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This month in Eyes on Evidence

Socioeconomic inequalities in cancer mortality
A cohort study found that British men in manual jobs were more likely than those in non-manual jobs to die from cancer, a disparity that remained broadly unchanged between 1978 and 2013.

Implementation of antibiotic prescribing guidance
A study of Public Health England's 'Start smart − then focus' antibiotic prescribing toolkit concluded that most hospital antibiotic policies in England 'start smart' by recommending broad-spectrum antibiotics for empirical therapy in severe infections. However fewer 'focus' by reviewing the ongoing need for antibiotics after a couple of days, as recommended.

Costs of autism spectrum disorders
An analysis of data in existing literature estimated that the lifetime direct and indirect costs associated with a person with an autism spectrum disorder in the UK was £1.5 million for those who also had an intellectual disability and £0.92 million for those without intellectual disability, although the range of costs was considerable.

Stenting versus endarterectomy for symptomatic carotid stenosis
An international multicentre randomised trial found that carotid stenting was as effective as endarterectomy at preventing fatal or disabling stroke for up to 10 years in people with symptomatic carotid stenosis.

Imaging techniques to diagnose suspected kidney stones
A randomised controlled trial in the US found that using ultrasonography as initial imaging for suspected kidney stones in people presenting to A&E was associated with less radiation exposure than CT and did not increase the incidence of subsequent high-risk diagnoses with complications that could be related to missed or delayed diagnosis.

Evidence summaries from NICE's Medicines and Prescribing Programme
NICE has recently published medicines evidence summaries on:

- Chronic obstructive pulmonary disease: aclidinium/formoterol
- Infantile haemangioma: oral propranolol
- Asthma: tiotropium as add-on therapy to inhaled corticosteroids in moderate asthma
- Acute coronary syndromes: further evidence on duration of dual antiplatelet therapy after drug-eluting stent implantation

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Socioeconomic inequalities in cancer mortality

Overview: Previous studies have shown that patients with cancer who live in deprived areas are more likely to die from cancer than those who live in more affluent areas (Coleman et al. 2004). Between 1997 and 2011, around 19,200 cancer deaths a year in England could have been avoided if cancer as a cause of death (that is, population mortality rates from cancer) for the most deprived groups were as low as those for the least deprived (National Cancer Intelligence Network 2014).

Possible explanations for the lower cancer survival among cancer patients living in more deprived areas include diagnosis at a more advanced stage of disease, poorer general health (such as comorbid cardiovascular or respiratory disease), and variations in treatment (Lyratzopoulos 2015). In addition, people living in more deprived areas have a higher risk of developing cancer through their life course (National Cancer Intelligence Network 2014). The combined effect of inequalities in cancer incidence and disparities in cancer survival results in inequalities in cancer mortality.

Since 1996, various waves of health policy in England have aimed to target socioeconomic inequalities in cancer mortality, either by supporting earlier presentation and diagnosis or by better and more standardised treatment. The NHS Cancer Plan, published in 2000, explicitly aimed to tackle the inequalities in cancer mortality by commitments to reduce smoking and improve access to cancer treatment. The 2011 National Strategy for Cancer outlined the need for better data and performance indicators on inequalities in cancer and better targeting of information on prevention and symptom awareness.

Current advice: The NHS Constitution for England states that the NHS has a social duty to promote equality through the services it provides and to pay particular attention to groups or sections of society where improvements in health and life expectancy are not keeping pace with the rest of the population. Staff should contribute towards providing fair and equitable services for all and play a part, wherever possible, in helping to reduce inequalities in experience, access or outcomes between differing groups or sections of society requiring health care.

New evidence: A cohort study by Ramsay et al. (2014) assessed how socioeconomic inequalities in cancer mortality among men in Great Britain changed over time. The authors used data from a sample of 7735 men recruited to the British Regional Heart Study in 1978–1980. The men were aged 40–59 years at recruitment and drawn from 24 towns representing major British regions.

Socioeconomic status was based on the longest-held occupation of participants at study entry. Participants were grouped according to whether they had a manual job (semi-skilled, partly skilled, and unskilled manual occupations) or a non-manual job (professionals, managerial occupations, and semi-skilled non-manual jobs). Mortality and cause of death were established from death certificates.

This analysis comprised 7489 men who were followed up for 35 years between 1978 and 2013. At recruitment, men in the manual occupation group were more likely to be current smokers (48% versus 30% in the non-manual group), moderate-to-heavy drinkers (43% versus 29%), and physically inactive (44% versus 33%).

A total of 4627 deaths occurred during the study period, of which 1484 deaths were from cancer. The risk of death from any cancer during the study period was higher in men who had manual jobs than in men with non-manual jobs (hazard ratio [HR]=1.35, 95% confidence interval [CI] 1.21 to 1.50). The risk of mortality from smoking-related cancer was also higher in men who had manual jobs (HR=1.53, 95% CI 1.32 to 1.79).

The raised cancer mortality among men who had manual jobs compared with men who had non-manual jobs did not differ significantly over the 35-year study period. The absolute difference in survival to 70 years in men who had non-manual jobs versus those who had manual jobs was 2.53% in 1978–1980 to 1988–1990 and 2.87% in 1998–2000 to 2008–2013.

Limitations of this evidence include that the participants were all men, so the findings may not be generalisable more diverse populations. The analysis did not appear to account for confounding factors, and did not encompass likely mediators involved in the excess cancer mortality in poorer patients.

Commentary: “This research augments our understanding of the prevailing problem of socioeconomic inequalities in cancer mortality. Ramsay et al. (2014) found that in the past 3 decades, cancer has remained a more frequent cause of death among British men with a lower socioeconomic position. Some of this information could be possibly inferred by repeatable cross-sectional studies based on routine, population-based, statistics. However, in this study the authors estimated the evolution of cancer mortality inequalities during the life course of participants of a valuable cohort study.

“Socioeconomic inequalities in cancer mortality reflect inequalities in cancer incidence (because of differential exposure to risk factors such as smoking, heavy drinking and physical inactivity) combined with inequalities in cancer survival (once cancer has been diagnosed). The latter (inequalities in cancer survival) represents a particularly complex problem with several likely causes, including differences in screening uptake (such as bowel cancer screening, which has been introduced more recently) as well as variation in stage at diagnosis of symptomatic patients, comorbidity and cancer treatment.

“This new evidence provides a ‘reality check’ for the persistence of the complex problem of socioeconomic inequalities in cancer mortality. It should motivate further inquiries and efforts to address the differential in cancer incidence and survival between different socioeconomic groups. This task requires a concerted effort to help make public health policy more effective in reducing inequalities in cancer incidence, combined with public health and healthcare improvement measures to increase screening uptake and improve timeliness of presentation and treatment.” ***– Dr Georgios Lyratzopoulos, Cancer Research UK Clinician Scientist Fellow and Clinical Reader in Cancer Epidemiology, University College London***

Study sponsorship: British Heart Foundation.

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Implementation of antibiotic prescribing guidance

Overview: Appropriate use of antibiotics is important to reduce the serious threat of antibiotic resistance and the risk of healthcare-associated infections such as *Clostridium difficile*. The concept of antimicrobial stewardship was developed to support optimal prescribing of antimicrobials, prevent overuse, misuse and abuse, and minimise development of resistance. The term 'antimicrobial' includes antifungal, antiviral, and antiparasitic drugs as well as antibacterial drugs (more commonly known as antibiotics).

Healthcare professionals should ensure prescribing is in line with NICE guidance, Public Health England's guidance for primary care on managing common infections, the organisation's toolkit for secondary care 'Start smart − then focus', and local trust antibiotic guidelines. The total volume of all antibiotic prescribing and broad-spectrum antibiotic prescribing in primary and secondary care should be reviewed against local and national data.

The NICE key therapeutic topic on antibiotic prescribing – especially broad spectrum antibiotics summarises the issues around antibiotic prescribing and is supported by the NICE evidence summary: medicines and prescribing briefing on *Clostridium difficile* infection: risk with broad-spectrum antibiotics.

Current advice: Public Health England's 'Start smart − then focus' toolkit outlines best practice in antimicrobial stewardship in the secondary care setting.

'Start smart' states that antibiotics should be started within 1 hour of diagnosis (or as soon as possible) in people with severe and life-threatening infections (particularly where the cause of infection is uncertain), in line with local antibiotic prescribing guidance. In people with less severe infection, local prescribing guidance should recommend narrow-spectrum antibiotics that cover the expected pathogens.

'Focus' states that the clinical diagnosis and continuing need for antibiotics should be reviewed within 48−72 hours, with 5 options to consider:

- stop antibiotics if there is no evidence of infection
- switch antibiotic formulation from intravenous to oral
- change antibiotic – ideally to a narrower spectrum, but broader if required
- continue antibiotics and document next review date
- start outpatient parenteral antibiotic therapy.

NICE has produced several guidelines relating to healthcare-associated infections and antibiotic prescribing, including NICE guidelines on respiratory tract infections – antibiotic prescribing and pneumonia. The NICE pathways on self-limiting respiratory tract infections – antibiotic prescribing and pneumonia bring together all related NICE guidance and associated products on the 2 areas in sets of interactive topic-based diagrams.

NICE is also developing guidelines on antimicrobial stewardship (publication expected July 2015) and antimicrobial stewardship – changing risk-related behaviours (publication expected March 2016).

New evidence: Llewelyn et al. (2014) surveyed specialist antibiotic pharmacists in acute hospital trusts in England about empirical treatment of common infections ('start smart') and antibiotic prescription reviews ('focus'). The infections assessed were community- and hospital-acquired pneumonia, pyelonephritis, community-acquired abdominal sepsis and severe sepsis. Antibiotics were categorised as broad spectrum (cephalosporins, quinolones, carbapenems and penicillin combination antibiotics, such as co-amoxiclav

and piperacillin-tazobactam) or narrow spectrum (penicillin, amoxicillin, aminoglycosides, doxycycline and trimethoprim). Rates of *C difficile* infection were obtained from the national mandatory surveillance system.

A total of 105 of the 145 trusts contacted responded to the survey (response rate=72%). Broad-spectrum penicillin combination antibiotics were commonly recommended in hospital trust antibiotic policies for the infections assessed. A substantial number of responding trusts recommended narrow-spectrum antibiotics first line for community-acquired pneumonia (42/105 [40%]) and pyelonephritis (50/105 [48%]). Very few trusts recommended quinolones or cephalosporins for first-line treatment.

Across the indications, 18−28% of policies from responding trusts recommended giving first-line antibiotic treatment for 24−48 hours only. The most commonly recommended treatment duration for community- and hospital-acquired pneumonia, pyelonephritis and community-acquired abdominal sepsis was 7 days or more. Nearly all trust policies (100/105 [95%]) recommended antibiotic prescription reviews, but less than half of the trusts that provided details on reviews (46/96 [48%]) reported monitoring compliance.

Trusts with policies recommending broad-spectrum antibiotics for community-acquired pneumonia had significantly higher rates of *C difficile* infection than those that recommended narrow-spectrum antibiotics (p=0.06). No increased risk of *C difficile* was seen with broad-spectrum antibiotics compared with narrow-spectrum antibiotics for other infections assessed in the study.

The study has several limitations. It is possible that the 40 trusts (28%) that did not respond to the survey were less engaged in antimicrobial stewardship than those that did respond. Also, trusts with high rates of *C difficile* may have introduced antibiotic prescribing policies with greater use of narrow-spectrum antibiotics, which may have reduced the relationship between broad-spectrum antibiotics and rates of *C difficile*. It is also possible that trust antibiotic policies may not reflect actual use of antibiotics within the organisations.

Commentary: “Antimicrobial resistance remains a major clinical and public health issue. Antimicrobial use is a key driver of resistance. Antimicrobial stewardship, an organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials, will help to preserve their future effectiveness (Department of Health 2013). The 3 goals for an effective antimicrobial stewardship programme are:

- Optimising therapy for the individual patient
- Preventing overuse, misuse and abuse
- Minimising development of resistance at patient and community levels (Doran 2011).

“The study by Llewelyn et al. (2014) highlighted that most hospital trust policies recommended using antibiotics for at least 7 days for most indications and less than 50% of trusts monitored 48–72 hour review of antibiotic prescriptions. Such recommendations of at least 7 days of antibiotics for most indications could lead to unnecessary use of broad-spectrum antibiotics. This could increase the risk of *C difficile* if better systems are not put in place to improve treatment focus at 48–72 hours, as recommended by the ‘Start smart − then focus’ antimicrobial stewardship toolkit.

“The drive to reduce the number of *C difficile* infections and the risk of antibiotic resistance across the NHS has led to reduced use of cephalosporins and quinolones in recent years; this is reflected in the published data by Llewelyn et al. (2014). In the study, cephalosporins and quinolones were recommended in less than 6% of trust guidelines and only for upper and catheter-associated urinary tract infections. However, co-amoxiclav, potentially a high risk antibiotic for *C difficile* infection from observational data, was commonly recommended.

“Similarly, a survey of antimicrobial stewardship activities in 2014 by the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) showed that for 10 common infections, co-amoxiclav was 1 of the top 5 antibiotics recommended in trust guidelines. Cephalosporins and quinolones were recommended in less than 2% of trust guidelines. Antimicrobial consumption data reported by ESPAUR highlighted that between 2010 and 2013, co-amoxiclav use increased by 13%, piperacillin-

tazobactam by 46% and carbapenems by 31%.

“It is clear that many English hospital trusts are starting smart with their recommended antibiotic prescribing guidelines. However, greater emphasis is required on implementing and monitoring the focus element of ‘Start smart − then focus’ to reduce unnecessary use of broad-spectrum antibiotics.” ***– Dr Diane Ashiru-Oredope, Pharmacist Lead, Antimicrobial Resistance, Stewardship and Healthcare-associated Infection Programme, Public Health England***

Study sponsorship: This study was not funded.

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Costs of autism spectrum disorders

Overview: Autism is a lifelong neurodevelopmental condition characterised by persistent difficulties in social interaction and communication, the presence of rigid and repetitive behaviours, and resistance to change or restricted interests (NICE 2012). The umbrella term ‘autism spectrum disorder’ is used to describe all subgroups of autism, Asperger’s syndrome and atypical autism (or pervasive developmental disorder not otherwise specified). Approximately 50% of children and young people with autism also have intellectual disability (IQ below 70; Charman et al. 2007).

Autism spectrum disorders can be associated with financial costs for the affected people, their families, and society as a whole. Previous estimates put the lifetime cost of supporting a person in the UK with an autism spectrum disorder and intellectual disability at approximately £1.23 million, and approximately £0.80 million for someone with an autism spectrum disorder and no intellectual disability (Knapp et al. 2009).

The costs associated with autism spectrum disorder can include direct medical costs, non-medical costs (for example, special education, day care and after-school care), accommodation costs (private, supported living, residential or hospital) and out-of-pocket payments by families (such as travel to medical appointments and home modifications). In addition, opportunity costs may arise as a result of unemployment or underemployment in patients and their families.

Current advice: NICE has guidelines on the management and support of children and young people on the autism spectrum and on recognition, referral, diagnosis and management of adults on the autism spectrum. Both guidelines recommend that the assessment, management and coordination of care for children, young people and adults with autism should be provided through local specialist community-based multidisciplinary teams.

Children, young people and adults with autism should be offered psychosocial interventions for the core symptoms of autism and interventions focused on life skill. Psychosocial and pharmacological interventions should also be offered for the management of coexisting mental health or medical problems.

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

New evidence: Buescher et al. (2014) used existing data to estimate the annual and lifetime costs

associated with people with autism spectrum disorders in the UK and in the US in 2013. The costs analysed were accommodation, medical services, non-medical services, special education, employment support, and out-of-pocket payments by families. Opportunity costs were calculated as lost productivity as a result of lost or disrupted employment for people with autism spectrum disorders and their families. Lifetime costs assumed a life expectancy of 67 years for people with autism spectrum disorders and were discounted at a rate of 3.5%.

The number of people with autism spectrum disorders in the UK was estimated as 604,824. The annual cost to the UK of children under the age of 18 years with autism spectrum disorders was estimated as £3.1 billion a year, assuming a 40% prevalence of intellectual disability. The annual cost was £3.4 billion when the prevalence of intellectual disability was assumed to be 60%. These costs were largely driven by direct non-medical costs, such as special education, and indirect non-medical costs, such as parental productivity loss.

The annual cost of adults with an autism spectrum disorder was estimated as £29 billion a year assuming a 40% prevalence of intellectual disability and £31 billion a year assuming a 60% prevalence. The largest contributing factors to these costs were accommodation, direct medical costs, and productivity loss for the person with autism.

The cost of an autism spectrum disorder throughout a person's lifetime was estimated as £1.5 million for those with intellectual disability and £0.92 million for those without intellectual disability.

The authors conclude that the high direct and indirect economic effect of autism spectrum disorders reiterate the importance of searching for effective and cost effective interventions and support arrangements. In addition, the spread of costs across difference services highlights to need of effective coordination among health and social care professionals and the costs borne by families should be considered.

Limitations of this analysis include that the prevalence and cost estimates were compiled from a number of sources, which were not rated for quality and in some cases were not precise. Data were not available for some costs, so estimates of overall costs involved several assumptions. In addition, the authors did not consider the cost effectiveness of the interventions and support arrangements they studied.

Commentary: “This study provides a new and comprehensive estimate of the broad costs associated with autism spectrum disorders, rather than being confined to costs for particular domains of care such as education or medical care.

“Splitting the data according to intellectual disability is useful in that it allows comparison of costs on the basis of a factor that has great impact on care needs. However, the authors did not compare their estimates with the costs associated with children and adults who have intellectual disability but no autism, or the cost of having a child without any disability. This data would allow calculation of the additional costs associated with autism.

“A similar piece of research by Barrett et al. (2014) compared service use and costs over 6 months among young people in the UK with autism spectrum disorders, special needs and typical development. This study found that the total costs for service use were highly skewed by a small number of young people and the mean cost did not necessarily reflect the range. For example, the cost of 6 months of services for a young person with autism spectrum disorder ranged from £2525 to £40,959, with the average total cost estimated as £8968. The costs estimated by Buescher et al. (2014) could likewise be skewed by a few people with very high costs and thus be an overestimate.

“The Buescher et al. (2014) study has a number of limitations, and high on this list is the difficulty of routinely monitoring and aggregating costs associated with autism. However, the estimates in this analysis are likely to be the best possible given the data available. The prevalence of autism has also been changing, so that there are an increasing number of people diagnosed with autism spectrum disorder who do not have intellectual disability. The estimates calculated by Buescher et al. (2014) could therefore be too high because the prevalence rates for intellectual disability in autism they used could be too high.

"The conclusion is that autism is costly for families and society, and that the direct and indirect economic effect is greater for people with an autism spectrum disorder who also have intellectual disability, particularly impaired development of life skills (adaptive behaviour), and special educational needs." **–** ***Professor Gillian Baird, Consultant Paediatrician and Honorary Professor, Kings Health Partners and Guy's & St Thomas's NHS Foundation Trust, London***

Study sponsorship: Autism Speaks.

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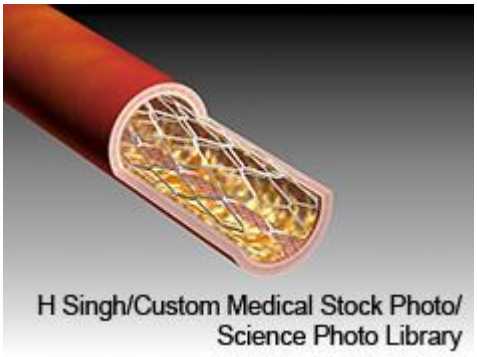
Stenting versus endarterectomy for symptomatic carotid stenosis



Overview: Carotid stenosis occurs when fatty deposits build up in the carotid arteries that carry blood to the brain, causing them to narrow and harden (NICE 2011). Blood clots that form on the plaques can detach and lodge in thinner arteries in the brain, causing symptoms like a transient ischaemic attack (TIA, sometimes called a 'mini stroke') or a stroke.

One approach to treating symptomatic carotid stenosis is carotid endarterectomy, where a cut is made in the neck to access the narrowed artery and remove the fatty plaques (NHS Choices 2014). Another less-invasive technique involves using a metal mesh tube called a stent to widen the narrowed carotid artery. The stent is inserted into an artery in the leg and moved into place in the carotid artery by using a fine wire.

Previous studies indicate that compared with carotid endarterectomy, stenting is associated with a higher risk of a procedure-related stroke or death in the first 30 days after treatment (Bonati et al. 2012). The long-term efficacy and safety of carotid artery stenting compared with endarterectomy is not clear.

Current advice: The NICE guideline on stroke recommends that all people with suspected non-disabling stroke or TIA who are considered candidates for carotid endarterectomy should have carotid imaging within 1 week of onset of symptoms.

People with stable neurological symptoms from acute non-disabling stroke or TIA who have symptomatic carotid stenosis of 50–99% according to North American criteria, or 70–99% according to European criteria, should be assessed and referred for carotid endarterectomy within 1 week of onset of symptoms. These people should undergo surgery within a maximum of 2 weeks of onset of stroke or TIA symptoms.

NICE guidance on carotid artery stent placement recommends carotid artery stenting for symptomatic extracranial carotid stenosis, provided that normal arrangements are in place for clinical governance and audit or research. During the consent process, clinicians should ensure that patients understand the risk of stroke and other complications associated with this procedure. Clinicians should also ensure that patients understand the reasons for advising carotid artery stent placement rather than endarterectomy in their particular case.

The National Stroke Strategy recommends considering immediate referral for appropriately urgent specialist assessment and investigation in all patients presenting with a recent TIA or minor stroke. Carotid intervention for recently symptomatic severe carotid stenosis should be regarded as an emergency procedure in patients who are neurologically stable, and should ideally be performed within 48

hours of a TIA or minor stroke.

The NICE pathway on carotid imaging and carotid endarterectomy for people with TIA or non-disabling stroke brings together all related NICE guidance and associated products on the area in a set of interactive topic-based diagrams.

New evidence: Bonati et al. (2014) reported the long-term results of the International Carotid Stenting Study (ICSS), a multicentre randomised clinical trial of stenting versus endarterectomy for the treatment of symptomatic carotid stenosis.

ICSS recruited 1713 people older than 40 years who had atherosclerotic carotid stenosis with symptoms (for example, a recent TIA or ischaemic stroke) and at least 50% reduction in the diameter of the affected artery. Participants were identified from 50 centres in Europe, Australia, New Zealand and Canada and randomised to undergo carotid stenting (including use of a cerebral protection device; n=855) or endarterectomy (standard or eversion; n=858). All participants received medical care, including antiplatelet therapy or anticoagulation if indicated. Participants were followed up at 30 days after treatment (end of the procedural period), 6 months after randomisation, and every year thereafter.

This analysis considered long-term data from up to 10 years of follow-up (median=4.2 years). In analysis of all participants randomised to treatment (n=1710), the incidence of fatal or disabling stroke was similar in the stenting group (52 events) and the endarterectomy group (49 events; hazard ratio=1.06, 95% confidence interval [CI] 0.72 to 1.57). The cumulative 5-year risk of fatal or disabling stroke did not differ significantly between the stenting group (6.4%) and the endarterectomy group (6.5%; absolute risk difference at 5 years =–0.2%,–2.8 to 2.5).

People in the stenting group were significantly more likely to experience any stroke than those in the endarterectomy group (hazard ratio=1.71, 95% CI 1.28 to 2.30, p<0.001). This difference was driven largely by a higher incidence of non-disabling stroke in the stenting group (73 events versus 27 events in the endarterectomy group). Functioning at 5 years (measured by the distribution of modified Rankin scale scores) did not differ significantly between groups.

Limitations of this analysis include that the assessment of functioning could not take into account subjective perception of wellbeing or subtle changes in physical or mental functioning. As such, the study cannot rule out any differences in long-term complications of stroke between the treatment groups. In addition, stenting was a relatively new procedure when ICSS started. Experience with the procedure and safety may have improved since the study was initiated.

Commentary: “In modern clinical practice, patients with symptoms suggestive of a TIA or a minor stroke are assessed for risk of a subsequent disabling stroke. The aim is to identify those with severe carotid stenosis and refer them for surgery within a short time period from symptom onset (2 weeks ideally). The reason for this urgency is that the risk of a disabling stroke is highest within the first 2 weeks after symptom onset. This is because the majority of subsequent strokes are caused by a blood clot detaching from the ‘at risk’ carotid plaque and causing a blockage rather than the plaque itself blocking the artery. In addition, patients with TIA and carotid stenosis are now treated much earlier and more aggressively with medical treatments – often high dose statins and dual antiplatelet regimens – to ‘stabilise’ an ‘at risk’ plaque.

“Participants were recruited to the ICSS study between 2001 and 2008, mostly predating the 2007 National Stroke Strategy and the 2008 NICE stroke guidance. Consequently, patients were randomised to surgery or stenting much later than the 2 weeks from symptom onset recommended by NICE (most ‘within 6 months’ of symptom onset). This means that ICSS represents a study of intervention, whether stent or operation, in people with relatively much more stable (less risky) atheromatous plaques.

“Within this biological caveat, the results from the 4–5 year follow-up in ICSS are promising. The study shows that stenting carries less risk of an early truly disabling stroke than originally thought and that long-term outcome is similar with stenting and endarterectomy. These findings are unlikely to challenge current NICE guidance. However, for patients with delayed presentations (and more stable plaques) and those with significant comorbidities and frailty, stenting may provide a safer alternative option to endarterectomy.

“Given improvements in stent technology, whether early stenting is safe and effective for symptomatic carotid stenosis and is superior to optimal medical management should be the subject of ongoing research.” ***– Dr Elizabeth Warburton, Consultant Physician in Stroke Medicine, Department of Clinical Neurosciences, University of Cambridge and NICE Fellow***

Study sponsorship: Medical Research Council, Stroke Association, Sanofi-Synthélabo and the European Union.

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Imaging techniques to diagnose suspected kidney stones

Overview: Kidney stones (nephrolithiasis) occur when calcium or other minerals in the urine crystallise into a hard compact mass in the kidney (NHS Choices 2014). These stones can pass out of the kidney and become lodged in the ureter or other parts of the urinary tract (urolithiasis). Stones in either the kidney or the ureter can cause abdominal or flank pain (renal colic) and other symptoms such as blood in the urine (haematuria) and nausea.

People with symptoms of kidney stones may be referred for imaging to confirm the diagnosis or to identify where a kidney stone is. Non-contrast CT can accurately identify stones in the kidney (Kim et al. 2005), but entails exposure to ionising radiation and the attendant long-term cancer risk (Smith-Bindman et al. 2009). Another option is ultrasonography, which is cheaper than CT and does not involve radiation. However, ultrasonography may not be as accurate as CT (Ray et al. 2010).

Current advice: The European Association of Urology guidelines on urolithiasis recommend that the clinical diagnosis of acute renal or ureteric colic should be supported by appropriate imaging. Ultrasonography should be used as the primary diagnostic imaging tool for patients with urinary stones. Non-contrast CT should be used to confirm stone diagnosis in patients with acute flank pain.

Guidelines for the acute management of first presentation of renal/ureteric lithiasis from the British Association of Urological Surgeons likewise recommend non-contrast CT within 24 hours if presentation is acute and to confirm diagnosis of kidney stones.

New evidence: Smith-Bindman et al. (2014) performed a randomised controlled trial of ultrasound compared with CT as initial imaging for suspected kidney stones. The study recruited people with flank or abdominal pain who presented to the emergency room at one of 15 hospitals in the USA. Cases where imaging was ordered to diagnose kidney stones were randomly assigned to ultrasonography performed by the doctor (point-of-care ultrasonography), ultrasonography performed by a radiologist, or abdominal CT. The primary outcomes were the subsequent incidence of high-risk diagnoses with complications, such as pneumonia with sepsis and renal infarction, that could be related to missed or delayed diagnoses, and cumulative radiation exposure from imaging.

A total of 2759 patients were randomly assigned to point-of-care ultrasonography (n=908), radiology ultrasonography (n=893), and CT (n=958). The incidence of high-risk diagnoses with complications within 30 days after the emergency department visit was similar in the 3 study groups. Overall, 6 patients (0.7%) assigned to point-of-care ultrasonography, 3 (0.3%) assigned to radiology ultrasonography, and 2 (0.2%)

assigned to CT had high-risk diagnoses (p=0.30). People who underwent point-of-care ultrasonography or radiology ultrasonography were exposed to considerably less radiation over the 6 months from randomisation than those assigned to CT (10.1 mSv and 9.3 mSv, respectively, versus 17.2 mSv; p<0.001).

When the diagnosis at initial imaging was compared with confirmed stone diagnosis at 30-day follow-up (n=2382), the 3 techniques had similarly high sensitivity (point-of-care ultrasonography=85%, radiology ultrasonography=84%, CT=86%; p=0.74). Specificity for the 3 imaging modalities was lower (point-of-care ultrasonography=50%, radiology ultrasonography=53%, CT=53%; p=0.38).

A considerable proportion of patients in the ultrasonography groups (40.7% in the point-of-care group and 27.0% in the radiology group) underwent CT during the initial visit to the emergency department. The authors caution that their results do not suggest that patients should undergo only ultrasound imaging, but rather that ultrasonography could be used as the initial diagnostic imaging test, with further imaging studies performed at the discretion of the doctor. Other limitations of this study include that investigators, patients and physicians could not be blinded to the study group assignment.

Commentary: “This US trial evaluates a pragmatic alternative to across-the-board CT –that is, ultrasonography with selective CT – rather than directly comparing ultrasonography with CT. This approach makes the findings highly applicable to the trial setting but more difficult to generalise elsewhere. Diagnostic imaging is used more sparingly in the UK than the US, so it is not clear what the relevant pragmatic comparison would be in the UK.

“The distinction between US and UK practice is also relevant when considering the study population. Patients with a high probability of nephrolithiasis were selected, and people were excluded if there was a high risk of alternative serious pathology. Typical UK practice often involves selective use of imaging to concurrently rule out a serious alternative diagnosis as well as evaluate kidney stones. Patients with a clear diagnosis of renal or ureteric colic and low risk of alternative pathology may not receive imaging in A&E.

“Another factor, considered by the authors, is the need for appropriately trained staff to undertake imaging. Ultrasound in emergency settings is developing in the UK, but few emergency medicine doctors are currently able to maintain the skills required to accurately diagnose kidney stones.

“These points may limit the potential for this impressive study to guide practise in the UK. However, the comparison of diagnostic accuracy reported here could prompt an increase in the use of ultrasound as a first-line test. Previous studies suggest that CT is more sensitive than ultrasound. This study found that both techniques have good sensitivity but limited specificity. This finding probably reflects the use of a pragmatic reference standard (confirmation by the patient of the stone passing or by surgery) that will miss small stones that pass unnoticed. The higher sensitivity for CT reported in previous studies could potentially reflect detection of insignificant stones. If so, it is possible that ultrasound detects the pathology that matters without the radiation-related risks of CT.” ***– Professor Steve Goodacre, Professor of Emergency Medicine, University of Sheffield***

Study sponsorship: Agency for Healthcare Research and Quality.

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Evidence summaries from NICE's Medicines and Prescribing Programme

NICE has recently published the following Evidence summary: new medicine:

Chronic obstructive pulmonary disease: aclidinium/formoterol
Two randomised controlled trials found that aclidinium/formoterol significantly improved lung function and breathlessness over 24 weeks compared with placebo and aclidinium and formoterol monotherapies.

Evidence summaries: new medicines form part of NICE's service to provide high quality medicines and prescribing information to the NHS and patients in England. The summaries are aimed at commissioners, budget holders and groups such as Area Prescribing Committees to help them make informed decisions and aid local planning on the introduction of key new medicines. Evidence Summaries: New Medicines do not constitute formal NICE guidance but are designed to support the managed introduction of selected new medicines or new indications for existing medicines not covered by NICE's Technology Appraisal programme.

NICE has also recently published the following Medicines evidence commentaries:

Infantile haemangioma: oral propranolol
A multicentre, double-blind, randomised controlled trial in 460 infants with proliferating infantile haemangioma who required systemic therapy found that propranolol 3 mg/kg/day for 6 months was more effective than placebo.

Asthma: tiotropium as add-on therapy to inhaled corticosteroids in moderate asthma
Two large, double-blind, randomised controlled trials in people with moderate asthma already treated with an inhaled corticosteroid (n=2103) found that, compared with placebo, tiotropium improved lung function but did not produce a clinically meaningful improvement in asthma control score or any other patient-oriented outcomes.

Acute coronary syndromes: further evidence on duration of dual antiplatelet therapy after drug-eluting stent implantation
A randomised controlled trial found that continuing dual antiplatelet therapy beyond 12 months after implantation of a drug eluting stent significantly reduced the risk of stent thrombosis, and major cardiovascular and cerebrovascular events at 30 months, compared with switching to aspirin monotherapy.

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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.

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