This month in Eyes on Evidence

**Social integration and risk of suicide in men**
A cohort study in the US found that professional middle-aged men who were socially well integrated had a lower risk of suicide than men with fewer family, friendship and religious connections.

**Surgical versus non-surgical treatment for fracture of the heel**
A small, 2-year randomised controlled trial in the UK reported that surgical treatment appeared to be no better than non-surgical treatment at improving function and pain in patients with intra-articular fracture of the heel, and was associated with a higher rate of complications.

**Improving cardiovascular disease through networks of general practices**
An observational study in London found that grouping general practices into managed networks and emphasising clinical engagement and education was associated with small improvements in outcomes related to cardiovascular disease, although it was not clear which elements of the networks were most important.

**Antibiotics in fetal and early life and subsequent childhood asthma**
A Swedish observational study found an association between antibiotic use in fetal and early life and asthma. However, this link was reduced or disappeared in analyses that compared children with siblings who did not have asthma, suggesting that factors shared in families may explain any observed association between antibiotic exposure and asthma.
Detecting atrial fibrillation in people who have had a stroke
Two randomised controlled trials reported that long-term electrocardiogram monitoring was more effective at detecting atrial fibrillation than 24-hour or intermittent electrocardiogram monitoring in people who had experienced apparent cryptogenic stroke or transient ischaemic attack.

Case studies from the Quality and Productivity collection
We highlight 2 new examples from the Quality and Productivity collection demonstrating how NHS organisations have implemented new local practices that have both cut costs and improved quality:

- Mobile clinics for chronic stable glaucoma management
- Ensuring appropriate use of monitored dosage systems

Evidence Updates
NICE has recently published Evidence Updates on:

- Fertility
- Psychosis and schizophrenia in children and young people
- Occupational therapy and physical activity interventions to promote the mental wellbeing of older people in primary care and residential care
- Promoting physical activity for children and young people

Changes to NICE evidence awareness products
NICE has announced some changes to 2 of its evidence awareness products: Evidence Updates and Eyes on Evidence. Evidence Updates are being replaced by guideline surveillance reports, and Eyes on Evidence has moved to a new home on the NICE website.

Social integration and risk of suicide in men

Overview: In 2012, 5,981 people aged 15 or over committed suicide in the UK (Office for National Statistics 2014). The rate of suicide in men was more than 3 times higher than the rate in women, with 18.2 male deaths per 100,000 population compared with 5.2 female deaths per 100,000 population. The highest suicide rate was among men aged 40–44 years, at 25.9 deaths per 100,000 population. Historically, however, suicide rates have generally been highest among young men aged 15–44, peaking for this group at 18.6 per 100,000 in 2008 (Office for National Statistics 2012).

Poor social integration – for example, not being married or having a small number of friends – has been linked with risk of suicide (Duberstein et al. 2004). The link between poor social integration and suicide is thought to be stronger in men than in women (Berkman et al. 2004).

Current advice: NICE guidance on depression in adults recommends that the quality of interpersonal relationships and living conditions, and social isolation, should be considered when assessing a person who may have depression. People with depression should always be asked directly about suicidal ideation and intent. If there is a risk of self-harm or suicide, the person’s level of social support should be assessed.

NICE guidance on common mental health disorders also emphasises the importance of considering living conditions and social isolation when assessing people with mental health problems. When discussing treatment options with a person with a common mental health disorder, healthcare professionals should
consider the presence of any social or personal factors that may have a role in the development or maintenance of the disorder.

The NICE Pathways on depression and common mental health disorders in primary care bring together all related NICE guidance and associated products on the conditions in sets of interactive topic-based diagrams.

**New evidence:** A cohort study by Tsai et al. (2014) investigated the relationship between social integration and suicide among middle-aged men in the USA. The authors used a prospective database called the Health Professionals Follow-up Study, which enrolled men aged 40–75 years who were dentists, optometrists, osteopaths, pharmacists, podiatrists and veterinarians.

A total of 51,529 men were enrolled in 1986 and sent questionnaires every 2 years. In 1988 and 2006, the questionnaires included a 7-item index of social integration. This index comprised questions about marital status, social network size, frequency of contact with social ties, religious participation and participation in other social groups. The primary outcome was death from suicide between the baseline questionnaire in 1988 and 2012.

A total of 34,901 men with a mean age of 56.6 years responded to the social integration questions in the 1988 survey (67.7% response rate). There were 147 suicides over the 708,945 person-years of follow-up.

In analyses adjusted for baseline characteristics and other causes of death, men with a low social integration index at baseline were around twice as likely to have died from suicide over the 24-year follow-up as men with a high social integration index. The rate of suicide was highest in men in the lowest category of social integration in 1988 (39 deaths per 100,000 person–years) and lowest among men in the highest category of social integration (14 deaths per 100,000 person–years).

When the different elements of the social integration index were examined separately, marital status, social network size and attendance at religious services were identified as having the most significant protective effect on risk of suicide.

Limitations of this study include the lack of information on the mental health of the participants. The findings were in professional US men, so may not be applicable to other populations such as those with different professions, women, those from a different age group or generation, and socioeconomically diverse populations.

The authors conclude that their results support the development of targeted social integration interventions aimed at strengthening existing social network structures or creating new ones. They highlight in particular population-level policies and programmes targeting social integration and selective prevention strategies such as church- and community-based programmes for contacting and supporting isolated people.

**Commentary:** “These findings shed considerable light on our understanding of the links between poor social integration and increased risk of suicide in men. There is a breadth of literature that documents how men often struggle to cope with difficult life transitions – for example, the impact of recession and unemployment, relationship break-up or divorce, or retirement. Such transition points frequently seem to result in a disruption of men’s social and community networks.

“Within a men’s health and suicide prevention policy context in Ireland, we have learned that interventions with vulnerable or ‘at risk’ groups of men can only succeed if they tackle the core issues of isolation and disconnection in men. Moving men out of isolation and reconnecting them to strong social and community networks needs to be at the heart of a more gendered approach to suicide prevention policy and practice.”

– Dr Noel Richardson, National Centre for Men’s Health, Institute of Technology Carlow, Ireland

**Study sponsorship:** National Institutes of Health and Robert Wood Johnson Foundation.
Surgical versus non-surgical treatment for fracture of the heel

Overview: Fractures of the heel bone (calcaneus) can be broadly divided into intra-articular injuries (where the joint surfaces are damaged) and extra-articular fractures (where the joint surfaces remain intact). Intra-articular calcaneal fractures where the bones become misaligned (displaced fractures) can be serious. These fractures typically occur after a fall from a height, such as from scaffolding or a ladder, or as a result of a road traffic incident.

Calcaneal fractures are more common in men than in women: of the 2425 people in England admitted to hospital with fracture of the calcaneus in 2013–14, 2063 (85%) were men (Health and Social Care Information Centre 2015). These fractures are also more common among people in their 20s and manual labourers (Mitchell et al. 2009).

Outcomes after calcaneal fractures can be poor: often the calcaneus is deformed and the alignment of the leg through the ankle to the heel is lost. Many patients need to use a walking stick after injury, and some may experience severe, painful osteoarthritis of the subtalar joint.

Conservative, non-surgical treatment of calcaneal fracture usually comprises elevation, use of ice, early mobilisation and use of a splint (Schepers et al. 2007). Calcaneal fractures can also be treated with surgery, which realigns the bone fragments, fixes them with plates and screws, and restores the subtalar joint. However, the efficacy of surgical versus non-surgical treatment for calcaneal fracture is unclear owing to a paucity of randomised controlled trials (Bruce and Sutherland 2013).

Current advice: Guidance from the American College of Occupational and Environmental Medicine recommends surgical management or non-surgical cast immobilisation for calcaneal fractures. It also recommends pneumatic compression of the foot to reduce swelling for patients with significant oedema after closed calcaneus fractures (that is, fractures where no bone is exposed).

NICE is currently developing guidelines on fractures, with anticipated publication in February 2016.

New evidence: A randomised controlled trial by Griffin et al. (2014) compared surgical treatment with non-surgical treatment for people with intra-articular calcaneal fractures.

Adults with a recent (within the past 3 weeks) closed, intra-articular, displaced calcaneal fracture were recruited from 22 hospitals in the UK. People randomised to surgical treatment underwent open reduction and internal fixation within 3 weeks of injury. Postsurgical care comprised a splint and a standardised physiotherapy rehabilitation regimen. People randomised to non-surgical treatment received gentle mobilisation of the ankle and subtalar joints as pain allowed, a removable splint, and the same standardised physiotherapy rehabilitation regimen as the surgical treatment arm.

The primary outcome was pain and function at 2 years after injury, as reported by patients using the Kerr–Atkins calcaneal fracture score (range 0–100, with 100 points indicating normal pain and function).

Overall, 2006 people presented with calcaneal fractures during the 2 year recruitment period; 502 had severe fractures that met the eligibility criteria. Of these people, 151 (7.5%) agreed to take part and were randomly assigned to surgical treatment (n=73) or non-surgical treatment (n=78). Participants were aged 46.5 years on average (range 18–80 years), and only 24 (16%) were women.

At 2 years, pain and function did not differ significantly between the surgical treatment group (mean Kerr–Atkins score=69.8) and the non-surgical treatment group (mean Kerr–Atkins score=65.7; adjusted
difference=-0.03, 95% confidence interval [CI] −7.08 to 7.02). Regression analysis showed no evidence that outcomes after surgery were affected by fracture severity (p=0.697). Pain and function improved for 18 months after injury in both groups and were then stable until 2 years. General health and quality of life did not differ significantly between treatment groups at 2 years, and a similar proportion in each group had returned to work.

The rate of complications was significantly higher in the surgical treatment group (23%) than in the non-surgical treatment group (4%; odds ratio=7.5, 95% CI 2.0 to 41.8, p<0.001). The most common complication in the surgical treatment group was surgical site infection (19% of participants), followed by reoperations (11%).

This study is limited by the low recruitment rate of eligible patients. The authors suggested that longer term follow-up may show significant differences in outcomes between surgical and non-surgical treatment because other factors, such as arthritis, would have time to become apparent.

Commentary: “This study by Griffin et al. (2014) suggests that surgery is no better than non-surgical treatment for people with calcaneal fractures, but the study has several limitations that may undermine this conclusion. This study included only 7.5% of the people with calcaneal fractures who attended the hospitals involved. This small number of cases after application of the exclusion criteria means that the 27 surgeons in the 22 different hospitals operated on a median of only 2 fractures. The infection rate of 19% of the surgically treated patients is by no means the standard wound complication rate and is hugely worrying.

“Previous studies have shown that initial fracture severity and fracture severity classifications correlate with clinical outcome after surgery (Rammelt et al. 2013), but Griffin et al. (2014) were unable to power their trial to investigate this. Instead they estimated this relationship via regression analysis, drawing the conclusion that there was no evidence that the effect of surgery was affected by fracture severity. It may be inappropriate to conclude this given that the study may have inadvertently excluded the more severe fractures.

“The authors rightly highlight that their results may change over the duration of patient follow-up. In a similar multicentre randomised controlled trial in Sweden, clinical outcomes for surgically and non-surgically treated calcaneal fractures were similar at 1 year. However, in the same cohort of patients, there was a tendency toward improved pain and physical quality of life at 8–12 years’ follow-up in the surgery group, in addition to reduced incidence of radiographically detectable subtalar joint osteoarthritis.

“Overall, it is inappropriate to conclude on the basis of the current evidence that surgery provides no benefit to the treatment of calcaneal fractures.” – Mr Stephen Bendall, Orthopaedic Surgeon, Brighton & Sussex University Hospitals, and Past President, British Orthopaedic Foot and Ankle Society

Study sponsorship: Arthritis Research UK, the University of Warwick, and the University Hospitals of Coventry and Warwickshire NHS Trust.
Improving cardiovascular disease through networks of general practices

Overview: Cardiovascular disease is a leading cause of preventable mortality in the UK. Various risk factors and clinical conditions increase a person’s risk of developing cardiovascular disease (NICE 2014). Modifiable risk factors include high blood level of cholesterol, and hypertension is one of the conditions linked to cardiovascular disease.

The Quality and Outcomes Framework (QOF) offers financial incentives to general practices in England for achieving clinical, public health and quality targets. Individual practices receive payments for meeting various targets, including achieving target levels of blood pressure and cholesterol in people with hypertension, coronary heart disease and stroke. Evidence suggests that quality of care could be improved by grouping general practices into networks and providing incentives for the networks rather than for individual practices (Hull et al. 2013).

Current advice: The NICE guideline on hypertension recommends initially offering lifestyle advice to people with raised blood pressure. Antihypertensive drugs should be offered to people aged under 80 years who have a blood pressure of 140/90 mmHg or higher and who meet 1 or more criteria, such as established cardiovascular disease.

Clinic blood pressure measurements should be used to monitor the response to antihypertensive treatment with lifestyle modifications or drugs. Healthcare professionals should aim for a target clinic blood pressure below 140/90 mmHg in people aged under 80 years with treated hypertension.

The NICE Pathway on hypertension brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence: An observational study in east London by Robson et al. (2014) assessed how grouping general practices into collaborative networks affected outcomes related to cardiovascular disease. A total of 34 general practices in the former Tower Hamlets Primary Care Trust (PCT) were grouped by geographical area into networks of 4–5 practices.

Practices in each network worked together to target 3 elements of cardiovascular disease: hypertension, coronary heart disease and stroke. The networks collectively received financial incentives for hitting targets – such as for blood pressure (less than 150/90 mg/Hg) and cholesterol (less than 5 mmol/l) – in people with these disorders. Patients who did not meet these targets were recalled more frequently.

To help them meet the specified targets, networks were provided with clinical guidelines, ran education meetings and clinical case discussion meetings, and set up peer education support. Each network also had a network manager, who provided IT support and monthly reporting of network performance and incentives received.

Once the networks had been set up, blood pressure and cholesterol control in people with hypertension, coronary heart disease and stroke improved considerably faster in Tower Hamlets than in London as a whole or in England.

In the 3 years after the networks were in place, the proportion of people with hypertension, coronary heart disease and stroke who met the blood pressure target increased by 1.24% a year in Tower Hamlets. The proportion of people with these disorders who hit the blood pressure target increased more slowly each year in London (0.22% a year) and in England as a whole (0.28% a year; p<0.001 for both).

The proportion of people with coronary heart disease who met the serum cholesterol target increased by 0.61% a year in Tower Hamlets after introduction of the networks. Over the same 3 year period, the
proportion of people with coronary heart disease who met the cholesterol target decreased each year in London (−0.40% a year) and in England (−0.67% a year; p<0.05 for both).

In the 3 years after the networks were introduced, mortality from myocardial infarction declined by 43% in Tower Hamlets, a greater drop than the average decrease of 25% for the top 10 ranked PCTs in England.

This analysis did not appear to account for factors that may have changed during the follow-up period and affected the study results, such as demographics, affluence of people registered at the network practices, and patient behaviour. The study took place in an inner-city area, so the results may not apply to less urban areas. The results cannot prove that improvements in care as a result of the networks definitively affected outcomes such as mortality from cardiovascular disease.

Commentary: “This study by Robson et al. (2014) shows the value and impact of primary care adopting a collaborative approach towards optimising the management of cardiovascular disease.

“Within a relatively short time frame, the project led to significant improvements in risk factor modification in the local population, including blood pressure and lipid profiles. Reassuringly, these benefits appeared to translate into improved clinical outcomes, including mortality from myocardial infarction.

“The key intervention within the managed practice networks appeared to be clinical engagement and leadership within each network, supported by peer-to-peer education, clear, concise guidelines and reliable, intuitive IT infrastructure to manage data and recall systems.

“Another significant aspect of the intervention was the focus on the more challenging ‘off target’ patients, who were not achieving the thresholds for blood pressure and cholesterol control. These people are often ‘exempted’ in QOF and not included in practice performance statistics. By providing additional nurse specialist support for these patients, the networks might reduce exemption rates and improve outcomes in these often hard to reach and inherently higher risk cohorts.

“It is worth noting that significant resource was required to establish and support the networks during the programme, which may be a limiting factor in replicating this intervention elsewhere. In addition, it is difficult to define precisely from the study which particular intervention (educational support, financial incentives, adherence to guidelines, peer learning or specialist CVD nurse support) had the greatest impact. It would have been helpful to define this in order to identify which intervention(s) could potentially be adopted by other localities, who may find themselves more constrained in terms of expertise and resource.

“The results of this study are encouraging however, not only in terms of their impact on risk factor modification and clinical outcomes, but also in respect of the positive aspects of collaborative working between practices. The study design suggests that, with appropriate leadership and resource, the network model could prove to be a valuable template for Clinical Commissioning Groups and primary care colleagues nationally who may be considering developing similar models of care.” – Dr Chris Arden, GP, Chandlers Ford; GP with a special interest in Cardiology, Southampton; and Cardiovascular Lead, West Hampshire Clinical Commissioning Group

Study sponsorship: This study did not receive specific funding.

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Antibiotics in fetal and early life and subsequent childhood asthma

Overview: Antibiotic resistance poses a significant threat to public health, particularly because antibiotics underpin routine medical practice in both primary and secondary care. It is important to prescribe antibiotics according to the principles of antimicrobial stewardship, such as prescribing antibiotics only when they are needed and reviewing the continued need for them.

Antibiotic prescribing has been linked to an increased prevalence of childhood asthma, with some studies suggesting that exposure to antibiotics in fetal and early life may increase the risk of developing asthma. A systematic review of 22 observational studies (Murk et al. 2011) found that exposure to antibiotics during the first year of life slightly increased the risk of childhood asthma (odds ratio [OR]=1.52, 95% confidence interval [CI] 1.30 to 1.77; 20 studies). Exposure in utero was associated with a smaller, but significant, increase in risk of asthma (OR=1.24, 95% CI 1.02 to 1.50; 3 studies). The authors suggested that reverse causality, where early symptoms of undiagnosed asthma were attributed mistakenly to respiratory infection and treated with antibiotics, may have been a possible confounder (a factor that can influence the outcome independently of the intervention).

Current advice: Public Health England advises that an antibiotic should be used only when there is likely to be a clear clinical benefit, and a no or delayed antibiotic prescribing strategy should be considered for acute self-limiting upper respiratory tract infections and mild symptoms of urinary tract infections.

NICE guidance on respiratory tract infections states that an immediate antibiotic prescription should only be offered for a respiratory tract infection if a person is systemically very unwell, has symptoms of serious illness and/or complications, is at high risk of complications, or is older than 65 years and satisfies certain criteria.

See the NICE Key Therapeutic Topic on antibiotic prescribing – especially broad spectrum antibiotics (KTT9) for a summary of the evidence base on antibiotic prescribing, especially broad-spectrum antibiotics.

NICE is currently developing a guideline on antimicrobial stewardship, with an anticipated publication date of July 2015.

New evidence: A Swedish observational cohort study by Örtqvist et al. (2014) investigated the association between exposure to antibiotics in fetal and early life and the development of childhood asthma. This population-based registry study included Swedish children born to mothers who were pregnant between July 2005 and December 2010. Siblings who had not been diagnosed with asthma were used as controls to access the impact of familial factors, such as genetic predisposition to respiratory infections, and factors in the home environment. Exposure to antibiotics in fetal and early life was determined by filled prescriptions of systemic antibiotics.

A cohort of 493,785 children were identified, of whom 180,894 children were eligible for sibling analysis. Analyses were adjusted for multiple maternal and child confounding factors.

Exposure to any antibiotic during fetal life increased the risk of childhood asthma in the full cohort (adjusted hazard ratio [HR]=1.28, 95% CI 1.25 to 1.32). The association disappeared in the sibling control analysis, with no significant risk of asthma associated with any antibiotic (adjusted HR=0.99, 95% CI 0.92 to 1.07). Separate analyses of antibiotics used to treat respiratory tract infections and antibiotics for urinary tract or skin infections found similar results.
Antibiotic use during childhood was associated with increased risk of developing asthma in the full cohort, with the greatest risk associated with antibiotics used to treat respiratory tract infections prescribed in the first 6 months of life (adjusted HR=4.12, 95% CI 3.78 to 4.50). The risk of asthma was not as high when antibiotics used to treat respiratory tract infections were prescribed for older children (for example, for children aged 2 or more: adjusted HR=1.79, 95% CI 1.68 to 1.92). The risk also was not as high when antibiotics used for urinary tract or skin infections were prescribed for children aged up to 6 months (adjusted HR=1.54, 95% CI 1.24 to 1.92); this risk reduced further for children older than 12 months.

In the sibling control analysis, the risk of asthma with childhood antibiotic use was lower, but remained significant for children prescribed antibiotics used to treat respiratory tract infections in the first 6 months of life (adjusted HR=2.38, 95% CI 1.78 to 3.13). The risk was non-significant for urinary tract or skin antibiotics in children aged up to 6 months (adjusted HR=0.85, 95% CI 0.47 to 1.55).

The authors concluded that the association between antibiotics and asthma may be caused by confounding factors shared within families. Other possible explanations are that children with respiratory infections might be at increased risk of developing asthma, or that early symptoms of undiagnosed asthma might be attributed mistakenly to respiratory infection and treated with antibiotics.

**Commentary:** “This population-based study discounts the association between use of antibiotics in pregnancy and early life and the development of asthma in children. Nevertheless, the conclusions reached do not contradict present guidance, which discourages the use of antimicrobials in the absence of clear indications for use.

“Although use of antimicrobials appears not to increase the risk of developing asthma, the principles of antimicrobial stewardship still apply. Örtqvist et al. (2014) draw attention to the risk of emergence of resistant organisms associated with overuse of antimicrobials. Antimicrobials should be reserved for those cases where there is evidence that the patient is systemically unwell or is suffering from complications caused by bacterial infection, or is at risk of complications as a result of co-existing morbidity.

“These principles apply to antimicrobial use in any clinical situation. Prescribers should delay or withhold antimicrobials in accordance with published guidelines, which have been produced in an effort to limit the emergence and spread of resistant organisms and to preserve the effectiveness of antimicrobial drugs.” – Dr Christopher Cefai, Consultant Microbiologist, Wrexham Maelor Hospital

**Study sponsorship:** The Swedish Research Council.
Short-term electrocardiogram (ECG) monitoring can be used to detect atrial fibrillation, but this approach cannot identify paroxysmal fibrillation. Previous studies have suggested that monitoring heart rhythms for a longer period after ischemic stroke or TIA can improve detection of atrial fibrillation and ensure patients are offered anticoagulation therapy (Higgins et al. 2013).

**Current advice:** The NICE guideline on atrial fibrillation recommends performing manual pulse palpation to assess for the presence of an irregular pulse that may indicate underlying atrial fibrillation in people presenting with stroke or TIA. An ECG should be performed in all people, whether symptomatic or not, in whom atrial fibrillation is suspected on the basis of an irregular pulse. In people with suspected paroxysmal atrial fibrillation undetected by standard ECG recording:

- use a 24-hour ambulatory ECG monitor in those with suspected asymptomatic episodes or symptomatic episodes less than 24 hours apart
- use an event recorder ECG in those with symptomatic episodes more than 24 hours apart.

The guidance adds that the CHA2DS2-VASc stroke risk score should be used to assess stroke risk in people with symptomatic or asymptomatic paroxysmal, persistent or permanent atrial fibrillation. Anticoagulation with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist should be considered in people with non-valvular atrial fibrillation and previous stroke or TIA.

The NICE guideline on stroke adds that people with disabling ischaemic stroke who are in atrial fibrillation should be treated with aspirin 300 mg for the first 2 weeks before considering anticoagulation treatment.

The NICE Pathways on atrial fibrillation and stroke bring together all related NICE guidance and associated products on the conditions in sets of interactive topic-based diagrams.

**New evidence:** Two randomised controlled trials assessed long-term ECG monitoring to detect atrial fibrillation in people who had experienced a stroke or TIA and had no known atrial fibrillation.

**Gladstone et al. (2014)** enrolled people in Canada aged 55 years or older who had experienced a stroke and had no atrial fibrillation detected with conventional 24-hour screening. Participants were randomly assigned to ambulatory ECG monitoring either for 30 days with an event recorder or for 24 hours with a Holter monitor.

A total of 572 participants were randomised (287 to the 30-day monitoring group and 285 to the 24-hour monitoring group), and 557 (97.7%) were included in the intention-to-treat analyses. ECG monitoring for 30 days identified more people with atrial fibrillation (45 people, 16.1%) than 24-hour ECG monitoring (9 people, 3.2%; absolute difference=12.9 percentage points, 95% confidence interval [CI] 8.0 to 17.6 percentage points, p<0.001). By 90 days, patients in the 30-day monitoring group were more likely to be on anticoagulation therapy (18.6%, up from 5.6% at baseline) than those in the 24-hour monitoring group (11.1%, up from 6.7%).

**Sanna et al. (2014)** enrolled people aged 40 years or older with stroke or TIA and no evidence of atrial fibrillation from Europe, Canada and the USA. Participants were randomly assigned to continuous ECG monitoring with an implantable subcutaneous cardiac monitor or to standard arrhythmia monitoring (ECG monitoring performed at study visits at the discretion of the investigator). All participants were followed up at 1, 6 and 12 months and every 6 months thereafter until the study closed.

A total of 441 participants were randomised (221 to the ECG monitoring group and 220 to the standard monitoring group) and included in the intention-to-treat analyses. During the first 6 months of follow-up, 65 patients in the standard monitoring group had conventional ECG monitoring, 17 patients had 24-hour Holter ECG monitoring, and 1 patient had ECG monitoring with an event recorder.

Continuous ECG monitoring detected more people with atrial fibrillation (19 people, 8.9%) than did standard monitoring (3 people, 1.4%) in the first 6 months of follow-up (hazard ratio=6.4, 95% CI 1.9 to 21.7, p<0.0001). By 12 months, people in the continuous ECG monitoring group were more likely to be on
anticoagulation therapy (14.7% versus 6.0% in the standard monitoring group) and less likely to have experienced an ischaemic stroke or TIA (7.1% versus 9.1%).

Limitations of these studies include that neither was able to make a causal association between atrial fibrillation and the index stroke or TIA. In addition, randomisation occurred more than a month after the index stroke or TIA in both studies, and neither could record all instances of atrial fibrillation owing to the memory size of the ECG monitoring devices.

Commentary: “These studies clearly show that we need to look harder and look longer for underlying atrial fibrillation in patients presenting with stroke, before labelling someone as having ‘cryptogenic stroke’. The diagnosis of ‘cryptogenic stroke’ is really a diagnosis of exclusion, after very strenuous efforts to exclude atrial fibrillation. Many patients with paroxysmal atrial fibrillation are asymptomatic, and relying on symptoms alone is inadequate for diagnosis.

“A stroke confers the highest risk of a subsequent stroke, and if atrial fibrillation is detected, effective stroke prevention is needed. Prevention essentially comprises oral anticoagulation therapy, whether given as a vitamin K antagonist (VKA; for example, warfarin) with good quality anticoagulation control (average time in therapeutic range >65%), or a non-VKA oral anticoagulant.

“More prolonged atrial fibrillation monitoring improves the detection rate. As part of the standard work-up, 2–4 week ECG monitoring or, where there is a high index of suspicion, an implanted monitoring device, should be considered. This would improve diagnosis of atrial fibrillation, and, by using thromboprophylaxis with oral anticoagulation, reduce the risks of a subsequent stroke that may be fatal or disabling.” – Professor Gregory Y H Lip, Professor of Cardiovascular Medicine, University of Birmingham, and Aalborg University, Denmark

Study sponsorship: Gladstone et al. (2014) was funded by the Canadian Stroke Network and Sanna et al. (2014) was funded by Medtronic.

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Case study from the Quality and Productivity collection: mobile clinics for chronic stable glaucoma management

Glaucoma affects 1–2% of people aged over 40 years and 10% of people aged over 70 years (NICE 2009). Glaucoma is a treatable condition, but it is the reason for more than 10% of all registrations for blindness in the UK, so has a significant impact on whether people are able to live independently.

Because glaucoma is so common, it places a large burden on all hospital eye departments. People with chronic glaucoma need lifelong monitoring so that any progression of visual damage can be detected.

An initiative by Ipswich and East Suffolk Clinical Commissioning Group and Ipswich Hospital NHS Trust aims to improve productivity by reducing demand for appointments from low-risk people in hospital eye clinics. It provides local care to people with stable or low-risk glaucoma using a mobile clinic, allowing the hospital to see people with more complex disease.

The clinic, named the ‘i-van’, is based in a community setting and regularly visits 4 locations throughout rural Suffolk. All necessary tests are performed in 1 appointment. In the previous system, people required on average 2.75 appointments to undertake the same tests.

The service can see up to 20 people a day. All results are recorded electronically and reviewed by consultant ophthalmologists using a web-based system, to ensure the quality of decision-making.
John Havard, Senior Partner at Saxmundham Health general practice in Suffolk, said: “There has been a very positive response from people who have used the service. The initiative brings an improvement in care quality for people with stable, low-risk glaucoma because they are seen sooner and are less likely to miss appointments. All optometrist decisions are reviewed electronically by consultant ophthalmologists. People with unstable, higher risk glaucoma also benefit because reduced demand means there are more appointments available at the hospital eye clinic.”

It is predicted that the annual saving from this initiative will be around £96,000 per 100,000 population. This estimate is based on a reduction in the number of appointments needed to complete the required tests, and a reduced follow-up outpatient tariff.

The NICE Quality and Productivity collection provides users with practical case studies that address the quality and productivity challenge in health and social care. All examples submitted are evaluated by NICE to assess the degree to which the initiative meets the Quality and Productivity criteria: savings, quality, evidence and implementability.

Visit the NICE website for more details of mobile clinics for chronic stable glaucoma management and other examples of quality and productivity initiatives.

Case study from the Quality and Productivity collection: ensuring appropriate use of monitored dosage systems

Monitored dosage systems (also known as compliance aids or multi-compartment medicines systems) provide medication in time-specific packs to ensure that the correct medication is taken at the correct day and time. Many patients are admitted to hospital with monitored dosage systems or are issued with them during their stay at the request of carers, where their use might not be appropriate.

There is often great expectation that these devices will ensure reliable and safe administration of medication, but in practice this is not necessarily the case. It has been suggested that monitored dosage systems may make patients less knowledgeable about their medicines and how, when and why they should be taken (Royal Pharmaceutical Society 2013). This reduction in knowledge may in turn reduce patient autonomy and choice. There is also the risk of human error when preparing the devices, which could have serious consequences. The preparation and checking of unnecessary monitored dosage systems creates a significant additional workload for hospital pharmacies.

An initiative from Taunton & Somerset NHS Foundation Trust aimed to reduce the inappropriate use of monitored dosage systems. The hospital pharmacy began a programme to ensure monitored dosage systems were only issued where patients were already using the devices before admission and were not found to be capable of managing medicines from original packaging. Dosage systems could also be issued when a consultant had assessed the patient as requiring a device to address a specified problem with medicines adherence.

This approach is in line with NICE guidance on medicines adherence (NICE 2009), which states that monitored dosage systems should be considered an option to improve adherence on a case-by-case basis, and only if there is a specific need to overcome practical problems. This decision should follow a discussion with the patient to explore possible reasons for non-adherence and the options available to improve adherence, if that is their wish.

The predicted productivity savings associated with this strategy are about £20,800 for a population of 340,000, equivalent to £6100 per 100,000 population.

Jon Beard, Chief Pharmacist and Accountable Officer for controlled drugs from Taunton & Somerset NHS
Foundation Trust, said: “Although the savings per unit population are low, the costs to implement this strategy are negligible and it can be implemented quickly. This initiative has only recently been implemented, but initial results demonstrate an 80% reduction in the number of monitored dosage systems issued.”

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- Fertility
- Psychosis and schizophrenia in children and young people
- Occupational therapy and physical activity interventions to promote the mental wellbeing of older people in primary care and residential care
- Promoting physical activity for children and young people

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 fertility was published by NICE in March 2015. It includes commentary from the EUAG on 15 new articles (relevant to NICE clinical guideline 156), covering the following topics:

- Investigation of suspected tubal and uterine abnormalities
- World Health Organization (WHO) Group II ovulation disorders
- Controlled ovarian stimulation in IVF
- Luteal phase support after IVF
- Admissions to hospital for children born after IVF
- Risk of thromboembolism in pregnancies after conception using IVF
- Effects of culture media on outcomes of IVF
- Oxygen concentration during embryo culture
- Endometrial injury to improve outcomes of assisted reproduction procedures.

The Evidence Update on psychosis and schizophrenia in children and young people was published by NICE in March 2015. It includes commentary from the EUAG on 12 new articles (relevant to NICE clinical guideline 155), covering the following topics:

- Long-term outcomes of early-onset schizophrenia
- Cognitive deficits in people at risk of psychosis
- Cognitive behavioural therapy (CBT) for people at risk of psychosis
- CBT with or without an antipsychotic for people at risk of psychosis
- Antipsychotic medication for children and young people with first episode psychosis
- Group psychoeducation for young people with psychosis and their families
- Risk of neutropenia with clozapine
- Genetic basis of weight gain associated with antipsychotic drugs.

The Evidence Update on occupational therapy and physical activity interventions to promote the mental wellbeing of older people in primary care and residential care was published by NICE in March 2015. It includes commentary from the EUAG on 6 new articles (relevant to NICE public health guidance 16), covering the following topics:

- Occupational therapy for older people living in the community
- Occupational therapy for older people in residential care
- Mixed exercise programmes
- Non-face-to-face advice on physical activity
- Promoting participation in walking schemes.

The Evidence Update on promoting physical activity for children and young people was published by NICE in March 2015. It includes commentary from the EUAG on 13 new articles (relevant to NICE public health guidance 17), covering the following topics:

- School-based versus community-based after-school programmes
- Sharing school facilities with community organisations
- Safe Routes to School programme
- A physical activity programme for early years daycare centres
- Professional development training in after-school programmes
- Active free play with non-traditional play materials and managing adult risk perception
- Impact of school break-time interventions on physical activity
- Physical activity interventions for pre-school children, such as a movement skills intervention
- Promoting motor development in disabled pre-school children
- Community and family interventions
- Reducing sedentary behaviour
- Online interventions to promote physical activity.

Changes to NICE evidence awareness products

NICE has announced some changes to 2 of its evidence awareness products: Evidence Updates and Eyes on Evidence.

From April 2015, NICE will no longer produce Evidence Updates. However, information on important new evidence in relation to NICE guidelines will still be available through NICE surveillance reports.

NICE surveillance reports contain a summary of new evidence related to the guideline and an in depth commentary on a selection of this evidence. In addition, surveillance reports give a decision on whether the relevant guideline should be updated and the rationale behind this decision.

Surveillance reports go further than Evidence Updates in that they include the decision that NICE has taken about the need to update the relevant clinical guideline in light of the new evidence. Evidence
Updates were developed to help inform the review proposal on whether or not to update a NICE clinical guideline, but the process of developing an Evidence Update was separate to the process of developing a guideline review proposal. Therefore Evidence Updates were only able to discuss potential impacts on recommendations and did not include information on the decisions NICE had taken in light of the new evidence.

From April 2015, NICE will have one process that will produce the new surveillance reports and the guideline update decision. The reports explain how potential impacts on guidelines from new evidence have been considered by NICE and the plan for responding to them. To receive the surveillance reports, please email surveillance@nice.org.uk.

The Eyes on Evidence awareness service has moved to a new home on the NICE website. Information about Eyes on Evidence and how to subscribe to the service is now available on the NICE newsletters and alerts page. Previous Eyes on Evidence articles can be found in NICE Evidence Search by searching for “Eyes on Evidence”. Previous issues will be available on the NICE newsletters and alerts page.

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