controlled trial – in NE London; Coventry and Warwickshire. 78 care homes with 891 residents ≥65 years.
Intervention: Depression awareness training for care-home staff, 45 min physiotherapist-led exercise session twice per week and whole home encouragement in more physical activity.
Control: Depression awareness training only.

Results/conclusion: The primary outcome was the number of depressive symptoms on the GDS-15 over 12 months. The results showed no significant impact on depressive symptoms.

Importance: A very robust study which obtained a clear answer to the research question. Future research should consider evaluating a multifactorial intervention targeted specifically at care home residents with depression.

Publication: Underwood et al., 2013 Lancet; 382: 41-9.

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8. TXT2STOP

Aim: To assess the effect of an automated smoking cessation programme delivered via mobile phone text messaging on continuous abstinence.

Method: A RCT of 5800 smokers who were willing to make a quit attempt. 2915 smokers were allocated to the txt2stop intervention and 2885 were allocated to the control group.

Intervention*:* A mobile phone text messaging smoking cessation programme comprising of motivational messages and behavioural-change support. The group received five text messages per day for the first five weeks, then three per week for the next 26 weeks. They also had the option of texting the word 'crave' or 'lapse' to receive an instant message of support when a craving struck.

Control*:* Text messages were sent unrelated to quitting.

Results/conclusion: The primary outcome was self-reported continuous smoking abstinence, biochemically verified at 6 months. This was available for 5524 (95%) participants. Biochemically verified continuous abstinence at 6 months was significantly increased, double in fact, in the txt2stop group (10·7% txt2stop vs 4·9% control).

Importance: A very successful study with an intervention that is cost effective, easy to replicate and has been proven to work well across all age and social groups. It is now available as part of the NHS SMOKEFREE campaign.

Publication: The Lancet Volume 378, No.9785, p 49-55, 2 July 2011

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9. ESTEEM

Aim: To assess the effectiveness and cost consequences of GP-led and nurse-led telephone triage compared with usual care for patients seeking same-day consultations in primary care.

Method: A cluster RCT and economic evaluation between March 1, 2011, and March 31, 2013, at 42 practices in four centres in the UK. Practices were randomly assigned (1:1:1) to GP-led triage, nurse-led computer-supported triage, or usual care. Patients who telephoned the practice seeking a same-day face-to-face consultation with a GP were included.

Results/conclusion: The primary outcome was primary care workload (patient contacts, including those attending accident and emergency departments) in the 28 days after the first same-day request. 42 practices were randomly assigned to GP triage (n=13), nurse triage (n=15), or usual care (n=14), and 20 990 patients (n=6695 vs 7012 vs 7283) were randomly assigned, of whom 16, 211 (77%) patients provided primary outcome data.
GP triage was associated with a 33% increase in the mean number of contacts per person over 28 days compared with usual care (2·65 [SD 1·74] vs 1·91 [1·43]); and nurse triage with a 48% increase (2·81 [SD 1·68]). Although triage interventions were associated with increased contacts, estimated costs over 28 days were similar between all three groups (roughly £75 per patient).

Importance: Evidence supporting the use of telephone triage to manage workload in primary care has been scarce until this study was undertaken. Although the introduction of GP-led or nurse-led telephone triage was associated with an increase in the number of primary care contacts in the 28 days after the first same-day request, costs were similar to those of usual care. The study team concluded that 'telephone triage might be useful in aiding the delivery of primary care' but that the whole-system implications should be assessed when introducing such a system.

Publication: The Lancet Volume 384, No. 9957, p1859–1868, 22 November 2014

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10. PAST-BP

Aim: An open label RCT to assess whether using intensive BP targets leads to lower BP in a community population of people with prevalent cerebrovascular disease.

Method: The study ran in 99 general practices throughout England recruited from 2009-11. Participants included people with a history of stroke or transient ischaemic attack whose SBP was 125 mm Hg or above.

Intervention*:* Intensive SBP target (<130 mm Hg or 10 mm Hg reduction from baseline if this was <140 mm Hg) or standard target (<140 mm Hg).

Control*:* Participants were allocated to the standard target of < 140mm Hg.
Apart from the different target, patients in both arms were actively managed in the same way with regular reviews by the primary care team (practice nurse to monitor the BP and a GP responsible for modifying BP treatment). The practice nurse saw all patients at three month intervals (if their BP was below target) or after one month (if previous BP was above target). The research nurse (separate to the practice nurse) measured participant's BP at baseline, six and twelve months. GPs were provided with treatment protocols that reflected national guidelines at the time of the trial and had access to a computer based algorithm that actively suggested drugs and dosage if the participant was above target.

Results/conclusion: Primary outcome measure was a change in SBP between baseline and 12 months. 529 patients (mean age 72) were enrolled, 266 to the intensive target arm and 263 to the standard target arm. 379 were included in the primary analysis (182 (68%) intensive arm; 197 (75%) standard arm).

Treatment to a more intensive target was associated with a significantly greater reduction in SBP at 12 months but associated with increased workload (one extra consultation a year each for GP and nurses) but not more side effects, although more changes to treatment occurred because of side effects during the trial.

In the intensive target arm mean SBP dropped by 16.1 mm Hg to 127.4 mm Hg. In the standard arm it reduced by 12.8 mm Hg to 129.4 mm Hg (difference between groups 2.9 (95% confidence interval 0.2 to 5.7) mm Hg; P=0.03).

Aiming for a SBP target below 130 mm Hg rather than 140 mm Hg in people with cerebrovascular disease in primary care led to a small additional reduction in BP. Furthermore, active management was associated with clinically important reductions in blood pressure in both arms—the 13 mm Hg reduction achieved in the below 140 mm Hg arm equates to more than 40% and 20% reduction in the risk of stroke and coronary heart disease respectively

Importance: Decreasing BP after stroke is associated with a lower risk of stroke recurrence, but uncertainty exists about what the target BP should be. This trial showed that patients set a target of <130 mm Hg or a 10 mm Hg reduction if initial BP was <140 mm Hg achieved lower SBPs than those set a target of <140 mm Hg. However, the difference (about 3 mm Hg) in the context of the reductions seen in both arms (13mm Hg and 16 mm Hg) was small. Active management of BP after stroke/transient ischaemic attack is more important than the target that is set.

Publication: BMJ 2016;352:i708

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11. DUTY – Diagnosis of Urinary Tract infection in Young children

Aim: To develop algorithms to accurately identify pre-school children in whom urine should be obtained; assess whether or not dipstick urinalysis provides additional diagnostic information; and model algorithm cost-effectiveness

Method: One hundred and seven clinical characteristics (index tests) were recorded from the child's past medical history, symptoms, physical examination signs and urine dipstick test. Prior to dipstick results clinician opinion of UTI likelihood ('clinical diagnosis') and urine sampling and treatment intentions ('clinical judgement') were recorded. All index tests were measured blind to the reference standard, defined as a pure or predominant uropathogen cultured at ≥ 10^5 colony-forming units (CFU)/ml in a single research laboratory. Urine was collected by clean catch (preferred) or nappy pad. Index tests were sequentially evaluated in two groups, stratified by urine collection method: parent-reported symptoms with clinician-reported signs, and urine dipstick results. Diagnostic accuracy was quantified using area under receiver operating characteristic curve (AUROC) with 95% confidence interval (CI) and bootstrap-validated AUROC, and compared with the 'clinician diagnosis' AUROC. Decision-analytic models were used to identify optimal urine sampling strategy compared with 'clinical judgement'.

Results/conclusion: A total of 7163 children were recruited, of whom 50% were female and 49% were < 2 years old. Culture results were available for 5017 (70%); 2740 children provided clean-catch samples, 94% of whom were ≥ 2 years old, with 2.2% meeting the UTI definition. Among these, 'clinical diagnosis' correctly identified 46.6% of positive cultures, with 94.7% specificity and an AUROC of 0.77 (95% CI 0.71 to 0.83). Four symptoms, three signs and three dipstick results were independently associated with UTI with an AUROC (95% CI; bootstrap-validated AUROC) of 0.89 (0.85 to 0.95; validated 0.88) for symptoms and signs, increasing to 0.93 (0.90 to 0.97; validated 0.90) with dipstick results. Nappy pad samples were provided from the other 2277 children, of whom 82% were < 2 years old and 1.3% met the UTI definition. 'Clinical diagnosis' correctly identified 13.3% positive cultures, with 98.5% specificity and an AUROC of 0.63 (95% CI 0.53 to 0.72). Four symptoms and two dipstick results were independently associated with UTI, with an AUROC of 0.81 (0.72 to 0.90; validated 0.78) for symptoms, increasing to 0.87 (0.80 to 0.94; validated 0.82) with the dipstick findings. A high specificity threshold for the clean-catch model was more accurate and less costly than, and as effective as, clinical judgement. The additional diagnostic utility of dipstick testing was offset by its costs. The cost-effectiveness of the nappy pad model was not clear-cut.

Importance: Clinicians should prioritise the use of clean-catch sampling as symptoms and signs can cost-effectively improve the identification of UTI in young children where clean catch is possible. Dipstick testing can improve targeting of antibiotic treatment, but at a higher cost than waiting for a laboratory result. Future research is needed to distinguish pathogens from contaminants, assess the impact of the clean-catch algorithm on patient outcomes, and the cost-effectiveness of presumptive versus dipstick versus laboratory-guided antibiotic treatment.

Publication: **doi: 10.1370/afm.1954** Annals of Family Medicine **July/August 2016** vol. 14 no. 4 **325-336** **http://www.annfammed.org/content/14/4/325**

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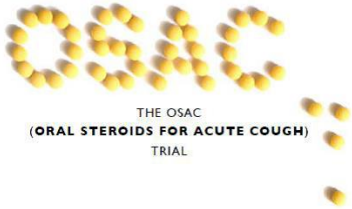
12. OSAC

Aim: The majority of UK adults experience at least one lower respiratory tract infection (LRTI, or acute bronchitis) a year. Despite an absence of evidence in this patient group, some GPs prescribe inhaled or oral corticosteroids. OSAC sought to demonstrate 'proof of concept' symptomatic effectiveness of a moderate dose of oral corticosteroid for adults without asthma or COPD with acute LRTI.



Method: OSAC was a double blind, placebo controlled RCT set in GP practices in England, powered to investigate if oral prednisolone reduces the duration of moderately bad or worse cough and/or the severity of its associated symptoms, when compared to placebo, by at least 20%. Adults (≥18 years) with acute (≤28 days) cough, for whom same-day antibiotics were not clinically indicated, and without asthma or COPD, received 40 mg oral prednisolone or matched placebo for 5 days. Symptom diaries, completed for up to 28 days, measured two primary outcomes: the duration of moderately bad or worse cough; and the average severity of all symptoms on days 2 to 4 on a scale of 0–6. We sought to demonstrate a minimum clinically important reduction of 20% in each outcome.

Results/conclusion: 398 participants were randomised to either prednisolone or placebo tablets (198 and 200 respectively) from 54 UK primary care sites. Attrition was lower than expected, giving over 85% power for the two primary outcomes. Data were analysed on an intention-to-treat basis. The median duration of moderately bad or worse cough was 5 days in both groups (IQRs 2–8 and 3–8 for prednisolone and placebo respectively). Adjusting for trial centre and baseline characteristics, this gave a hazard ratio of 1.11 (95% CI 0.89 to 1.39, p = 0.35). Symptom severity was lower in the prednisolone group (mean 1.99 vs 2.16), adjusted difference -0.090 (-0.212 to 0.003, p = 0.152).

Publication: *Thorax* 2015;70:A50 doi:10.1136/thoraxjnl-2015-207770.93

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13. WALKING

Aim: Perceived behavioural control (PBC) is a consistent predictor of intentions to walk more. A previously successful intervention to promote walking by altering PBC has been adapted for delivery in general practice. This study aimed to evaluate the effect of this intervention on Theory of Planned Behaviour (TPB) constructs in this context.

Method: Cluster randomized controlled trial, with *n* = 315 general practice patients. Practice nurses and Healthcare Assistants delivered a self-regulation intervention or information provision (control). Questionnaires assessed TPB variables at baseline, post-intervention, 6 weeks and 6 months. Walking was measured by pedometer.

Results/conclusion: The control group reported significantly higher subjective norm at all follow-up time points. There were no significant differences between the two groups in PBC, intention, attitude or walking behaviour. TPB variables significantly predicted intentions to walk more, but not objective walking behaviour, after accounting for clustering. The lack of effect of the intervention was probably due to a failure to maintain intervention fidelity, and the unsuitability of the behaviour change techniques included in the intervention for the population investigated.

Importance: This previously successful intervention was not successful when delivered in this context, calling into question whether practice nurses are best placed to deliver such interventions.

Publication: Williams, SL et al. The effects of a brief intervention to promote walking on Theory of Planned Behavior constructs: A cluster randomized controlled trial in general practice. Patient Educ Couns (2015) http://dx.doi.org/10.1016/j.pec.2015.01.010

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14. ICCD

Aim: Configuring high quality care for the rapidly increasing number of people with type 2 diabetes (T2D) is a major challenge worldwide for both providers and commissioners. In the UK, about two thirds of people with T2D are managed entirely in primary care, with wide variation in management strategies and achievement of targets. Pay for performance, introduced in 2004, initially resulted in improvements but disparities exist in ethnic minorities and the improvements are levelling off. Community based, intermediate care clinics for diabetes (ICCDs) were considered one solution and are functioning across the UK. However, there is no randomised trial evidence for the effectiveness of such clinics.

Method: This is a cluster-randomised trial, involving 3 primary care trusts, with 49 general practices randomised to usual care (n = 25) or intervention (ICCDs; n = 24). All eligible adult patients with T2D were invited; 1997 were recruited and 1280 followed-up after 18-months intervention. Primary outcome: achievement of all three of the NICE targets [(HbA1c#7.0%/53 mmol/mol; Blood Pressure ,140/80 mmHg; cholesterol ,154 mg/dl (4 mmol/l)]. Primary outcome was achieved in 14.3% in the intervention arm vs. 9.3% in the control arm (p = 0.059 after adjustment for covariates). The odds ratio (95% CI) for achieving primary outcome in the intervention group was 1.56 (0.98, 2.49). Primary care and community clinic costs were significantly higher in the intervention group, but there were no significant differences in hospital costs or overall healthcare costs. An incremental cost-effectiveness ratio (ICER) of +£7,778 per QALY gained, indicated ICCD was marginally more expensive at producing health gain.

Results/conclusion: Intermediate care clinics can contribute to improving target achievement in patients with diabetes. Further work is needed to investigate the optimal scale and organisational structure of ICCD services and whether, over time, their role may change as skill levels in primary care increase.

Publication: Wilson A, O'Hare JP, Hardy A, Raymond N, Szczepura A, et al. (2014) Evaluation of the Clinical and Cost Effectiveness of Intermediate Care Clinics for Diabetes (ICCD): A Multicentre Cluster Randomised Controlled Trial. PLoS ONE 9(4): e93964. doi:10.1371/journal.pone.0093964 http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0093964

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15. BEST

Aim: Low-back pain is a common and costly problem. We estimated the eff ectiveness of a group cognitive behavioural intervention in addition to best practice advice in people with low-back pain in primary care.

Method: In this pragmatic, multicentre, randomised controlled trial with parallel cost-eff ectiveness analysis undertaken in England, 701 adults with troublesome subacute or chronic low-back pain were recruited from 56 general practices and received an active management advisory consultation. Participants were randomly assigned by computergenerated block randomisation to receive an additional assessment and up to six sessions of a group cognitive behavioural intervention (n=468) or no further intervention (control; n=233). Primary outcomes were the change from baseline in Roland Morris disability questionnaire and modifi ed Von Korff scores at 12 months. Assessment of outcomes was blinded and followed the intention-to-treat principle, including all randomised participants who provided follow-up data. This study is registered, number ISRCTN54717854

Results/conclusion: 399 (85%) participants in the cognitive behavioural intervention group and 199 (85%) participants in the control group were included in the primary analysis at 12 months. The most frequent reason for participant withdrawal was unwillingness to complete questionnaires. At 12 months, mean change from baseline in the Roland Morris questionnaire score was 1·1 points (95% CI 0·39–

1·72) in the control group and 2·4 points (1·89–2·84) in the cognitive behavioural intervention group (difference between groups 1·3 points, 0·56–2·06; p=0·0008).

The modified Von Korff disability score changed by 5·4% (1·99–8·90) and 13·8% (11·39–16·28), respectively (diff erence between groups 8·4%, 4·47–12·32; p<0·0001). The modified Von Korff pain score changed by 6·4% (3·14–9·66) and 13·4% (10·77–15·96), respectively (difference between groups 7·0%, 3·12–10·81; p<0·0001). The additional quality-adjusted life-year (QALY) gained from cognitive behavioural intervention was 0·099; the incremental cost per QALY was £1786, and the probability of cost-effectiveness was greater than 90% at a threshold of £3000 per QALY. There were no serious adverse events attributable to either treatment.

Publication: Lancet 2010; 375: 916–23 Published Online February 26, 2010 DOI:10.1016/S0140-6736(09)62164-4

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16. BLISS

Aim: The aim of this programme is to recruit a unique UK primary care COPD cohort, as a platform for testing novel health service interventions resulting in patient benefit, both within this proposal and in future outside the programme. The cohort will comprise both new and existing cases of COPD recruited using the local PCRN-CE network of general
practices, and will also reflect the ethnic diversity of the West Midlands.

BLISS
Birmingham Lung Improvement Studies

Method: In this cluster-randomised controlled trial, participating general practices in the West Midlands, UK, were randomly assigned (1:1), via a computer-generated block randomisation sequence, to either a targeted case-finding group or a routine care group. Eligible patients were ever-smokers aged 40–79 years without a previously recorded diagnosis of COPD. Patients in the targeted case-finding group were further randomly assigned (1:1) via their household to receive either a screening questionnaire at the general practitioner (GP) consultation (opportunistic) or a screening questionnaire at the GP consultation plus a mailed questionnaire (active). Respondents reporting relevant respiratory symptoms were invited for post-bronchodilator spirometry. Patients, clinicians, and investigators were not masked to allocation, but group allocation was concealed from the researchers who performed the spirometry assessments. Primary outcomes were the percentage of the eligible population diagnosed with COPD within 1 year (defined as post-bronchodilator forced expiratory volume in 1 s [FEV_1] to forced vital capacity [FVC] ratio <0·7 in patients with symptoms or a new diagnosis on their GP record) and cost per new COPD diagnosis. Multiple logistic and Poisson regression were used to estimate effect sizes. Costs were obtained from the trial. This trial is registered with ISRCTN, number ISRCTN14930255.

Results/conclusion: From Aug 10, 2012, to June 22, 2014, 74 818 eligible patients from 54 diverse general practices were randomly assigned and completed the trial. At 1 year, 1278 (4%) cases of COPD were newly detected in 32 789 eligible patients in the targeted case-finding group compared with 337 (1%) cases in 42 029 patients in the routine care group (adjusted odds ratio [OR] 7·45 [95% CI 4·80–11·55], p<0·0001). The percentage of newly detected COPD cases was higher in the active case-finding group (822 [5%] of 15 378) than in the opportunistic case-finding group (370 [2%] of 15 387; adjusted OR 2·34 [2·06–2·66], p<0·0001; adjusted risk difference 2·9 per 100 patients [95% CI 2·3–3·6], p<0·0001). Active case finding was more cost-effective than opportunistic case finding (£333 *vs* £376 per case detected, respectively).

Importance: In this well-established primary care system, routine practice identified few new cases of COPD. An active targeted approach to case finding including mailed screening questionnaires before

spirometry is a cost-effective way to identify undiagnosed patients and has the potential to improve their health.

Publication: Lancet Vol. 4, No. 9 18th July 2016 ; Published Online September DOI: http://dx.doi.org/10.1016/S2213-2600(16)30149-7

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17. Rapid Reduction

Aim: To examine the success of quitting smoking by gradual compared with abrupt quitting.

Method: Participants quit smoking abruptly or reduced smoking gradually by 75% in the 2 weeks before quitting. Both groups received behavioural support from nurses and used nicotine replacement before and after quit day.

The primary outcome measure was prolonged validated abstinence from smoking 4 weeks after quit day. The secondary outcome was prolonged, validated, 6-month abstinence.

Results/conclusion: At 4 weeks, 39.2% (95% CI, 34.0% to 44.4%) of the participants in the gradual-cessation group were abstinent compared with 49.0% (CI, 43.8% to 54.2%) in the abrupt-cessation group (relative risk, 0.80 [CI, 0.66 to 0.93]). At 6 months, 15.5% (CI, 12.0% to 19.7%) of the participants in the gradual-cessation group were abstinent compared with 22.0% (CI, 18.0% to 26.6%) in the abrupt-cessation group (relative risk, 0.71 [CI, 0.46 to 0.91]). Participants who preferred gradual cessation were significantly less likely to be abstinent at 4 weeks than those who preferred abrupt cessation (38.3% vs 52.2%; *P* = 0.007).

Importance: Quitting smoking abruptly is more likely to lead to lasting abstinence than cutting down first, even for smokers who initially prefer to quit by gradual reduction.

Publication: Gradual Versus Abrupt Smoking Cessation: A Randomized, Controlled Non-inferiority Trial, Ann Intern Med. 2016;164(9):585-592. doi:10.7326/M14-2805
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18. SCOT

Aim: Selective cyclooxygenase-2 inhibitors and conventional non-selective non-steroidal anti-inflammatory drugs (nsNSAIDs) have been associated with adverse cardiovascular (CV) effects. We compared the CV safety of switching to celecoxib vs. continuing nsNSAID therapy in a European setting.

Method: Patients aged 60 years and over with osteoarthritis or rheumatoid arthritis, free from established CV disease and taking chronic prescribed nsNSAIDs, were randomized to switch to celecoxib or to continue their previous nsNSAID. The primary endpoint was hospitalization for non-fatal myocardial infarction or other biomarker positive acute coronary syndrome, non-fatal stroke or CV death analysed using a Cox model with a pre-specified non-inferiority limit of 1.4 for the hazard ratio (HR).

Results/conclusion: In total, 7297 participants were randomized. During a median 3-year follow-up, fewer subjects than expected developed an on-treatment (OT) primary CV event and the rate was similar for celecoxib, 0.95 per 100 patient-years, and nsNSAIDs, 0.86 per 100 patient-years (HR = 1.12, 95% confidence interval, 0.81–1.55; P = 0.50). Comparable intention-to-treat (ITT) rates were 1.14 per 100 patient-years with celecoxib and 1.10 per 100 patient-years with nsNSAIDs (HR = 1.04; 95%

confidence interval, 0.81–1.33; P = 0.75). Pre-specified non-inferiority was achieved in the ITT analysis. The upper bound of the 95% confidence limit for the absolute increase in OT risk associated with celecoxib treatment was two primary events per 1000 patient-years exposure. There were only 15 adjudicated secondary upper gastrointestinal complication endpoints (0.078/100 patient-years on celecoxib vs. 0.053 on nsNSAIDs OT, 0.078 vs. 0.053 ITT). More gastrointestinal serious adverse reactions and haematological adverse reactions were reported on nsNSAIDs than celecoxib, but more patients withdrew from celecoxib than nsNSAIDs (50.9% patients vs. 30.2%; P < 0.0001).

Importance: In subjects 60 years and over, free from CV disease and taking prescribed chronic nsNSAIDs, CV events were infrequent and similar on celecoxib and nsNSAIDs. There was no advantage of a strategy of switching prescribed nsNSAIDs to prescribed celecoxib. This study excluded an increased risk of the primary endpoint of more than two events per 1000 patient-years associated with switching to prescribed celecoxib.

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19. START2QUIT

Aim: National Health Service Stop Smoking Services (SSSs) offer help to smokers motivated to quit; however, attendance rates are low and recent figures show a downward trend. We aimed to assess the effectiveness of a two-component personalised intervention on attendance at SSSs.

Method: We did this randomised controlled trial in 18 SSSs in England. Current smokers (aged ≥16 years) were identified from medical records in 99 general practices and invited to participate by their general practitioner. Individuals who gave consent, were motivated to quit, and had not attended the SSS within the past 12 months, were randomly assigned (3:2), via computer-generated randomisation with permuted blocks (block size of five), to receive either an individually tailored risk letter and invitation to attend a no-commitment introductory session run by the local SSS (intervention group) or a standard generic letter advertising the local SSS (control group). Randomisation was stratified by sex. Masking of participants to receipt of a personal letter and invitation to a taster session was not possible. The personal letter was generated by a research assistant, but the remainder of the research team were masked to group allocation. General practitioners, practice staff, and SSS advisers were unaware of their patients' allocation. The primary outcome was attendance at the first session of an SSS course within 6 months from randomisation. We did analysis by intention to treat. This trial is registered with Current Controlled Trials, number ISRCTN 76561916.

Results/conclusion: Delivery of personalised risk information alongside an invitation to an introductory session more than doubled the odds of attending the SSS compared with a standard generic invitation to contact the service. This result suggests that a more proactive approach, combined with an opportunity to experience local services, can reduce patient barriers to receiving treatment and has high potential to increase uptake

Importance: There has been a significant decrease in the number of smokers accessing the SSS in the past few years. Efforts to reverse this trend should be a priority as services offer smokers a significantly higher chance of stopping smoking compared with trying to quit without support.

Publication:
https://www.sciencedirect.com/science/article/pii/S0140673616323790?dgcid=raven_sd_aip_email

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