This month in Eyes on Evidence

**General health checks in adults**
A Cochrane review suggests that general health checks are not associated with reductions in mortality or morbidity.

**Hand eczema in healthcare workers**
A randomised controlled trial indicates that accurate diagnosis of hand eczema and a preventive education intervention in healthcare workers may improve symptoms and quality of life.

**Effect of menstrual cycle on mood in a general population of women**
A systematic review suggests a lack of clear evidence for a relationship between negative mood and the premenstrual phase in the general population.

**Adherence to a warfarin dosing algorithm in atrial fibrillation**
Adherence to a warfarin dosing algorithm by clinicians treating people with atrial fibrillation may be associated with improved coagulation control and clinical outcomes.

**Trends in new medicine launches in the UK**
A retrospective observational study indicates that although short-term trends indicate a decline, longer-term data for 1971 to 2011 show a small increase in new medicine launches.

**Case studies from the Quality, Improvement, Productivity and Prevention (QIPP) collection**
We highlight 2 new examples from the QIPP collection demonstrating how NHS organisations have implemented new local practices that have both cut costs and improved quality.

- Reducing bed days and outpatient appointments with Arrhythmia Care Coordinators
- Improving efficiency and safety of out-of-hours care through wireless working in hospitals

**Evidence Updates**
NICE has recently published Evidence Updates on:

- Depression in children and young people
- Surgical site infection
General health checks in adults

Overview: General health checks are intended to reduce deaths and ill health by enabling early detection and treatment of disease. However, there are potential negative implications, for example potentially unnecessary diagnosis and treatment of conditions that might never have caused symptoms or shortened life.

Current advice: The NHS Health Check programme aims to help prevent heart disease, stroke, diabetes, kidney disease and certain types of dementia. Everyone between the ages of 40 and 74 years, who has not already been diagnosed with one of these conditions, is invited to have a check every 5 years to assess their risk of heart disease, stroke, kidney disease and diabetes and is given support and advice to help them reduce or manage that risk.

New evidence: A Cochrane review (Krogsbøll et al. 2012) assessed the benefits and harms of general health checks in adults with an emphasis on outcomes such as morbidity and mortality. It identified 14 randomised controlled trials of health checks assessing more than 1 disease or risk factor in general populations compared with no health checks. Data were available for 182,880 adults with follow-up times of 1–22 years (median 9 years).

Total mortality was reported in 9 trials and no difference was seen for health checks compared with no health checks (risk ratio [RR] = 0.99, 95% confidence interval CI 0.95 to 1.03). Similar results were seen for 8 trials reporting cardiovascular mortality (RR = 1.03, 95% CI 0.91 to 1.17) and for 8 trials reporting cancer mortality (RR = 1.01, 95% CI 0.92 to 1.12).

No effects were seen for clinical events or other measures of morbidity. General health checks seemed to have no impact on hospital admissions, disability, worry, specialist referrals, additional visits to doctors or time off work, but most of these outcomes were rarely reported. Important harmful outcomes such as the number of follow-up diagnostic tests or short-term psychological effects were often not studied.

Commentary: This review suggests that health checks targeted at the general population may have no proven benefits and possible harms are studied inadequately. Health checks are currently being offered by the NHS and by private providers. Why are they so popular? The most likely answer is the intuitive appeal of the approach. Clinically motivated testing and preventive activities for individual patients by doctors are of value. Therefore, it seems logical to assume that a population-based programme would be even better.

“This logic is employed by advocates and politicians who understandably desire to ‘do something’ about heart disease, men’s health, cancer, and health inequalities. Nonetheless, the conclusion from this review seems to be that the evidence does not support these programmes. However, many of the studies included in the Cochrane review date back to the 1960s, so may not be representative of current clinical practice. General health checks currently undertaken may take a different approach. The appropriate action would be to conduct randomised trials of health checks – not to continue with a population-based intervention with unknown risks and benefits.” – Professor Phil Hanlon, Professor of Public Health, University of Glasgow

Study sponsorship: Nordic Cochrane Centre, Denmark. One author was partly supported by a grant from the non-profit foundation Trygfonden, Denmark.
Overview: Eczema (also known as dermatitis) is red, dry, itchy skin that has many underlying causes, including allergy, and contact with irritant substances. The UK Health and Safety Executive notes that some workers, such as hairdressers or healthcare workers, may develop dermatitis more often than the general population. The most common causes of occupational dermatitis are working with wet hands, and contact with soaps and cleaning materials.

Current advice: The British Association of Dermatologists' guidance on contact dermatitis (NICE accredited) notes that most contact dermatitis involves the hands, so gloves are the mainstay of prevention. It also notes that evidence suggests benefits in using soap substitutes and after-work creams in reducing the incidence and prevalence of contact dermatitis. These products should be encouraged and made readily available in the workplace.

New evidence: Ibler et al. (2012) conducted a randomised controlled trial in Denmark of skin care education and individual counselling (n=123) compared with usual care (n=132) in healthcare workers with hand eczema. People in the intervention group were given advice on avoiding exposure to irritants at work and at home, how to avoid relevant allergens (identified by skin prick testing), and how to protect their skin at work. Correct techniques for applying emollient and hand washing were taught to participants. Participants were advised to disinfect hands rather than washing them if they were not visibly dirty, and to use protective gloves for wet work, handling drugs, cleaning and cooking.

After 5 months, the intervention group had significantly lower mean scores on the hand eczema severity index than the usual care group (difference of means=-3.56, 95% CI -4.92 to -2.14, p<0.001). The intervention group also had significantly lower scores on the dermatology quality of life index (difference of means=-0.78, p=0.003), in which higher scores are associated with a lower quality of life. The authors described this change in quality of life as from 'having a small impact on a patient's life' to 'having no impact on a patient's life'.

Commentary: "This well conducted study demonstrates that accurate diagnosis of the cause of hand eczema (through thorough assessment involving patch and prick testing) and education in preventive measures statistically significantly improves eczema and quality of life in healthcare workers. The quality of life scores were not particularly high before the intervention. This may reflect that healthcare workers expect to develop hand eczema because of the exposures associated with healthcare work (for example frequent hand washing and occlusive rubber glove use).

"The intervention has not had a rigorous health economic analysis, so the cost effectiveness of patch testing and education remains to be seen. But patients are likely to appreciate having the opportunity to have their hand eczema addressed. It is likely that workers in other occupational groups with similar exposures and high rates of hand eczema (chefs, food handlers and hairdressers) would also benefit from this intervention." – Dr John English, Consultant Dermatologist, Nottingham University Hospital NHS Trust

Study sponsorship: Region Zealand's Research Fund and Danish Working Environment Research Fund.
Overview: Premenstrual syndrome (PMS) is a condition in which distressing physical, behavioural, and psychological symptoms regularly occur in the second half (luteal phase) of the menstrual cycle, and are significantly improved or resolved by the end of menstruation. Psychological symptoms include depressed mood, mood swings, anxiety, irritability, and loss of confidence. The exact cause of PMS is uncertain, but around 5% of women present with premenstrual symptoms of severe enough functional consequence to seek treatment.

See the NICE Evidence Services topic page on premenstrual syndrome for an overview of the condition.

Current advice: The NICE clinical knowledge summary for premenstrual syndrome advises that when making a diagnosis of PMS, other conditions with similar presentations such as depression, anxiety, hypothyroidism, anaemia, irritable bowel syndrome, endometriosis, chronic fatigue syndrome, and fibromyalgia need to be considered. Management of PMS should be tailored to the severity and type of symptoms, the woman's treatment preferences, and any desire to become pregnant.

New evidence: A systematic review assessed the strength of evidence for PMS among the general female population (Romans et al. 2012). The review found 47 studies involving 4320 women, but differences between the studies prevented a meta-analysis of results.

Among the 47 studies:

- only 7 (15%) reported a 'classical' PMS pattern of negative mood associated with the premenstrual phase
- 18 (38%) found no link between negative mood and any menstrual cycle phase
- 18 (38%) reported negative mood in the premenstrual phase in combination with other menstrual cycle phases (most commonly menstruation)
- 4 studies (9%) found a link between non-premenstrual phases and negative mood.

Some of the studies included as few as 6 participants, and over half included fewer than 50 participants. However, analysis of only studies with more than 15 participants gave similar results to the overall analysis. The purpose of the investigation was not hidden in 26 studies, so existing beliefs among participants about their menstrual cycle may have influenced results. In 16 studies, only undergraduate students were recruited therefore many of those analysed by the review were young women.

The authors stated that there seemed to be no clear evidence for a relationship between negative mood and the premenstrual phase in the general population. They discussed findings in the context of cultural beliefs, attitudes and stereotypes surrounding menstruation, which may often be negative. The authors concluded that the lack of a firm scientific basis for current thinking about PMS means that beliefs in this area may need to be challenged. They also noted that better studies with adequate sample sizes and wider age groups were needed.

Commentary: "This review attempts to clarify how menstrual cycle phases affect mood in the general population of women. Sadly, the literature in this area is poor and studies that merit inclusion almost exclusively include young women up to about 30 years of age. Current advice from NICE clinical knowledge summaries addresses the significant minority of women of all menstrual ages who have symptomatic physical and psychological changes that they associate with menstrual phase. Importantly, this does not include the fewer suffering more severe premenstrual dysphoric disorder who are at greater risk of depression postnatally and postmenopause.

"Current advice remains relevant therefore for the larger population of 3–6% of women who need clinical advice about perimenstrual symptoms and who may benefit from increasing exercise and other lifestyle changes. However, this review strengthens the argument for significant changes in societal and clinical understanding of symptoms in women attributed to hormonal changes, and for encouraging a more positive view of menstruation as a sign of health and fertility. The review does not address the general population of women menstruating between ages 35 and menopause, who may be more likely
Adherence to a warfarin dosing algorithm in atrial fibrillation

Overview: Atrial fibrillation is a heart condition that causes an irregular and often abnormally fast heart rate. People with atrial fibrillation have a 5-fold increased risk of stroke and thromboembolism, and antithrombotic therapy is an important treatment option to reduce this risk.

See the NICE Evidence Services topic page on atrial fibrillation for a general overview of this condition.

Current advice: NICE guidance on managing atrial fibrillation (which is currently being updated) recommends antithrombotic therapy with either dose-adjusted warfarin or aspirin depending on the risk of stroke. The outcome for people taking warfarin depends partly on how well therapeutic control is maintained. This can be measured in terms of the time the patient's international normalised ratio (INR) is in therapeutic range.

NICE technology appraisals also recommend the newer oral anticoagulants apixaban, dabigatran etexilate and rivaroxaban as options for the prevention of stroke and systemic embolism in atrial fibrillation.

New evidence: Van Spall et al. (2012) used data from 6022 patients in the Randomized Evaluation of Long-term Anticoagulation Therapy (RE-LY) trial. RE-LY was a large randomised controlled trial (912 centres in 44 countries) of dabigatran versus warfarin over 2 years in patients with atrial fibrillation and risk factors for stroke. The trial protocol specified that investigators should manage warfarin according to local practice with the following provisions: the target INR was 2.0–3.0 (2.0–2.5 in Japan), with no more than 4 weeks between INR tests.

An algorithm for warfarin dosing recommended no change for in-range INR and 10–15% weekly dose adjustments for out-of-range INR. A multilevel regression model was used to compare variations in 'time in therapeutic INR range' (TTR) by centre and country. The importance of warfarin dosing practice in predicting TTR and clinical outcomes was also evaluated.

Adherence (intentional or not) to a simple warfarin dosing algorithm predicted improved TTR and accounted for considerable variation in TTR between centres and countries. The degree of adherence by clinicians accounted for 87% of between-centre and 55% of between-country variation. After adjusting for patient, centre and country characteristics, each 10% increase in adherence by centres, there was also an 8% decrease in the rate of the composite clinical outcome (stroke, systemic embolism or major haemorrhage), which was of borderline statistical significance (hazard ratio 0.92, 95% CI 0.85 to 1.00, p=0.05).

This study determined whether dose adjustments were consistent with algorithm recommendations, but could not verify whether clinicians actually used the algorithm. Patients participating in this clinical trial may have been more adherent to treatment than in a real-world setting. The association between algorithm consistency and clinical outcomes could be due to better overall care in centres with higher TTRs.

Commentary: ‘Despite over 50 years’ experience using vitamin K antagonists, such as warfarin, management remains suboptimal. Treatment centres continue to use warfarin apparently without the use of simple dosing algorithms, despite evidence to the contrary. In this study, TTR was clearly shown to be associated with better patient outcomes. Adjusting weekly warfarin doses by 10–15% when out of the INR range of 2.0–3.0 was the single most important factor influencing TTR in this large trial.'
population.

"How does this translate to UK practice? The use of computerised decision support software containing such simple algorithms is almost universal; in fact clinics in Northern Europe and Australia had the best TTR values in the RE-LY study. Should we compare TTR performance between clinics as part of a continuous quality improvement programme? Probably, although in real-world practice other factors influence TTR, not least treatment adherence in patients who would normally be excluded from trials. Also, not all clinics manage equivalently complex cases.

"What about newer oral anticoagulants? NICE technology appraisals for apixaban, dabigatran etexilate and rivaroxaban, all recommend that these newer oral anticoagulants are options for the prevention of stroke and systemic embolism in atrial fibrillation; and that the potential risks and benefits of switching from warfarin to a new oral anticoagulant should be considered in light of the level of INR control. From a clinical perspective, there may be less reason to consider a switch to a new oral anticoagulant in people whose INR is well maintained on warfarin than in people with poor control; and this paper highlights the importance of optimising warfarin dosing." – Dr Will Lester, Consultant Haematologist, University Hospitals Birmingham NHS Foundation Trust

Study sponsorship: Boehringer-Ingelheim.

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Trends in new medicine launches in the UK

Overview: In 2011 an editorial in The Lancet reviewed European Medicines Agency (EMA) data and showed a decline in positive opinions and finalised marketing authorisation applications for new medicines in 2010 compared with 2009. The potential underlying issues suggested included the pharmaceutical industry’s diminishing return on investment following research and development of new medicines, and subsequent delay in bringing these to market.

Current advice: To reduce the time to marketing authorisation, in 2006 the EMA implemented a new system for accelerated assessment of new medicines applications for innovative medicines offering significant clinical benefit. In 2011 the Department of Health published Innovation, Health and Wealth to support the adoption and diffusion of new medicines into the NHS. Aims of this report included reducing variation and strengthening compliance in the adoption of positive NICE technology appraisals, and supporting growth in the life sciences industry.

New evidence: A new retrospective observational study (Ward et al. 2013) analysed how many new medicines were added to the British National Formulary (BNF) each year from 1982 until 2011. The BNF is a useful proxy measure of drug launches, but does not provide an exhaustive list of all drugs available in the UK. Further data from published literature were then used by the authors to extend the regression analysis back to 1971.

The primary analysis, using data from 1982 to 2011, found that the mean number of new medicines incorporated into the BNF per year was 23.9 (standard error 1.16). The lowest number of new medicines incorporated in the BNF was 11 in 1985, the highest number was 34 both in 1997 and 2010. The secondary analysis extended the period studied back to 1971. Over this longer period the mean number of new medicines was 22.7 (standard deviation 6.0) with the lowest number being 9 in 1985, peaking at 34 in 1997 and 2010.

These results indicated a small but statistically significant increase in new medicines launches of 0.16 per year between 1971 and 2011 (p=0.04), but neither an increase nor decrease in more recent years (p=0.25). Subanalysis of data from 1997 to 2006 found a statistically significant (p=0.001) reduction in the number of new medicines launched.
On analysis of the homogeneity of the results, the authors suggested that previous studies showing decline in the number of new medicines launches were most likely due to short-term trends resulting from the periods studied. The study was limited to describing the trends in new medicine launches rather than explaining the underlying cause of any change; it did not discriminate between new treatments for different diseases nor did it address the novelty or clinical importance of the new medicines included.

**Commentary:** "The data from 1997 to 2006 indicated a decline in new medicine launches. During this period, national appraisal mechanisms evolved and became impactful and contributed to a perception of 'incremental innovation blight'. The data do not support a consideration of the wider issues that lead to the belief that the pharmaceutical research and development (R&D) and Health Technology Assessment (HTA) uptake model is 'broken'. For example, the study cannot differentiate between areas of high R&D activity, such as oncology, and those in which pharmaceutical R&D has declined, for example neurology.

"The cost of R&D (especially HTA) is increasing and there is a growing demand for medicines for smaller patient populations being treated with each new medicine. Therefore, even when the number of new medicines increases, the population treated may decline. Conflict therefore exists between the cost of high-risk investment in R&D and uncertain investor returns in an era when payers need to be more circumspect than ever in investing healthcare budgets. In summary, this research adds to the debate but more comprehensive analyses should be undertaken before we congratulate ourselves on the UK being a good place to innovate." – *Mr Leslie Galloway, Chairman, Ethical Medicines Industry Group*

"This study challenges the view that the pipeline of new medicines is declining and supports the anecdotal experiences of those responsible for assessing new products within the local NHS, in terms of the number of meeting requests from the pharmaceutical industry about new medicines. The analysis shows a small upwards trend but the authors point out that more detailed investigation is needed to examine the underlying trends of 'me-too drugs' versus 'first in class'.

"Although there have been efforts to decrease approval times, it takes on average 12 years for a medicine to come to market and the cost per medicine is increasing. As pharmaceutical companies search for new opportunities, the future impact of pharmacogenomics and personalised medicine will be considerable. The NHS needs to take account of these issues, while focusing on the medicines optimisation opportunities. This means ensuring patients take the most appropriate medicines for them through better understanding of their conditions and improving delivery and supply systems. The medicines optimisation clinical guideline being produced by NICE will be welcome." – *Alison Tennant, Head of Service Improvement, Dudley Clinical Commissioning Group*

**Study sponsorship:** UK National Institute for Health Research Horizon Scanning Centre.

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**QIPP case study: reducing bed days and outpatient appointments by introducing arrhythmia care coordinators**

Cardiac arrhythmia affects over 700,000 people in England, with atrial fibrillation absorbing almost 1% of the entire NHS budget. The National Service Framework for coronary heart disease stated that people with long-term conditions should receive support in managing their illness from a named arrhythmia care coordinator. To meet this objective the British Heart Foundation (BHF) piloted and evaluated the nursing role of Arrhythmia Care Coordinator (ACC) across 19 NHS sites in England and Wales.

The initiative aimed to reduce bed days and outpatient appointments and improve quality of care through more efficient management of arrhythmia via a single named specialist nurse contact. ACC nurses liaise with relevant professionals to ensure coordinated management of the condition, provide easy access to support and advice, and ensure optimum use of medication.
Simplifying the care pathway improves the patient and carer experience. An independent evaluation of the ACC programme (Ismail and Lewin 2010) measured aspects of patient functioning and wellbeing using standardised tools, before and after the ACC nurse intervention. This demonstrated small but significant improvements in a range of measures related to physical and mental wellbeing and independence.

ACC nurses can perform diagnostic tests that might otherwise have to be administered by cardiologists or through additional hospital and outpatient appointments. Nurse-led preoperative assessment of patients and consent-taking resulted in more people who needed elective devices implanted being treated as day cases. The ACC nurse also educates patients and healthcare professionals such as general practitioners, practice nurses and matrons in the optimum care of arrhythmia.

The ACC role saved, on average, £29,357 per year largely from improvements in productivity resulting in fewer bed days. All 19 trusts participating in the pilot realised savings and continued to fund ACC nurse posts after the pilot.

Catherine Kelly, Programme Director of Prevention and Care at the British Heart Foundation said: “ACC nurses provide a single point of contact for patients and carers following a diagnosis of arrhythmia. This improves access to advice and information and decreases the stress and burden of managing a long-term condition across different areas. Qualitative data from interviews show that patients greatly appreciated having a named contact to coordinate their care.”

Jenny Tagney, Cardiology Nurse Consultant at the University Hospital Bristol NHS Foundation Trust, which employed 2 band 7 ACC nurses said: “The role of arrhythmia care coordinator is usually undertaken by specialist nurses working to improve communication, expedite investigations, diagnosis and treatments and encourage self-management. Investment in these posts improves patient experience, reduces outpatient costs and reduces length of stay, thus the posts more than pay for themselves. They are equally valuable in primary care or hospital-based settings.”

Visit NICE Evidence Services for more details of this initiative and other QIPP examples.

QIPP case study: improving efficiency and safety of out-of-hours care through wireless working in hospitals

Hospital working hours of 9 am to 5 pm from Monday to Friday means that the out-of-hours period covers more than 75% of the week. During this time services may be more stretched and patients are at highest risk. In accordance with national guidance, care in hospitals at night is provided by a small team of doctors, nurse coordinators and healthcare assistants, which covers work in all specialties, often across a large area.

Coordination and communication between hospital wards and team members has been a major issue. Standard pager and landline telephone systems are prone to delays because tasks must be interrupted to answer the page, and the originator of the request must wait by the phone for an answer. Repeating the message, in the absence of standards of details to be communicated, results in loss of information. Handover between shifts is also of concern because the current system does not record the work undertaken in detail.

An initiative by Nottingham University Hospitals NHS Trust aimed to improve the efficiency and safety of out-of-hours care in hospitals by replacing the standard pager and telephone-based system with a wireless IT system that also records in detail the work undertaken.

The objectives were to reduce information loss and to improve the quality and speed of communication between doctors and nurses and improve satisfaction for clinicians and patients. The initiative captured data on every task requested (including type, priority, location and duration) to help understand the workload and organise resources.
The initiative demonstrated a saving of £30,280 per 100,000 population. This takes into account the cost of training staff on the use of the wireless system. Cash savings were achieved through a reduction in length of stay and fewer adverse events.

A reduction in data errors, more detailed information available to clinicians and healthcare staff, and a reduction in information loss ensured that the quality of care provided to patients was improved. Use of the system also resulted in more time for direct patient care.

John Blakey, Senior Lecturer, of Liverpool School of Tropical Medicine, who was a Clinical Lecturer at Nottingham University Hospitals NHS Trust during the data collection, said: "The wireless working initiative has been a multidisciplinary effort and has realised improvements in several areas. Particularly pleasing has been the significant reduction in reported incidents concerning handover and response out-of-hours."

Visit NICE Evidence Services for more details of this initiative and other QIPP examples.

**Evidence Updates**

NICE has recently published Evidence Updates on:

- Depression in children and young people
- Surgical site infection

These Evidence Updates highlight and provide commentary on selected new evidence published since the NICE guidance was issued. For each topic, the evidence was considered by an Evidence Update Advisory Group (EUAG), a panel of experts, most of whom were involved in developing the original NICE guidance.

The Evidence Update on depression in children was published by NICE in June 2013. It includes commentary from the EUAG on 8 new articles (relevant to NICE clinical guideline 28), covering the following topics:

- Impact on treatment response of parental marital discord, abuse and other factors
- Modular approach to psychotherapeutic interventions
- Classroom-based and computerised CBT
- Prescribing antidepressants for children and young people

The Evidence Update on surgical site infection was published by NICE in June 2013. It includes commentary from the EUAG on 26 new articles (relevant to NICE clinical guideline 74), covering the following topics:

- Preoperative showering, hair removal, and antibiotic use
- Intraoperative use of surgical face masks, skin antiseptics
- Maintaining patient homeostasis
- Wound closure techniques and dressings
- Negative pressure wound therapy

Eyes on Evidence helps contextualise important 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.