

# In Contact

Spring 2016



**National Institute for  
Health Research**

Clinical Research Network  
West Midlands



## Working Together for Better Health

Launch of the new RCGP Ready<sup>®</sup> website

CTU merger

**Delivering research to make patients, and the NHS, better**

## **NHS** National Institute for Health Research

Clinical Research Network  
West Midlands



Max Feltham

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# Hello, goodbye

Dear colleagues,

On the 10th February 2016 the National Institute for Health Research published its 100th research summary. The research featured, showed that engaging clinicians and healthcare organisations in research is linked to improvements in the delivery of healthcare. The paper published in the BMJ Open by Boaz and colleagues, found that most of the improved healthcare performances related to processes of care (ie, following best practice according to guidelines) and outcomes for patients (ie, better survival).

The NHS has a duty to promote research and innovation, which aims to improve patient outcomes. The commissioning system promotes and supports participation by NHS organisations and NHS patients in clinical research. Your GP practice and community pharmacy can be supported by the clinical research networks (CRN) to meet benchmarking standards for delivery of research to time and target recruitment levels. NHS organisations that have deliberately integrated the research function into their structures demonstrate how research engagement can, among other factors, contribute to improved healthcare performance. Our team of primary care research facilitators and nurses are dedicated to support high-quality clinical research in your GP practice and community pharmacy.

We are delighted to welcome three new members to our CRN: Primary Care delivery team. Sue Read has taken up the role as Senior Research Nurse for Primary Care and will lead our team of six Research Nurses who are embedded across Birmingham and The Black Country. Furthermore, she can offer support and advice to your practice nurse on how to deliver research in your surgery. Marie Crook and Georgi Dotchin have joined our Research Facilitator team and have already started conducting practice visits for the All-HEART, HEAT and IMPRESS-AF studies.

I am pleased to announce that Kaldeep Singh, Community Pharmacy Champion for the West Midlands, received a national award for their contribution to the development of an innovative model for commercial research recruitment. Kaldeep received his award from the Chief

Scientific Advisor for the Department of Health during an event hosted by the British Medical Association in London. Community Pharmacy continues to play a key role in raising awareness of research and they are contributing towards recruitment to the TIME study, which is comparing evening dosing of usual antihypertensive therapy with conventional morning dose.

We showcased Commercial Research to GP practices in November and new practices now receive regular invitations to participate in industry research. This has led to GP practices now being involved in cardiovascular and dermatitis research. In February, we hosted our inaugural event for research site initiative (RSI) practices at Edgbaston Cricket Ground. The event was attended by GPs and Practice Managers from 50 practices and we presented research findings from the Primary Care Patient Safety Toolkit and the Weigh 2 Go study. Furthermore, GP practices had an opportunity to learn more about a new study that is investigating the effects of web support for exercise referral schemes. The general feedback was very positive and we will organise a similar annual RSI event for our community pharmacies.

In this final paragraph, I would like to take the opportunity to announce that I am moving away from the Clinical Research Network on 30 April. Working as the Research Manager over the past three years to lead the team based at the University of Birmingham to deliver Primary Care research in your GP practice, community pharmacy and care home has been enjoyable and fulfilling. Together we recruited 9,000 participants into clinical research, where we aim to improve the delivery of healthcare and make patients better. This figure excludes patients who were recruited into secondary care studies after being initially identified in primary care, so our impact has been even greater. Recruiting this number of patients requires the support of so many people and I hope I get an opportunity to say 'thank you' to all the Primary Healthcare providers involved in research over the coming months. I wish you all the very best for the future.

### Dr Max Feltham

Research Manager – Primary Care  
NIHR Clinical Research Network: West Midlands

# News

## Notification of CTU merger

We wish to inform you that the Primary Care Clinical Research and Trials Unit (PC-CRTU) combined with Birmingham Clinical Trials Unit (BCTU) in April this year to form a new BCTU, with Professor Peter Brocklehurst taking over directorship of the new unit mid-2016. The new unit is now one of the largest and most effective clinical trials units in the UK, undertaking high quality late phase clinical trials, diagnostic and test evaluation studies, systematic reviews and

methodological research across a wide range of disease areas in both primary and secondary care settings. BCTU has specialist statistical, methodological, trial management, research governance, quality assurance and computing expertise, who currently oversee the design, setup, coordination, analysis and reporting of the Unit's clinical trial research. BCTU will continue to work with the CRN: West Midlands to facilitate primary care research.



## Launch of the new RCGP Research Ready® website



The RCGP Research Ready® programme has now been running for approximately ten years. April saw the launch of the newly developed programme and website. Previously, practices may have focused on the quality badge element of the programme; from now on, the programme will seek to provide greater support in the development and implementation of primary care research projects. A prime example of this is the online RCGP eLearning Research Ready® package (see below for further details).

### The programme has two principal aims:

- To make available a 'quality badge', signalling to interested parties – eg, Care Quality Commission (CQC), National Institute for Health Research (NIHR), potential research project participants – that accredited GP practices are cognisant of meeting current UK research standards/requirements (ie, 'readiness' to undertake research)
- To give information, guidance and support to staff at GP practices in order to improve awareness of standards/requirements and how to meet them, as well as practical guidance in designing and delivering research projects

Accredited practices will join the RCGP's largest network – around 1,000 practices, covering 14% of the UK's patient population. Updates on research opportunities from the Clinical Research Network (CRN), RCGP and partner organisations are communicated regularly, on a local, regional and national basis, allowing for enhanced integration, communication and co-operation.

### How do I register to become Research Ready® Accredited?

Practices register via a three-step process on the website:

1. Provide practice information (eg, contact details, research interests)
2. Complete a short assessment, establishing 'research competency'
3. Pay an administration fee\*: £100 for one year's accreditation; £250 for three years' accreditation

### FREE eLearning research course

Launched alongside the new system is an online eLearning research course designed for all GP practice staff, both clinical and non-clinical, who may have involvement in research projects. The online training package covers diverse aspects of primary healthcare, and offers a full package based on Research Ready®.

The four modules cover:

- Becoming 'research ready'
- Obtaining informed consent
- Assessing project feasibility
- Data management

Access is completely free for every practice joining the Research Ready® programme (and is priced at £300 to non-accredited practices).

More details can be found at: [www.rcgp.org.uk/learning/online-learning/ole/rcgp-research-ready.aspx](http://www.rcgp.org.uk/learning/online-learning/ole/rcgp-research-ready.aspx)

### Further Information

More details on the Research Ready programme can be found on the RCGP website: [www.rcgp.org.uk/researchready](http://www.rcgp.org.uk/researchready).

*\*Please note that practices within Birmingham and Black Country that are part of the Research Site Initiative (RSI) Scheme receive funding for Research Ready® accreditation. For further information on the RSI scheme and how your practice could join, please contact Sheila Bailey ([s.m.bailey.20@bham.ac.uk](mailto:s.m.bailey.20@bham.ac.uk)) or 0121 414 7956.*



# The Clinical Research Ambassador Group – Valuing Patient and Public involvement in research

Improved care and better outcomes are strongly associated with research active organisations. At the Heart of England NHS Foundation Trust (HEFT), we have a commitment to ensure research is an integral part of the clinical care that is provided to our patients. As part of this commitment, we have a research Patient and Public Involvement (PPI) group called The Clinical Research Ambassador Group (CRAG) in order to engage with patients, carers and members of the public to enable them to voice their opinions and offer their perspective on the research we do at HEFT.

Public involvement in research is essential to enable us to gather a different perspective and outlook on the research we do within the Trust. It allows us to draw on others personal

knowledge and experiences to provide an alternative perspective on the array of research topics we are involved with in the Trust. This can ensure the research methods and outcomes are important and relevant to the public and patient's needs.

CRAG was formed in 2012 for people who have an interest in research to meet, through meetings and events held at the trust, to discuss, inform and update on research within the Trust. Membership of the group is open to anyone within the HEFT catchment area and the level of involvement is up to the individual. This can vary from being involved with designing research projects to ensuring research questions being asked are understandable and relevant to the public.

## Learn More

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## New Study – PIC Study

### REACT: REtirement in ACTion study

*Please note that this study attracts patient accruals and would therefore meet study commitment for RSI practices. An opportunity for your practice to be involved in a major study to help older people stay fitter and live independently for longer.*

REACT (REtirement in ACTion) is a new intervention study aimed at improving mobility and maintaining independence in older people, using an exercise-based rehabilitation programme. REACT is based on the LIFE trial conducted in the USA where the study intervention was found to reduce the incidence of major mobility limitation in older adults. REACT will adapt the LIFE study intervention to ascertain whether it is an effective and cost-effective approach to reducing mobility-related disability in older adults in a UK setting.

REACT will recruit sedentary, community living, older persons aged 65 and over, with functional limitations (ie, who are at risk of major mobility limitations), but who are still ambulatory. The aim is to target a non-disabled, but at-risk

population. The REACT intervention is a 12-month programme with a strong social element. It starts as a centre-based exercise programme, but adds support for gradually 'translating' exercise and physical activity into participants' day-to-day lives. It will be delivered in community centres when low-cost daytime capacity is available. Sessions will be organised as group activities (15 per group) with individually tailored elements, and will include cardiovascular, strength, co-ordination and flexibility/balance exercises. Increased daily walking will also be encouraged and social engagement and enjoyment will be prioritised.

#### What is involved for practices?

- Search GP database
- GP to check the list
- Mail-out to eligible patients
- Follow-up mailing to non-responders if recruitment targets not met

**Patients will respond direct to the study team based at the University of Birmingham.**



#### Remuneration:

- Based on recruitment of 32 patients either: £664 or £315 (Docmail option)

The target number of participants is 768 across all the trial centres (Bath, Bristol, Birmingham and Devon) with the aim of recruiting around 32 patients per practice (dependent on list size).

For the pilot study, we are looking to recruit practices from the Harborne, Perry Barr, Kingstanding and Oscott areas. The main study is planned to commence Autumn 2016.

#### Learn More

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REACT is funded by the National Institute for Health Research Public Health Research Programme.

# Current Studies – Site Studies

## Treatment in Morning Versus Evening (TIME) Study



Funded by British Heart Foundation, the main objective is to determine if anti-hypertensive therapy taken in the evening has improved cardiovascular outcome compared with more conventional morning dosing. The study is trying to recruit approximately 10,000 patients from across the UK in order to find an answer to a clinically important question.

Patients diagnosed and treated for hypertension (all forms) with at least one antihypertensive drug, aged  $\geq 18$  and having a valid email address are randomised into two groups where one group takes the treatment in the morning and the other group in the evening. Moreover, the study also regularly monitors and records the number of heart-attacks, strokes and vascular deaths from each group.

Practices will be asked to conduct a search to identify potentially eligible patients and the patient list will be checked by GP for exclusions. Patient invitation letters will be sent out using DOCMAIL.

There are study posters available in order to bring it to the attention of anti-hypertensive patients. Interested patients register themselves on the study secure website:

[www.timestudy.co.uk](http://www.timestudy.co.uk)

They will confirm consent and enter their personal details. All study management is done by emails between study team and the patient with information being updated online. The study documents are available on the TIME website:

[www.timestudy.co.uk/GPRegistration.aspx](http://www.timestudy.co.uk/GPRegistration.aspx)

### Learn More

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## Global Anticoagulant Registry in the FIELD (GARFIELD-AF)



GARFIELD-AF is an ongoing observational, multicentre, international registry of newly diagnosed atrial fibrillation patients with at least one additional, investigator determined risk factor for stroke. The aim of the study is to evaluate the management and outcomes of patients with newly diagnosed non-valvular AF at risk of stroke. The registry aims to enrol 55,000 patients at more than 1,000 sites in 50 countries.

Enrolment is taking place in five independent, sequential cohorts and patients are followed up for a minimum of two years. UK participants are recruited in primary care with the University of Birmingham as the recruiting centre.

GARFIELD-AF is now recruiting to the fifth and final cohort and recruitment is expected to end in July 2016. The UK continues to be a leading recruiter to GARFIELD-AF with 3,567 UK participants enrolled to date.

Thank you to all the practices that are participating in GARFIELD-AF.

### Learn More

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# Current Studies – Site Studies

## FAST

### Febuxostat versus Allopurinol Streamlined Trial.

The trial will evaluate the long term cardiovascular safety profile of febuxostat in comparison with allopurinol in patients aged 60 years or older with chronic hyperuricaemia in conditions where urate disposition has already occurred. Eligible patients will be randomly allocated to either febuxostat or allopurinol treatment. The study research nurses, or local network nurses, will follow-up the patients for an average of 3 years. The trial aims to recruit 5,706 patients.

#### Practice Involvement

Practices will be asked to:

- Nominate a Lead GP to undertake Good Clinical Practice Training (can be provided as part of the trial)
- Search GP database for eligible patients
- Nominate Lead GP to review the patient list and remove unsuitable patients
- Nominate Lead GP to report any Serious Adverse Events via the FAST Web portal or by contacting the study centre

It is expected that each participating GP practice will recruit a minimum of 6 patients per practice.

#### Practice Remuneration

Each practice will receive £500 search fee for the initial practice database search, plus £5 per month per patient for follow-up data.

#### Learn More

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## ACCU-RATE

### How accurate are home blood pressure monitors used by patients?

'Accu-rate' is a NIHR funded cross sectional survey that aims to determine whether patients' own blood pressure monitoring equipment is sufficiently accurate to be integrated into daily practice.

It will ascertain which digital blood pressure monitors are currently used by patients, how well they perform, and whether there is any evidence of decreasing accuracy over time or with greater usage.

We would like to invite interested practices to contact us to take part. The additional workload is minimal. Service support costs will be reimbursed to cover recruitment. Patients will be recruited from 8 practices across Birmingham.

Eligible patients on the hypertension register who currently self monitor with either a wrist or upper arm blood pressure monitor will be invited to attend device accuracy sessions at their own practices. Using standard calibration equipment and following a standard testing procedure as recommended by the British Hypertension Society, each monitor will be tested over a range of pressures. Machines with a difference in pressure of  $\leq 3$ mmHg at all levels will pass. Each patient will receive individual feedback for their monitor.

Trial participation involves:

- Identification and screening of eligible patients using the hypertension register (health care professional)

- Mail-out of a study invitation letter
- Receipt of monitors (frontline staff)
- Room hire

#### Learn More

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## Current Studies – Site Studies

### Validation of home blood pressure monitors in patients with atrial fibrillation

This research aims to determine if automatic blood pressure (BP) monitors, already independently validated to take measurements in the home environment and shown to be amongst the most accurate in the general population, can be reliably used in patients with Atrial Fibrillation (AF).

No automatic BP monitors are currently validated for use in AF. If monitors are shown to take accurate blood pressure readings in patients with AF, the use of home BP monitoring could be recommended in this high risk group to improve the effectiveness of hypertension diagnosis and management. Home BP monitoring allows many more BP readings to be taken, and therefore might help provide a more accurate picture of the true underlying BP levels in AF patients.

The proposed research will assess the potential of home BP monitoring in AF through validation studies of different home BP

monitors in patients with AF to assess their accuracy in this population, including additional analysis of the minimum number of measurements required before we can be confident in the accuracy of the obtained BP values for AF patients. Devices will be validated against standardised protocols to ensure consistent and reliable assessment.

Eligible patients, recorded as having permanent chronic AF, will be invited to participate. The validation studies will follow the standard British Hypertension Society (BHS) and European Society of Hypertension International Protocol (ESH-IP) protocols, and will take place in the NIHR Wellcome Trust Clinical Research Facility in Birmingham, which is accredited by the BHS as a site for monitor validation, and where validation studies are regularly conducted.

We are looking to recruit up to 10 practices, and would like to invite interested practices to

contact us to take part or for further information. The additional workload is minimal and service support costs to cover time recruiting patients will be reimbursed.

Study participation involves:  
Identification and screening of eligible patients  
Mail-out of study invitation letter

#### Learn More

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## Current Studies – PIC Studies

### Brains in Transition Study



It is possible to identify young people at risk for psychotic illnesses such as schizophrenia through a combination of symptoms and personal or family history. Around 20% of such people develop psychosis within 12 months of being identified. There are differences in the brains of at risk cases when compared to similar participants not at risk and these differences get greater with the onset of psychotic illness. We don't yet know, however, when in the progression these changes occur. They may come before (and somehow cause) the increase in symptoms, implying that trying to prevent these brain changes could prevent the illness. The Brains in Transition (BrIT) study (funded by the Medical Research Council) will investigate the course of brain changes across

the transition from being at risk for psychosis to the development of a psychotic illness, and determine if those changes can be used to predict outcome and improve early detection.

Participation in the study involves assessments of symptoms and functioning, as well as brain scans (MRI). Participants are followed for one year and receive £20 in recognition of their time and expenses each time they take part.

GP practices taking part will be eligible to receive payment via service support costs to cover the time spent identifying and mailing out to eligible patients. GP practices will be informed in writing of a patient's participation in the study.

#### Learn More

**Brains in Transition (BrIT) team**

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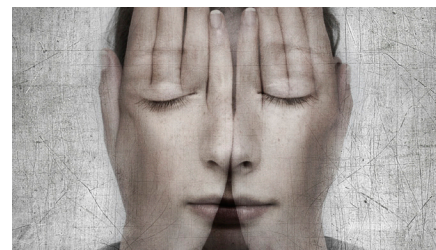
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# Current studies – PIC Studies

## Early treatment of Atrial fibrillation for Stroke Trial



We would like to invite you to take part in an exciting European study which is seeking to improve cardiovascular outcomes for patients with newly diagnosed Atrial Fibrillation (AF).

This is a Patient Identification Centre (PIC) study so we are simply inviting you to identify potential patients who can be invited to take part in the study. In Birmingham, the study is based around 2 secondary care sites; City Hospital and University Hospital Birmingham. Professor Paulus Kirchhof, Chair in Cardiovascular Medicine, Clinical and Experimental Medicine, University of Birmingham, is the International Principal Investigator.

The study will compare the usual treatment of AF with a management that uses early rhythm control therapy on top of usual care to explore whether earlier rhythm control has the potential

to prevent strokes and other cardiovascular complications. Earlier treatment may involve the use of anti-arrhythmic medicines as well as AF ablation. All treatments selected will comply with usual NHS guidance/technology appraisals and patient preferences will be discussed and agreed.

Patients will be randomly assigned to receive either usual care or early rhythm control, and followed up for a minimum of three years. Participants will have their travel expenses reimbursed. Recruitment to the study is currently due to end in 2016.

Practices will be remunerated for their involvement in the study.

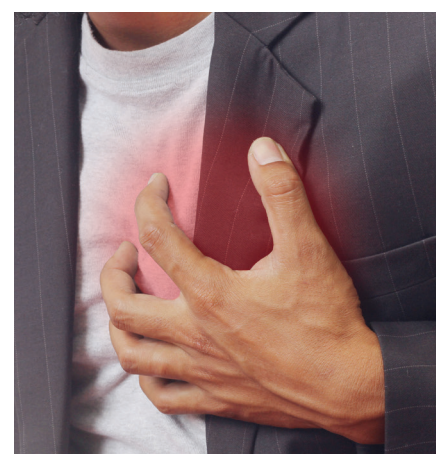
### Learn More

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## HI-Light



Vitiligo affects around 0.5-1% of the world's population. Current clinical guidelines recommend the use of potent or super potent topical corticosteroids (TCS), topical calcineurin inhibitors, or narrowband UVB light therapy (NB-UVB) for the first line treatment of vitiligo.

A Cochrane systematic review of 'Interventions for vitiligo' was last updated in 2010; one of the main conclusions of the update was that combination treatments seem to be more effective than mono-therapies in treating vitiligo but the trial evidence supporting their use is currently limited.

The trial's objectives are to assess the effectiveness of TCS and home based NB-UVB therapy for the treatment of patients with early or limited non-segmental vitiligo, used as mono-therapy and in combination for up to nine months.

a) To assess whether NB-UVB light therapy is better than potent TCS for the treatment of early and limited non-segmental vitiligo.

b) To assess whether combination of NB-UVB light therapy with potent TCS is better than either treatment used alone for the treatment of early and limited non-segmental vitiligo.

The sponsor of the study is University of Nottingham, the study is funded by NIHR Health Technology Assessment Ref 12/24/02 and Chief Investigator is Dr Jonathan Batchelor, Consultant Dermatologist, The University of Nottingham.

The HI-Light trial is a multi-centre double-blind, 3-arm randomised controlled trial (RCT) comparing potent topical corticosteroid to home based light therapy using hand-held devices, and to a combination of the two treatments.

Participants will receive up to 9 months of treatment. There will be 2 initial assessments at the hospital on consecutive days, then a 3, 6 and 9 month assessment at the hospital – which will be mainly answering questions, then follow up questionnaires at 12, 15, 18 and 21 months

All the research activities are taking place in Royal Wolverhampton Hospital NHS Trust (Adults), Birmingham Children's Hospital (Children) and Solihull Hospital (Adults and Children).

**Patients choose the research site based on their convenience.**

### Learn More

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# Current studies – PIC Studies

## Would you like to take part in National Research into COPD?



A randomised, double-blind placebo controlled trial of the effectiveness of low dose oral theophylline as an adjunct to inhaled corticosteroids (ICS) in preventing exacerbations of chronic obstructive pulmonary disease (COPD).

The study is trying to determine the clinical effectiveness and cost-effectiveness of adding low dose theophylline to ICS therapy in patients with COPD. Its objective is to improve the quality of life of COPD patients and to reduce the burden of COPD on the NHS.

Practices will be asked to conduct a search to identify potentially eligible patients and the patient list will be checked by the GP for any exclusions. Patient invitation letters will then be sent out from the practice inviting eligible patients to take part in the study.

There are study posters available to display in your practice to provide information about the study to patients. Patients who agree to take part in the study will attend three research clinics at the Queen Elizabeth Hospital, Birmingham (their travel expenses will be reimbursed at £10 per visit). They will also receive three telephone contacts from the study team and be asked to complete some questionnaires.

Participating patients may benefit from a possible reduction in COPD exacerbations and reduced hospital admissions as well as receiving assessments (health outcome and spirometry) by a hospital based specialist respiratory team. Practices will benefit from receiving study and spirometry data for any of their patients taking part in the study which can be used to meet QOF targets.

We would be very grateful for your support and involvement in this study.

### Learn More

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## In Follow Up

### TASMINH 4

Recruitment to the TASMINH 4 trial has now finished and, in total, 1,181 patients were recruited to the study nationally. Patient follow up will continue until February 2017.

The study team would like to say a huge 'thank you' to staff at all the 28 practices in our region that have helped to recruit patients and made the study such a success. Currently, our follow up response to 6 month follow-up clinics averages 83%. This response rate represents a lot of hard work from all the surgeries and researchers involved in the study and we would like to extend our sincere thanks and gratitude.

We really do appreciate the efforts that colleagues are taking to see participants and keep them engaged with the study.

#### What is the TASMINH 4 trial?

This research is a patient randomised controlled trial to evaluate the management of hypertension in primary care using self monitored blood pressure values, with or without tele-monitoring, compared to that using clinic monitored blood pressure. It will also consider the effect of self-monitoring and tele-monitoring on adherence, side effects, quality of life, adverse events and costs.



### Learn More

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# Study Findings

## If you want to quit smoking, do it now

Smokers who try to cut down the amount they smoke before stopping are less likely to quit than those who choose to quit all in one go, Oxford University researchers have found. Their study is published in journal *Annals of Internal Medicine*.

Most experts say that people should give up in one go, but most people who smoke seem to try to stop by gradually reducing the amount they smoke before stopping. This research helps to answer the questions 'Which approach is better?', and 'Are both as likely to help people quit in the short and long term?'

Dr Nicola Lindson-Hawley from the Nuffield Department of Primary Care Health Sciences led the research. She explained: 'We recruited 697 smokers who had chosen to stop smoking. They were split into two groups. One group – the 'abrupt cessation' group – set a quit day and stopped all smoking on that day. The second group – the 'gradual cessation' group – set a quit day but gradually reduced their tobacco use in the two weeks leading up to that date. 'Both groups had advice and support and access to nicotine patches and nicotine replacement therapy, like nicotine gum or mouth spray.' Once quit day had passed, volunteers were assessed weekly for the next four weeks, and after six months. As well as asking them about how they were doing, the researchers measured the amount of carbon monoxide they were breathing out – an objective way to check whether people were actually sticking to their quit plan.

At four weeks, 39% of the gradual cessation group had kept off tobacco, compared to 49% of the abrupt cessation group, meaning that the abrupt group were 25% more likely to quit. The difference between the groups began on quit day, when more of the abrupt group attempted to quit (defined as having at least 24 hours with no tobacco), compared to the gradual cessation group.

Dr Lindson-Hawley said: 'The difference in quit attempts seemed to arise because people struggled to cut down. It provided them with an extra thing to do, which may have put them off quitting altogether. If people actually made a quit attempt then the success rate was equal across groups. We also found that more people preferred the idea of quitting gradually than abruptly; however, regardless of what they thought, they were still more likely to quit in the abrupt group.'

'It is important to note that these results were found in people who wanted to quit soon and who were receiving counselling support and using nicotine replacement therapy. For these people the best advice appears to be to pick a day and stop smoking completely on that day. However, as we found that at the start of the



study many people cannot imagine being able to stop completely. For these people it is much better to attempt to cut down their smoking than do nothing at all and we should increase support for gradual cessation to increase their chances of succeeding.'

Mike Knapton, Associate Medical Director at the British Heart Foundation, which funded the study, said: 'This study shows that the most effective way to quit smoking is to stop all at once, rather than gradually reducing the number of cigarettes. This BHF funded research also highlights just how crucial it is that smokers have access to advice and support from NHS smoking cessation services.'

'Quitting smoking is the single best thing you can do for your heart health which is why we successfully encouraged thousands of smokers to quit for good this No Smoking Day, Wednesday March 9th. Setting a date, today, to ditch the cigarettes is the best start towards a smoke free life.'

The paper, Gradual versus Abrupt Smoking Cessation, is published in journal *Annals of Internal Medicine* on Tuesday 15 March (DOI: 10.7326/M14-2805).



# Study Findings

## Flu jabs 'more effective in morning'

Morning flu jabs provoke a stronger immune response than those given in the afternoon, a study shows.

The trial at 24 doctors' practices found people vaccinated before lunch produced the most defensive antibodies.

The University of Birmingham team suggested immunising people in tune with the body's natural rhythm could be a cheap way to save lives.

Experts said the study may mark the dawn of making use of 'the body clock in the clinic'. Our internal clock alters our alertness, mood, physical strength and even the risk of a heart attack in a daily rhythm.

And our immune system also waxes and wanes through the day.

The trial looked at 276 healthy people, aged over 65, getting the flu jab before the 2011, 2012 and 2013 flu seasons.

They were vaccinated either in a morning session (9.00 – 11.00am) or an afternoon appointment (1.00 – 5.00pm).

One month later, patients vaccinated in the morning had produced significantly more antibodies against two of the three flu strains in the jab.

Similar antibody levels were produced for the third strain, the results in the journal *Vaccine* showed.

Dr Anna Phillips, one of the researchers from the University of Birmingham, said the results were meaningful and doctors should 'definitely' think about performing flu jabs in the morning.

She told the BBC News website: 'A lot of surgeries just try and fit in vaccination anyway so it's not going to risk any patient, it's not going to cost anything and even if we're wrong you've nothing to lose by doing this.'

'I think it's fantastic, the idea of an intervention this easy to do and free is unheard of in terms of trying to change NHS practice.'

It is not clear exactly what the critical difference between the morning and afternoon immune system is.

Levels of immune messengers called cytokines, the stress hormone cortisol and sex hormones – all of which affect the immune system – fluctuate in a daily rhythm.

And individual white blood cells also have their own internal clocks that alter their activity too.

### 'Major gain'

Andrew Loudon and David Ray, a pair of body clock professors at the University of Manchester, told the BBC News website 'This may be the dawn of the body clock in the clinic.'

This is a most interesting study, and is among the first to show how the body clock can be used to make healthcare interventions more effective.'

'There have been major advances in understanding how the body clock can regulate immunity in laboratory animals, but very little of that exciting science has led to changes in healthcare.'

'This study shows that a simple intervention, giving the same vaccine at a different time of day, can result in a major gain in effectiveness.'

However, other vaccines stimulate the immune system in different ways so it is too simple to conclude that all immunisation should take place before lunch.

There have been some suggestions that hepatitis B vaccination may be more effective in the afternoon.

But the concept of timing medicine to the body clock – the field of chronotherapy – is powerful and is also showing promise in treating cancer and rheumatoid arthritis.

**BBC News website 26th April 2016**



# Study Updates

## The Million Women Study

A national study of women's health.

It is nearly 20 years since we started recruiting UK women to participate in the Million Women Study. With continued funding from the Medical Research Council and Cancer Research UK, the study is providing answers to many questions relating to women's health. We are most grateful to our participants and collaborators for their continued support.

### Million Women Study (MWS) investigations published in scientific journals since October 2014

Information provided by the MWS participants has been instrumental in our research to help clarify some of the uncertainties about risk factors for cancers and vascular disease in women, and provide novel insights into potential causes of these diseases. Summaries of all published studies are available on the study website ([www.millionwomenstudy.org](http://www.millionwomenstudy.org)), but here are a number of our recent findings:



Million Women Study investigators and staff at the Cancer Epidemiology Unit, University of Oxford.

### Hormone replacement therapy (HRT), oral contraceptives, and cancers of the ovary and the endometrium

MWS investigators combined efforts with other scientists in a global collaboration. HRT use increases the risk of ovarian cancer, with use for five years from around age 50 years associated with about one extra ovarian cancer per 1,000 users. In contrast, oral contraceptive use gives long-term protection against endometrial cancer, and oral contraceptives may have prevented 200,000 cases worldwide in the last ten years alone. *Beral V, et al. Lancet 2015;385:1835; Allen N, et al. Lancet Oncol 2015;16:1061.*

### Risk factors for 'rare' cancers

Our investigations into less common cancers suggest that oestrogen-only HRT use is associated with increased risks of brain tumours, but the risks are small (two extra cases per 10,000 users over five years). We also identified factors associated with increased risk of anal cancer, including smoking, and a history of cervical precancer. *Benson VS, et al. Int J Cancer 2015;136:2369; Coffey K, et al. Br J Cancer 2015;112:1568.*

### Determinants of heart disease and stroke

Physical activity is known to be beneficial to health. We found that at moderate levels, it was associated with lower risks of heart disease and stroke; but among women who were already

active, increasing its frequency does not seem to confer further reduction in risks. It has also been thought that participation in social activities may prevent heart disease. In the MWS, those who participated in social activities were more likely to be non-smokers, physically active, and have better self-rated health, which largely explained why they had a lower risk of heart disease than those who do not engage in social activities.

*Armstrong ME, et al. Circulation 2015;131:721; Floud S, et al. Eur J Prev Cardiol 2015 (E-pub).*

### Risk factors for dementia

A new area of research for the study is dementia. With such a large, long-term study we hope to add to what is known about lifestyle risk factors.

### Blood samples and genetic studies

We continue to collect blood samples for some women in the study, for genetic studies of breast cancer and of vascular disease.

**We would like to say a big 'thank you' to all the practices that have participated in the study and for continuing to support the Network.**

Learn More

Lynden Guiver

Email: [lynden.guiver@ceu.ox.ac.uk](mailto:lynden.guiver@ceu.ox.ac.uk)

Study website: [www.millionwomenstudy.org](http://www.millionwomenstudy.org)

## ExACT – Extended anticoagulation treatment for VTE: a randomised trial

Funded as part of an NIHR programme grant.

Recruitment to the ExACT study has now finished. The study team would like to say a big 'thank you' to Doctors and Staff at all the practices that have helped to recruit patients and make the study such a success.

In total, 281 patients have been recruited to the study and patient follow up continues until February 2017.

### Background to trial

Venous thromboembolism (VTE) is common with an incidence of approximately 1 per 1,000 per annum. It is associated with significant mortality and morbidity, including post-thrombotic syndrome (PTS). The annual recurrence rate following a first VTE is approximately 10% per annum irrespective of the duration of anticoagulation therapy.

This suggests that some patients should continue anticoagulation long-term. However, currently we are unable to identify this population.

### Aim of trial

To investigate whether extending anticoagulation treatment beyond 3–6 months, for patients with a first unprovoked proximal DVT or PE reduces the recurrence rate.

### Trial Intervention

Patients are randomised to either continue or discontinue oral anticoagulation and will be followed up every six months for two years. We will be looking at D-dimer levels (a product present in the blood after a blood clot), the development of PTS and associated quality of life.

We are also looking at the cost effectiveness of continuing oral anticoagulation treatment for these patients.

### For those of you who are already involved:

- We will be in contact as usual to organise rooms for follow up visits
- Please contact the study team on 0121 414 3354 if an ExACT patient experiences any adverse events

**There is a reimbursement for these services.**

Learn More

Sheriden Bevan

Tel 0121 414 3354

Email: [s.bevan@bham.ac.uk](mailto:s.bevan@bham.ac.uk)



# Courses/Training

## Getting to Hospital at a Single Stroke

**A free training initiative will be launched to help GP receptionists recognise the symptoms of stroke and TIA (transient ischaemic attack).**

'Getting to Hospital at a Single Stroke' offers two complementary ways to access training:

an online e-learning module and face-to-face training events. The project has been developed by Dr Liz Bates, GP and NIHR Clinical Lecturer in Primary Care, in response to the RECEPTS study carried out at the University and published in the British Journal of General Practice, last June.



It revealed that 20% of stroke patients called their GP, rather than an ambulance, at the onset of symptoms. After a successful pilot, the training will be launched later this year.

More details: <http://mymds.bham.ac.uk/eStroke/>

## University Accredited Courses 2016

The Institute of Applied Health Research at the University of Birmingham is pleased to introduce some new courses in 2016.



### Lung Cancer Study Day

**Monday 27 June**

This one day course is aimed at GPs and medical trainees with an interest in lung cancer, but is suitable for any healthcare professional regularly managing lung cancer patients. The course will cover diagnosis and management of all stages of disease through a combination of lectures and facilitated discussion of case studies.

#### Learning objectives

- How to diagnose lung cancer
- Surgery for lung cancer
- The essentials of chemotherapy and radiotherapy for lung cancer
- Understanding palliative care for lung cancer and dying at home

### Anticoagulation Masterclass for Nurses

**Tuesday 28 June**

This study day has been designed for nurses working with people receiving oral anticoagulants who wish to advance their knowledge and skills in using vitamin K antagonists (eg, warfarin) and direct oral anticoagulants (DOACs). It is a practical and clinically focused course, including lectures and workshops, making use of examples to show how to resolve complex problems. The course will help you further develop and enhance your skills and clinical knowledge for management of anticoagulation, and enable you to translate evidence into everyday practice for the benefit of patients.

*We are also continuing to offer the following courses over the spring and summer:*

#### Learning objectives

- Aetiology and epidemiology of thrombosis
- Symptoms and signs of DVT and PE
- Guidelines for treatment of thrombosis
- How to set up community management of DVT and PE
- NICE guidelines for VTE prophylaxis and what can be done in primary care

### Anticoagulation Management in Primary Care (MSc module)

**13–15 June**

- This course enables autonomous practice in dealing with fundamental and more complex problems in oral anticoagulation management.
- An understanding of the theory underpinning anticoagulation management
- An understanding of the pharmacology of vitamin K antagonists and the relevant medication, side effects, antidotes, interactions and dosing
- A knowledge of the management of anticoagulation and prevention of complications on the basis of current guidelines and existing research evidence
- An understanding of the requirements of clinical governance for anticoagulation management, eg, developing/adapting and applying audit tools with performance indicators



### An Introduction to Oral Anticoagulation Management

**21 June**

This course is targeted at nurses, and aims to provide an overview of the management of oral anticoagulation.

#### Learning objectives

- A knowledge of the principles of anticoagulation therapy, indication for use, side effects and interactions
- A knowledge of the principles of point of care, INR testing & quality assurance
- A knowledge of the professional guidelines for management of oral anticoagulation, audit procedures & protocol development

#### Learn More

Amy Partleton

Tel: 0121 414 2677

Email: [a.partleton@bham.ac.uk](mailto:a.partleton@bham.ac.uk)

# Research Design Service

## West Midlands

## What is RDS WM?

RDS WM exists to provide help to people preparing research proposals for submission to peer-reviewed funding competitions for applied health or social care research. RDS WM essentially consists of a team of methodologists based in universities and the NHS across the West Midlands, able to advise and provide practical support when you are developing your grant application. As RDS WM is funded by the NIHR for this purpose, such help is provided free of charge.

## Who can use the RDS?

We support a broad range of people, including:

- Doctors, nurses and allied health professionals
- Patients and service users
- Academics and NHS and social care managers

**For more information on RDS WM please contact  
Melanie Guthrie on 0121 414 8533 or  
[rds.wm@nhr.ac.uk](mailto:rds.wm@nhr.ac.uk)  
[www.rds-bham.ac.uk](http://www.rds-bham.ac.uk)**

## How can RDS WM help me?

RDS WM can advise on all aspects of the preparing grant applications, eg:

- Formulating research questions
- Building an appropriate research team
- How to apply for our public involvement fund scheme
- Designing a study
- Appropriate methodologies for quantitative research, eg, statistical issues, health economics
- Appropriate methodologies for qualitative research, eg, sampling, analytical strategies
- Identifying suitable funding sources
- Regulatory issues
- Writing lay summaries
- Identifying the resources required for a successful project

Advice and support is best provided face-to-face. RDS WM staff will be happy to meet with you at a convenient time and place to discuss your research. It is preferable to contact us at an early stage to discuss your ideas.



# Keep *In Contact*

Interested in taking part in research? We'd like to hear from you.

- You will always be able to choose your practice's level of involvement.
- You will be remunerated for practice time spent on research.

## Contact details:

Name:	<input type="text"/>
Job title:	<input type="text"/>
Practice address:	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
Postcode:	<input type="text"/>
Practice code:	<input type="text"/>
Email:	<input type="text"/>

Your email address will only be used to send you details of studies being undertaken by the CRN Primary Care.

Clinical Research Network: Primary Care is part of the National Institute for Health Research (NIHR). Only studies which have been independently peer-reviewed and funded through national competition; and commercial research asking relevant questions will be adopted onto the NIHR Portfolio of studies.

You can:

**Fax** back this form to **0121 414 2282** or

**Email** the details above to [crn-wm@contacts.bham.ac.uk](mailto:crn-wm@contacts.bham.ac.uk) or

**Phone** us on **0800 085 4229** for further information.

Alternatively, send the completed form to our postal address, as detailed on the back page.

#### **Primary Care**

University of Birmingham  
CRN: Primary Care,  
Murray Learning Centre,  
Edgbaston, Birmingham B15 2TT

Visit our website

[www.birmingham.ac.uk/crn-wm](http://www.birmingham.ac.uk/crn-wm)

#### **General Enquiries**

Tel: 0121 414 8843

Fax: 0121 414 2282

#### **Randomisation Service**

We now offer a telephone  
randomisation service for studies.  
Contact us for further details  
on 0800 6946943

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