This month in Eyes on Evidence

Community-based palliative care teams
A retrospective cohort study in Canada reported that use of specialist community-based palliative care teams was associated with fewer hospital admissions and more deaths at home among terminally ill people.

Preoperative chemotherapy for treatment of non-small-cell lung cancer
A meta-analysis of individual patient data suggested that preoperative chemotherapy followed by surgery improved survival compared with surgery alone in people with non-small-cell lung cancer.

Probiotics to prevent necrotising enterocolitis in preterm infants
A Cochrane review reported that prophylactic use of probiotics reduced the risk of severe necrotising enterocolitis and death in preterm infants.

Surgical safety checklists and short-term mortality
A population-based before and after study in Canada found that safety checklists did not reduce 30-day mortality or complications after surgery, although the study was limited by the variability in checklists, patients and hospitals and the lack of training for staff.

Risk of fall injuries in older people with commonly prescribed medicines
A NICE Medicines Evidence Commentary discusses a Swedish observational study in a large general population of older people that found that around half of the 20 most commonly prescribed medications are associated with severe fall injuries requiring hospitalisations.
Effects of inhaled corticosteroids on growth in children and young people with asthma

A NICE Medicines Evidence Commentary discusses 2 Cochrane reviews that found that, in children and young people with persistent asthma, inhaled corticosteroids are associated with reductions in certain measurements of growth.

Accreditation news

NICE has given its seal of approval to the process an independent group used to develop clinical guidelines on uveal melanoma, a rare form of eye cancer.

Community-based palliative care teams

Overview: Palliative care is defined as the active holistic care of people with advanced, progressive illness (NICE 2012). Palliative care can be provided by generalist or specialist teams in the community or in hospitals or hospices.

Community-based palliative care teams typically involve a group of interdisciplinary healthcare professionals – palliative care doctors, nurses and GPs – who provide integrated palliative care to patients in their homes. These teams manage symptoms, provide education, coordinate care and provide additional or enhanced support and care.

Community-based palliative care teams can improve symptoms and quality of life for patients with advanced illness (Bakitas et al. 2009), and many patients prefer to receive care at home (Higginson and Sen-Gupta 2000). This approach may also reduce the risk of hospitalisation and help people to die at home.

Current advice: NICE guidance on improving supportive and palliative care for adults with cancer advises that commissioners should ensure that an appropriate range and volume of specialist palliative care services are available to meet the needs of the local population. These services should, as a minimum, include specialist palliative care inpatient facilities and hospital and community teams. Specialist palliative care advice should be available on a 24-hour, 7-days a week basis. Community teams should be able to provide support to patients in their own homes, community hospitals and care homes.

NICE is currently preparing guidance on care of the dying adult.

New evidence: Seow et al. (2014) did a retrospective cohort study to assess the effect of specialist community-based palliative care teams on risk of hospitalisation and dying in hospital. This Canadian study compared patients treated at home by 1 of 11 specialist community-based palliative care teams with matched patients who received usual community-based palliative care.

The specialist community-based palliative care teams comprised a core group of palliative care doctors, nurses and general practitioners. Members of these teams collaborated to provide integrated palliative care to patients in their homes (symptom management, education and care) and were available 24/7. Patients on usual care received community-based palliative care (mostly nursing and personal care) from a number of service providers with little coordination between them, and the providers may not have been contactable at evenings and weekends. These patients may have separately received home visits from a general practitioner. The primary outcomes were hospital or emergency department visit in the last 2 weeks of life, and dying in a hospital inpatient unit.

A total of 3109 patients received specialist palliative care over the 2 year period studied; these people were matched to 3109 patients who received usual palliative care. Participants had an expected prognosis
of less than 6 months, and around 80% in each group had cancer. The specialist palliative care teams studied varied in size and composition. Compared with people who received usual palliative care, people who received specialist palliative care were less likely to be admitted to hospital (relative risk [RR]=0.68, 95% CI 0.61 to 0.76, p<0.001) or the emergency room (RR=0.77, 95% CI 0.69 to 0.86, p<0.001) in the last 2 weeks of life. People who received specialist palliative care were also less likely to die in hospital (RR=0.46, 95% CI 0.40 to 0.52, p<0.01).

Limitations of this study include that participants were matched with propensity score matching, which cannot adjust for unmeasured factors such as patient preference for hospital care. The study took place in Canada and participants were mostly cancer patients, which may limit the generalisability of the findings. In addition, 2 of the 11 specialist palliative care teams did not have a significant effect on outcomes compared with usual care.

Commentary: “Existing evidence shows that community-based specialist palliative care teams improve symptom control and quality of life, increase satisfaction with care, and provide better outcomes for families (Higginson et al. 2003, Abernethy et al. 2008). This paper complements these findings by showing that the teams can also reduce emergency department attendances, hospital admissions and hospital deaths of people considered to be in the last 6 months of life.

“These findings reinforce NICE guidance that commissioners should ensure availability of specialist palliative care in the community. This does not just mean telephone advice to professional carers, but direct access by phone or home visits for patients and families, both within and outside office hours. These were the features that were associated with reduced use of acute services in this study.

“The UK already uses specialist palliative care teams similar to those shown to be effective in this study. But specialist palliative care in the UK remains on average only 25% funded by the NHS, the remainder coming from charitable sources. Better provision, which this paper suggests would be of benefit to the healthcare sector as a whole, would need a specific share of any shift of resources into the community.

“This research is probably the best evidence yet that specialist palliative care teams in the community can reduce use of acute services and hence both save money and prevent patients being exposed to care settings that most of them do not wish to enter. However, there would need to be new investment in specialist provision in the community if change is to be driven further.” – Dr Nigel Sykes, Consultant in Palliative Medicine, St Christopher's Hospice, London

Study sponsorship: Canadian Institutes of Health Research.

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Preoperative chemotherapy for treatment of non-small-cell lung cancer

Overview: Lung cancer is the second most common cancer in England, accounting for 14% of all newly diagnosed cancers in men and 12% of all newly diagnosed cancers in women (Office for National Statistics 2013). Lung cancer is also the most common cause of cancer-related death in England and Wales for both sexes (Office for National Statistics 2011).

Lung cancer exists in 2 main types: non-small-cell lung cancer (NSCLC), which accounts for 80% of cases, and small-cell lung cancer, which is less common but develops more rapidly (NHS Choices 2013). Surgery is the treatment of choice for NSCLC, with chemotherapy and radiotherapy also treatment options. Using chemotherapy after surgery, with or without radiotherapy, has been shown to improve survival in patients
with NSCLC (NSCLC Meta-analysis Collaborative Group 2010). Using chemotherapy before surgery might also have beneficial effects on survival.

Current advice: NICE guidance on lung cancer recommends that patients with NSCLC who are medically fit and suitable for treatment with curative intent should be offered lobectomy surgery (either open or thoracoscopic) as the treatment of first choice.

Postoperative chemotherapy should be offered to patients with good performance status (that is, those who can carry on normal activities and go to work; WHO classification 0 or 1) and relatively small tumours that have limited spread to the lymph nodes (stage T1–3 N1–2 M0). Postoperative chemotherapy should also be considered in patients with good performance status (WHO classification 0 or 1) and tumours greater than 4 cm in diameter with no spread to the lymph nodes or elsewhere (T2–3 N0 M0). Cisplatin-based combination chemotherapy should be offered for postoperative chemotherapy. Preoperative chemotherapy should not be offered to patients with NSCLC who are suitable for surgery, except for in clinical trials.

The NICE Pathway on lung cancer brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams. The NICE Evidence Update on lung cancer highlights and provides commentary on selected new evidence published since the guideline was issued.

New evidence: The NSCLC Meta-analysis Collaborative Group (2014) conducted a meta-analysis of individual patient data to establish the effect of preoperative chemotherapy in patients with NSCLC who were suitable for surgery. The group searched for published and unpublished randomised trials comparing chemotherapy plus surgery with surgery alone. The population was chemotherapy-naive patients with NSCLC who were suitable for surgery and did not have any previous malignancies. The primary outcome was overall survival, defined as the time from randomisation until death from any cause.

A total of 15 trials (n=2385 patients) were included in this analysis (92% of all known eligible trials). Chemotherapy was used only before surgery in 10 trials, and both before and after surgery in 5 trials. All trials used platinum-based chemotherapy (cisplatin or carboplatin), except 1 that used docetaxel alone. The patients were mostly men (80%) with a median age of 62 years, and mainly had tumours that had spread to lymph nodes but no secondary or metastatic cancer (stage IB–IIIA; 93%).

Mortality was lower in patients who had preoperative chemotherapy than in those who had surgery alone (hazard ratio [HR]=0.87, 95% CI 0.78 to 0.96, p=0.007). This finding translates into a 5 percentage point absolute improvement in 5-year survival among people who had preoperative chemotherapy (from 40% to 45%). This improved survival was not affected by whether chemotherapy was given preoperatively only or both preoperatively and postoperatively. In addition, this finding was not affected by the number of drugs or platinum agent used, whether postoperative radiotherapy was given, or by patient characteristics (age, sex, performance status, histology or tumour stage).

Limitations of this analysis include the lack of information on study selection, data extraction and quality assessment. In addition, there was no assessment of publication bias, and 4 eligible trials (n=198) could not be included.

Commentary: “Current NICE guidance recommends the use of chemotherapy after surgery for patients with NSCLC who are suitable for surgery. The use of postoperative chemotherapy with combined vinorelbine and cisplatin is supported by several trials, such as the LACE pooled analysis, ANITA, and NCIC-CTG JBR.10 trials. These studies all reported superior overall survival for patients with stage II disease.

“This study by the NSCLC Meta-analysis Collaborative Group (2014) suggests that chemotherapy before surgery may also be beneficial in patients with NSCLC. Potential advantages of chemotherapy before surgery include better tolerability, early eradication of micrometastases and potentially easier resection. However, this approach may result in less accurate staging and possible delay to curative surgery.

“Although individual prospective randomised trials such as MRC LU22/NVALT 2/EORTC 08012 and the NATCH trial found no evidence of a difference in overall survival for the comparison of surgery only versus
platinum-based chemotherapy followed by surgery, the NSCLC Meta-analysis Collaborative Group analysis has shown that a positive effect does exist. However, the effect must be small because no individual study had the power to show an effect in its own right. This is not the case with chemotherapy after surgery, where multiple trials have shown positive benefit of chemotherapy independently.

"In summary, the study by the NSCLC Meta-analysis Collaborative Group has provided a robust and objective appraisal of the evidence supporting preoperative chemotherapy. However, there is currently insufficient data from prospective randomised trials to support a change in practice in favour of preoperative over postoperative therapy in patients with NSCLC, given the extensive randomised and meta-analysis data supporting the latter." – Professor Dean A Fennell, Chair of Thoracic Medical Oncology, Cancer Research UK Centre Leicester, University of Leicester and University Hospitals of Leicester NHS Trust

**Study sponsorship:** Medical Research Council UK.

**Probiotics to prevent necrotising enterocolitis in preterm infants**

**Overview:** Necrotising enterocolitis is characterised by inflammation and death of patches of bowel wall in newborn babies. Most cases of necrotising enterocolitis occur in preterm infants (Holman et al. 2006), in particular in very low birth weight infants (<1500 g). The cause of necrotising enterocolitis is unclear, but the condition is thought to be related to intestinal immaturity, an underdeveloped immune system and colonisation of the intestine by pathogenic bacteria (Tanner et al. 2014).

Probiotics are supplements containing live bacteria that colonise the gastrointestinal tract and are intended to beneficially alter the balance of gut microorganisms in the host. Probiotics could potentially reduce the risk of necrotising enterocolitis in preterm infants by competing against potential pathogens, preventing migration of bacteria and their products across the intestinal mucosa, and enhancing immune responses (Patel and Denning 2013).

Current advice: Necrotising enterocolitis can be managed either medically or surgically, depending on disease severity (Neu and Walker 2011). Options for initial medical management include gastric decompression, bowel rest, and intravenous broad-spectrum antibiotics, fluids and nutrition.

Surgical interventions are usually required in infants with bowel perforation or deteriorating clinical or biochemical status (for example, a decreasing platelet count). Surgical procedures may involve primary peritoneal drainage, exploratory laparotomy with resection of the dead or diseased bowel, or enterostomy with creation of a stoma.

**New evidence:** A Cochrane review by AlFaleh and Anabrees (2014) assessed whether administration of probiotics prevented severe necrotising enterocolitis in preterm infants. A search was conducted for randomised and quasi-randomised controlled trials in preterm infants aged less than 37 weeks or who had a birth weight of less than 2500 g, or both. Studies had to compare enteral administration of any live probiotic, at any dose for more than 7 days, with placebo or no treatment. The primary outcomes were severe necrotising enterocolitis (stage II or more on Bell’s criteria), hospital-acquired sepsis (positive culture of blood or cerebrospinal fluid taken after 5 days of age), and all-cause mortality.

A total of 24 trials were identified, which included 2761 infants treated with probiotics and 2768 control infants. Compared with placebo or no treatment, use of prophylactic probiotics was associated with a
significantly lower risk of severe necrotising enterocolitis in preterm infants (relative risk [RR]=0.43, 95% confidence interval [CI] 0.33 to 0.56, p<0.00001; 20 studies, n=5529). Probiotics were likewise effective at reducing severe necrotising enterocolitis in very low birth weight infants (RR=0.41, 95% CI 0.31 to 0.56, p<0.00001; 17 studies, n=4914).

Probiotics also reduced all-cause mortality (RR=0.65, 95% CI 0.52 to 0.81, p=0.00017; 17 studies, n=5112), but did not have a significant effect on the risk of sepsis (RR=0.91, 95% CI 0.80 to 1.03, p=0.12; 19 studies, n=5338). None of the included studies reported any cases of systemic infections caused by probiotics. Preparations containing either *Lactobacillus* species alone or a mixture of probiotics appeared to be most effective.

Limitations of this analysis include the heterogeneity of the included studies in: enrolment criteria; baseline risk of necrotising enterocolitis in the control groups; timing, dose and formulation of the probiotics; and feeding regimens. Only 11 of the 24 included trials were classified as high quality based on adequacy of allocation concealment procedures and blinding of the intervention. Insufficient data were available for analysis of the effect of probiotics in extremely low birth weight preterm infants (birth weight <1000 g).

**Commentary:** “Probiotic administration to neonates appears to be safe, cheap and readily implementable. Taking that into account, this Cochrane Review appears to make a convincing case for using these products in preterm neonates. However, probiotic administration is not yet used routinely on neonatal units.

“The case for routine probiotics has not been aided by initial data from a recently concluded large UK randomised controlled trial (PIPS) evaluating the use of *Bifidobacterium breve* BBG-001, which showed no advantage at all from the intervention (Costeloe et al. 2014). It would be naïve to expect all probiotic bacteria to be equally effective; the risk of recommending routine use of probiotics at the present time is that we do not know which regimen should be used.

“What is needed to definitively answer this question is a very large trial comparing different probiotic agents. Such a trial would have to be carefully designed to avoid interference from cross-colonisation of infants on the same unit (as observed in some placebo-controlled probiotic trials; Hickey et al. 2014), and may be prohibitively expensive.” – Dr Jim Gray, Consultant in Microbiology, Birmingham Children’s Hospital and Birmingham Women’s Hospital

**Study sponsorship:** McMaster University Medical Center, Canada; the Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, USA; and the Deanship of Scientific Research, King Saud University, Saudi Arabia.

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**Surgical safety checklists and short-term mortality**

**Overview:** In England and Wales, 129,419 patient safety incidents relating to surgical specialties were reported in 2007 (National Patient Safety Agency 2009). Surgical safety checklists can improve outcomes by increasing teamwork and communication in theatre and by ensuring that evidence-based interventions, such as antibiotic prophylaxis, are reliably used. The World Health Organization (WHO) has developed a Surgical Safety Checklist as part of its 2008 Safe Surgery Saves Lives initiative. This 19-item checklist has been shown to reduce the rate of in-hospital death from 1.5% to 0.8% (Haynes et al. 2009).
Current advice: The WHO’s Surgical Safety Checklist involves verbal confirmation by surgical teams of the completion of the basic steps for ensuring safe delivery of anaesthesia, prophylaxis against infection, effective teamwork, and other essential practices in surgery. A number of checks are completed before the induction of anaesthesia (‘sign in’), before incision of the skin (‘time out’) and before the patient leaves the operating room (‘sign out’).

The NHS has mandated the use of an adapted version of the WHO’s Surgical Safety Checklist in England and Wales. Healthcare organisations are required to:

- Ensure an executive and a clinical lead are identified to implement the surgical safety checklist within the organisation.
- Ensure the checklist is completed for every patient undergoing a surgical procedure (including local anaesthesia).
- Ensure that the use of the checklist is entered in the clinical notes or electronic record by a registered member of the team.

NICE guidance on surgical site infection provides recommendations on the procedures necessary before, during and after surgery to reduce the risk of infection. The NICE guideline on preoperative tests (currently being updated) covers tests that are carried out before elective surgery by doctors or nurses in hospitals, preoperative assessment clinics or, in some cases, the GP’s surgery or health centres.

New evidence: A population-based study by Urbach et al. (2014) assessed surgical outcomes before and after the introduction of mandatory surgical safety checklists in Ontario, Canada. This study assessed all surgical procedures at each Ontario hospital 3 months before and 3 months after introduction of the Canadian Patient Safety Institute checklist, the WHO checklist, or a unique checklist devised by the hospital. The primary outcome was death in the hospital or within 30 days after surgery (operative mortality).

Data were available from 101 hospitals, 97 of which used a special intervention or educational programme for checklist implementation. The number of surgical procedures performed per hospital ranged from 9 to 4422 (median=654) during the 3-month interval before the checklist was implemented and from 2 to 4522 (median=633) during the 3-month interval after implementation. Analyses were adjusted for patient age, sex, urban or rural residence, socioeconomic status, and comorbidities and for admission category (inpatient versus ambulatory), procedure type, procedure status (emergency versus elective), and month of surgery.

The adjusted risk of death within 30 days after the introduction of surgical checklists (0.65%, 95% confidence interval [CI] 0.60% to 0.70%) was not significantly different from the risk before implementation of checklists (0.71%, 95% CI 0.66% to 0.76%, p=0.07). Likewise the adjusted risk of surgical complications within 30 days of the procedure was not significantly lower after the use of checklists (3.82%, 95% CI 3.71 to 3.92%) than before (3.86%, 95% CI 3.76 to 3.96%, p=0.53). These results did not vary in any subgroup analyses, including in high-risk groups such as elderly patients, patients who underwent emergency procedures, and patients who underwent inpatient procedures.

The authors suggested that the absence of an effect of surgical checklists may reflect inadequate adherence to the checklists, although self-reported compliance from June 2010 was 98%. Other widespread interventions to improve surgical safety could have affected the results, but none were introduced during the period studied. No formal training on using checklists was provided, and implementation was not standardised. Additionally, the retrospective analysis of administrative records may be less useful than a prospective study.

Commentary: “Surgical safety is a key public health concern in low-, middle- and high-income countries. The WHO Surgical Safety Checklist has been implemented with varying degrees of success in different organisations.

“One of the key aspects of implementation is that introducing a checklist cannot be done via a top-down approach through the traditional information dissemination routes used in most healthcare institutions. For
any effect to be seen, staff must undergo sufficient training in the use of the checklist or the ‘5 steps to safer surgery’. In addition, a culture of patient safety must be developed that does not blame individuals but looks at systems in their entirety.

“The lack of effect in this study could be related to the retrospective analysis, the relatively small sample size, or the heterogeneity in types of patients and hospitals. While we wait for larger prospective studies that are more homogeneous in terms of types of hospitals, we should also be looking at data from local quality improvement programmes that include use of the surgical checklist.

“Checklists alone cannot be the answer to delivering safer care. A culture of reporting and learning from errors, better appreciation of human factors, and the ability to design, implement and evaluate large-scale quality improvement initiatives is desperately needed.” – Dr Sukhmeet Panesar, Honorary Fellow, Centre for Population Health Sciences, The University of Edinburgh

Study sponsorship: Canadian Institutes of Health Research and the Institute for Clinical Evaluative Sciences.

Risk of fall injuries in older people with commonly prescribed medicines

A NICE Medicines Evidence Commentary discusses a Swedish population-based, case-controlled study (Kuschel et al. 2014) that investigated the risk of falls associated with commonly prescribed medicines. The study included 64,399 people aged 65 years or older who sustained a fall injury requiring hospitalisation and 257,596 matched controls who had not been hospitalised for a fall injury.

The study found that around half of the 20 most commonly prescribed medications were associated with severe fall injuries requiring hospitalisations. The associated risk was greatest with central nervous system drugs such as antidepressants, hypnotics and analgesics. Opioids doubled the risk of severe injury due to falling. The NICE guideline on assessment and prevention of falls in older people recommends medication review as part of a multifactorial falls risk assessment for older people who have fallen or who are at risk of falls.

The Medicines Evidence Commentary ‘Falls: Swedish study highlights the risk of fall injuries in older people with commonly prescribed medicines’ was published in the 13–17 October issue of the Medicines Awareness Weekly e-bulletin. Medicines Evidence Commentaries form part of NICE’s Medicines Awareness Service and help contextualise important new evidence, highlighting areas that could signal a change in clinical practice. They do not constitute formal NICE guidance.

The full version of this article is available on the NICE Evidence Services website.

Effects of inhaled corticosteroids on growth in children and young people with asthma

A NICE Medicines Evidence Commentary discusses 2 Cochrane reviews that investigated the effect of inhaled corticosteroids on growth suppression in children and young people up to 18 years old with mild-to-moderate persistent asthma.

The first Cochrane review (Zhang et al. 2014) found that during the first year of treatment, low-to-
moderate doses of inhaled corticosteroids were associated with a statistically significant reduction of 0.48 cm/year in linear growth velocity and a 0.61 cm lower increase in height from baseline compared with placebo or non-steroidal asthma drugs. In the second year of treatment, there was no statistically significant difference between the inhaled corticosteroids and control groups in linear growth velocity or increase in height from baseline.

The second Cochrane review (Pruteanu et al. 2014) found that, compared with lower doses, higher doses of inhaled corticosteroids reduced linear growth velocity by 0.20 cm/year when used in children aged less than 12 years. However, there was no statistically significant difference between the groups in change in height over time periods longer than 3 months.

The benefits of using inhaled corticosteroids as regular preventer therapy in children and young people with persistent asthma are well established. The findings of these Cochrane reviews should serve as a reminder for clinicians about the risk of growth suppression in children when regular inhaled corticosteroids are used. Clinicians should follow the current British guideline on the management of asthma and prescribe the lowest dose of inhaled corticosteroids compatible with maintaining disease control.

This Medicines Evidence Commentary on ‘Asthma in children and young people: effects of inhaled corticosteroids on growth’ was published in the 3–7 November issue of the Medicines Awareness Weekly e-bulletin. Medicines Evidence Commentaries form part of NICE’s Medicines Awareness Service and help contextualise important new evidence, highlighting areas that could signal a change in clinical practice. They do not constitute formal NICE guidance.

The full version of this article is available on the NICE Evidence Services website.

Accreditation news

NICE has given its seal of approval to the process used to develop a clinical guideline on uveal melanoma, a rare form of eye cancer.

Funded by the charity Melanoma Focus, and produced by an independent guideline development group, the process behind the new guideline on uveal melanoma is the latest to be accredited by NICE.

The NICE Accreditation Programme assesses the quality of the processes used by UK and international organisations to produce guidance and advice about health and social care. Accreditation does not accredit the content of individual products, but awards a seal of approval – the NICE Accreditation Mark – to guidance producers that show they meet a defined set of accreditation criteria in processes used to develop their products.

The NICE Accreditation Mark helps health and social care professionals worldwide to identify the most robustly produced guidance developed using critically evaluated high-quality processes. The service thereby contributes towards driving up the quality of information used by health and social care professionals and enabling them to deliver high-quality care.

Visit the NICE website for more information about process used to develop the uveal melanoma guideline and the NICE Accreditation Programme.
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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