



Eyes on Evidence

Dear Sarah

This month Eyes on Evidence looks at new research supporting a biological explanation for the negative correlation between UV light exposure and MS disease risk and severity. We highlight conclusions from the recently published SCAST trial which suggest that candesartan is not beneficial in patients with acute stroke and high blood pressure, and trial results for apixaban in patients with atrial fibrillation for whom vitamin K antagonist therapy is unsuitable.

Soon Eyes on Evidence is introducing a new monthly notification service for new and significant evidence in all clinical areas and public health. We will let you know as soon as the new service is launched.

As always, we welcome [your comments](#) on any aspects of the service.



Vitamin D3 may reduce MS severity

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In This Issue :

- ▶ Vitamin D3 may reduce MS severity
- ▶ Should blood pressure be lowered in acute stroke?
- ▶ Apixaban as an alternative to aspirin in patients with AF
- ▶ NHS Evidence resources: The Prostate Cancer Charity
- ▶ NHS Evidence QIPP, case study: Care Funding

Overview: Multiple sclerosis (MS) is a complex neurodegenerative disease which affects approximately 85,000 people in the UK. It is possible for MS to occur at any age, however, in most cases symptoms are first seen between the ages of 20 and 40 and women are almost three times as likely to develop MS as men. Symptoms of the condition are numerous and unpredictable, and they affect each person differently.

The exact cause of MS is not fully understood. It is considered to be a T-cell-mediated autoimmune disease and there is substantial evidence to suggest that it is caused by a combination of genetic and environmental factors. The striking variation in MS prevalence with latitude – increasing further from the equator in both hemispheres – caused epidemiologists to first suggest that this might relate to sunlight in 1960, a theory that has gained ground with the understanding of the relationship between sunlight exposure, vitamin D and immune response.

Current treatment: There is no cure for MS, but there are a number of treatments which reduce the frequency of relapses and associated disability and others which aim to improve the symptoms and improve quality of life. Current disease modifying therapies seek to suppress the T-cell-mediated auto immune attack on the central nervous system, the origins of which are not known.

MS is a highly variable condition and [NICE guidance](#) recommends that treatment be tailored to the individual. Treatments for MS may involve drug therapies but also include physiotherapy, rehabilitation, and psychological and emotional support. No drug treatment may be required if MS is mild with infrequent relapses.

There is a growing body of evidence to suggest that vitamin D supplementation may be a useful intervention in people with MS. Supplementation is straightforward and safe – although the current RDA (200-

Calculator

Previous Issues

[Back copies](#) of Eyes on Evidence are available on the portal in a pdf format.

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NHS Evidence is changing

From May 10 we are broadening the types of information available on NHS Evidence and signposting users more clearly to the very best resources.

New features include:

- ▶ A new focus on medicines information – allowing users to search key sources simultaneously, including British National Formulary, National electronic Library for Medicine (NeLM) and National Prescribing

400IU/day) is insufficient to reliably maintain normal serum vitamin D levels. No significant problems have been associated with supplementation of 1000IU in children and 4000IU in adults.

New evidence: New research in an animal model by Mayne CG et al ([European Journal of Immunology, 41: 3, 822-832 March 2011](#)) investigated the protective effects of sunlight-dependent hormone, 1,25-dihydroxyvitamin D3 and how this might influence autoimmunity.

Using experimental allergic encephalomyelitis (EAE), an experimental model of MS, the team sought to identify the target cells of 1,25-dihydroxyvitamin D3 through selective deactivation of the vitamin D receptor gene, which is expressed in activated T lymphocytes.

They found that the hormone's protective effects were only evident when these receptors were present in autoimmune T lymphocytes. The results suggest that an action of vitamin D3 directly on pathogenic T cells may lead to enhanced elimination of these cells.

The team believes this to be the first evidence obtained entirely in vivo that 1,25-dihydroxyvitamin D3 acts directly on immune system cells and more specifically on T-lymphocytes involved in autoimmune disease control.

This evidence begins to provide a biological explanation for the apparent negative correlation between UV exposure and MS risk and severity.

Commentary: "Though prior experience should make us wary of strongly extrapolating results derived in animal MS models to human disease (for further discussion see [Farooqi et al, J Neurochemistry 2010; 115: 829-44](#)) the findings of Mayne et al are a further piece in the jigsaw linking the biology of vitamin D to

Centre (NPC).

- ▶ New clinical topic areas, bringing together the latest guidelines, high quality patient information, ongoing trials and other selected information.

- ▶ Access to NICE pathways – allowing users to easily visualise and browse associated NICE products online, guided through supporting documents.

- ▶ Summaries of recently published evidence, in the form of evidence updates.

- ▶ Notifications of the latest significant research in speciality areas.

To see what the new version of NHS Evidence will look like view the video available at www.evidence.nhs.uk

the enigmatic disease that is MS and further support a role not only in the aetiology but also in established relapsing onset disease.

"Clearly further basic science work on the precise immunological role of vitamin D will continue, however given the simplicity and evident safety of vitamin D3 supplementation the time is surely now ripe for large scale studies of this intervention either on a population basis or perhaps more realistically in those patients at the earliest stage of disease, where placebo controlled randomised trials retain equipoise." - *Mike Boggild, Consultant Neurologist, The Walton Centre & Honorary Senior Lecturer, Department of Neurosciences, University of Liverpool.*



Should blood pressure be lowered in acute stroke?

Overview: Blood pressure (BP) is often raised following an ischemic or haemorrhagic stroke and it is associated with an increased mortality rate. In acute haemorrhagic stroke it is argued that lowering blood pressure may slow the rate of haematoma expansion and reduce the risk of re-bleeding into the brain; similarly in acute ischemic stroke it is postulated that it might reduce vascular damage and cerebral oedema. However, it is also possible that lowering blood pressure could be harmful and increase the risk of cerebral ischemia.

Current treatments: [NICE recommends](#) that antihypertensive treatment should only be considered if there is a hypertensive emergency and the patient has a serious concomitant medical issue (hypertensive encephalopathy, hypertensive nephropathy, hypertensive cardiac failure/myocardial infarction, aortic dissection, pre-eclampsia/eclampsia, or intracerebral haemorrhage with systolic BP over 200mmHg). BP reduction should be considered in patients that are candidates for thrombolysis to achieve a target BP of 185/110mmHg or

Student Champion Scheme

In Autumn 2010 NHS Evidence recruited 26 nursing, pharmacy and medical students from Huddersfield, Bradford and Manchester universities to deliver presentations on the service to their fellow peers.

Over the course of eight weeks, 678 students attended the sessions to learn about how NHS Evidence can help them in their studies and future careers.

Final results show that before participating in the NHS Evidence learning session delivered by their respective student champion, 25 per cent of all students said they had used NHS Evidence

lower.

New evidence: The Scandinavian Candesartan Acute Stroke Trial (SCAST) ([Lancet 2011; 371: 741-50](#)) is a randomised, placebo-controlled double-blind trial of candesartan in 2029 patients with acute stroke that also present with raised blood pressure.

The trial assessed two co-primary end-points – a composite endpoint of vascular death, myocardial infarction or stroke during 6 months of follow up and a functional outcome assessed by the modified Rankin Scale at 6 months.

At 6 months it was shown that despite a 5/2 mmHg difference in level of BP reduction in the candesartan group at 7 days this did not result in significant difference in the rates of the composite outcome. The results were consistent across all pre-specified subgroups including ischaemic and haemorrhagic stroke and a range of presenting BP levels. They were also consistent with the results of 10 previous smaller trials that assessed this type of intervention.

Overall when the results of SCAST are added to the results of the 10 previous trials it is shown that lowering BP does not have an overall beneficial effect on functional outcome.

Commentary: "Elevated blood pressure is common in acute stroke and is associated with a poor prognosis after stroke, but the effect of treating it in the midst of an acute stroke is unclear. While current guidelines do not recommend that blood pressure be lowered during a stroke, it is sometimes attempted. Up until now there have been no large trials to inform practice in this area. The results from SCAST go some way to supporting the current practice of not treating raised blood pressure in acute stroke. There are other trials in particular, the ENOS trial which will hopefully inform us whether blood pressure lowering drugs

to help with their studies. At the time of the follow up 92.4 per cent of respondents said they had used NHS Evidence to help with their studies.

Almost two thirds of medical students told us they had no confidence in NHS Evidence prior to the learning session and three per cent told us they were confident or very confident.

Following the learning session, more than half of medical students said they were now confident or very confident about using NHS Evidence.

Following the success of the pilot NHS Evidence is now expanding the scheme nationwide. [Email NHS Evidence](#) for details on how to get involved.

that had been prescribed before a stroke should be continued during the acute phase of stroke." - *Sotiris Antoniou, Consultant Pharmacist - Cardiovascular Medicine, North East London Cardiovascular and Stroke Network, Barts and The London NHS Trust.*



Apixaban as an alternative to aspirin in patients with AF

Overview: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and if left untreated is a significant risk factor for stroke and other morbidities. Therefore patients with paroxysmal, persistent or permanent AF are assessed using a tool such as [CHADS2 score](#) to determine their risk of stroke or thromboembolism and offered anticoagulation (usually warfarin) or an antiplatelet agent (usually aspirin) according to that degree of risk.

Warfarin is more effective than aspirin for the prevention of stroke in patients with AF but has a narrower benefit to risk ratio and requires lifelong coagulation monitoring. Therefore it is usually reserved for suitably motivated patients deemed to be at higher risk of stroke.

Apixaban is a Factor Xa inhibitor which is still in clinical development and not yet licensed in the UK.

Current treatment: [NICE recommends](#) that aspirin (75mg- 300mg/day) is considered in the following patient groups:

- ▶ All patients deemed to be at high risk of a stroke/ thromboembolism (previous history stroke/transient ischaemic attack or aged 75 or older with hypertension or vascular disease or clinical evidence of valve disease, heart failure or impaired left ventricular function) and who have contraindications to warfarin.
- ▶ Patients deemed to be at moderate risk of a stroke/thromboembolism (aged 65 or

Accreditation news

The process used by the British Association for Sexual Health and HIV (BASHH) to produce UK national guidelines has been formally approved under the NHS Evidence Accreditation Scheme.

The independent NHS Evidence Advisory Committee concluded that BASHH has a robust process in place for producing clinical guidance and that this is clearly described in a process manual. The methods to balance benefits and risks in formulating recommendations were found to be well described, as were the methods for evaluating the strength of evidence.

In addition, the committee confirmed that the methods for peer review and

older with no high risk factors or aged less than 75 with hypertension, diabetes, or vascular disease) depending on their perceived risk/benefit of warfarin.

▶ All patients deemed to be at low risk of a stroke/thromboembolism (aged less than 65 with no moderate or high risk factors).

New evidence: Connolly et al ([N. Engl. J. Med 2011; 364:806-17](#)) conducted a trial in 5599 patients with AF for whom anticoagulation with a vitamin K antagonist was considered unsuitable. Patients were randomised to receive either apixaban (usually 5mg twice daily) or aspirin (81 to 324mg daily - dose selected at the discretion of the investigator). The primary outcome was occurrence of stroke or systemic embolism. The trial was stopped early on the advice of the data and safety monitoring board when it was shown that there was a treatment benefit in favour of apixaban at the first interim analysis after a mean follow up period of 1.1 years. The results suggest that for every 48 patients treated with apixaban instead of aspirin for one year, one less might be expected to have a stroke or systemic embolism. This reduction was consistent in terms of relative impact on rates of ischaemic stroke, hemorrhagic stroke, death and hospitalisation and across all patient subgroups assessed. Apixaban was however associated with a slightly increased rate of major bleeding events than aspirin but this difference was not statistically significant and this trend was also reflected in minor bleeding events.

Commentary: "Warfarin, with all its drawbacks in terms of interactions and monitoring requirements, has remained the 'gold-standard' treatment for AF patients for decades. However, the Stroke Improvement programme has shown that approximately a third of patients who should be on warfarin for AF (based on risk stratification) are not on warfarin. These patients are often prescribed aspirin and in

keeping guidance up to date are rigorous components of the process.

BASHH can now carry the NHS Evidence Accreditation Mark on its clinical guidelines produced under the accredited process, assuring staff that they are accessing some of the best information available online to make informed decisions about patient care.

Process review

The process NHS Evidence follows for accreditation has been in operation since April 2009 and has naturally evolved during that time.

To bring the process up to date with current practices and to incorporate suggested changes the process manual has been revised and is now

the future may be treated by one of the newer oral anticoagulants.

"Apixaban is one of several new agents that aim to provide an alternative to warfarin for stroke prevention in patients with atrial fibrillation. Interestingly, this agent was studied in patients unsuitable for warfarin and demonstrated superiority whereas the other agents have gone head to head with warfarin and were either superior or non inferior to warfarin.

"Further studies are planned against warfarin, with the choice of agent based on safety, efficacy and tolerability as well as cost noting the likely premium against warfarin." - *Sotiris Antoniou, Consultant Pharmacist - Cardiovascular Medicine, North East London Cardiovascular and Stroke Network, Barts and The London NHS Trust.*



NHS Evidence resources: The Prostate Cancer Charity

Information sheets and booklets produced by [The Prostate Cancer Charity](#) are now available through NHS Evidence to support men, their families and healthcare professionals in understanding the symptoms, diagnosis and treatment options for prostate cancer.

Information provided includes leaflets for newly diagnosed men, overviews of treatments available, guides to understanding the prostate-specific antigen (PSA) test and details about how to get involved in clinical trials.

In 2009, the charity won the Patient Information Award for Men's Health at the BMA Medical Book awards for its guide, 'Understanding the PSA test: A guide for men concerned about prostate cancer'.

The Charity's information booklets are evidence-based and developed in collaboration with an external Health

available for [public consultation](#) until May 13.

Easier searching

For quicker access to quality information download an [NHS Evidence search panel](#) to your website or intranet.

Follow us

Keep up to date on all the latest news from NHS Evidence via our [Facebook](#) and [Twitter](#) pages.

Updates include information on new and reconfigured sources, site updates and improvements as well as pictures, videos, press releases and events.

Professional Advisory Group and expert clinical reviewers.

A group of more than 200 people directly affected by prostate cancer – 'Prostate Cancer Voices' – also review all materials to ensure information provided is relevant and easy to understand.

NHS Evidence continues to expand its patient resources in order to help users make good care decisions and bring about improved health outcomes. All patient information available through NHS Evidence has been accredited under the DH Information Standard.



NHS Evidence QIPP, case study: Care Funding Calculator

The London boroughs of Barnet and Islington, Southwark, Havering and Harrow have delivered substantial savings in residential care for people with learning disabilities by using a fair pricing tool.

By implementing the Care Funding Calculator (CFC) – a tool developed to prevent councils paying different amounts for similar care packages – local purchasers can better understand the costs for accommodation-based care. This has allowed them to assess the level of staff support required to meet an individual's needs and agree a price based on relevant market knowledge.

By moving towards different types of accommodation - such as supportive living under a tenancy or enabling users to invest in shared ownership schemes - more individuals have been able to live in their home area rather than being restricted to 'out of borough' residential options. The average saving per PCT area in each London borough was £500,000 mainly achieved through a reduction in the number of high cost residential placements. This equates to almost £200,000 per 100,000 population.

Sarah Hollingworth, Department of Health lead on the initiative, said: "In some councils it is the social worker's responsibility to negotiate costs and terms with care providers – understandably their primary concern is sourcing and arranging the care needed as quickly as possible. By making a strategic shift towards to commissioning other types of living options we have delivered real cash savings, whilst still meeting the needs of individuals."

For more details see the [NHS Evidence QIPP collection](#).



Eyes on Evidence helps contextualise significant new evidence, highlighting areas that could signal a change in clinical practice. It does not constitute formal NICE guidance. The commentaries included are the opinions of contributors and do not necessarily reflect the views of NICE.

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