Inpatient survey shows modest improvements in patient experience

The first longitudinal study of patient experience by trust, *Patients' experience of using hospital services* (The King's Fund and Pickering Institute, 2015; www.kingsfund.org.uk/publications/patients-experience-using-hospital-services), finds that while overall there have been small improvements in patient experience between 2005 and 2013, the results show a tendency towards inertia or regression to the average. However, when this is set against tightening funding since 2010, the fact that patient experience hasn't deteriorated is reassuring.

Commenting on the study, Prof Sir Mike Richards, Chief Inspector of Hospitals at the Care Quality Commission, said: 'It is encouraging that patients are reporting improved care experiences in areas such as mixed sex accommodation and in cleanliness. We are clear that patient feedback should be a key driver for quality improvement in the NHS.'

Surgical breakthrough for patients with rectal cancer

Specialists have made a breakthrough which means that a number of patients with rectal cancer will be able to avoid surgery without their treatment being undermined, according to a study from The Christie NHS Foundation Trust research team (Renehan et al, 2015).

Professor Andrew Renehan said a series of tests would spare 15% of patients with rectal cancer from having major surgery. After surgery, up to nearly half of these patients require a permanent colostomy, but this can now be averted in many of these patients.

Cancer specialists could identify patients by giving them a magnetic resonance scan and an endoscopy which allows clinicians to view the bowel.

Renehan AG, Malcomson L, Emsley R et al (2015) Watch-and-wait approach versus surgical resection after chemoradiotherapy for patients with rectal cancer (the OnCoRe project): a propensity-score matched cohort analysis. *Lancet Oncol* (doi: 10.1016/S1470-2045(15)00467-2)

Statins: negative news stories linked to stopping treatment, more heart attacks and early death

Researchers in Denmark have found that negative news stories about statins are linked to some people choosing to discontinue their statin treatment, which, in consequence, is associated with an increased risk of heart attacks and dying from heart disease.

The study shows that for every negative nationwide news story about the cholesterol-lowering group of medicines, there was a 9% increased risk of people deciding to stop taking statins within 6 months of first being prescribed the drug (Nielsen and Nordestgaard, 2015).

'We found that exposure to negative news stories about statins was linked to stopping statins early and explained 2% of all heart attacks and 1% of all deaths from cardiovascular disease associated with early discontinuation of statins,' said Professor Børge Nordestgaard, Chief Physician at Copenhagen University Hospital in Denmark.

He added: 'People who stop statins early have a 26% increased risk of a heart attack and an 18% increased risk of dying from cardiovascular disease when compared to people who continue to use them.'

'Although we cannot say for sure that statin-related negative news stories cause the early discontinuation of statins, our findings suggest that this is likely. And although this type of association research cannot prove causality, our data suggest that early discontinuation of statins leads to unnecessary heart attacks and deaths from cardiovascular disease,' he said.

Professor Nordestgaard and his colleague Dr Sune Nielsen, a senior scientist at Copenhagen University Hospital, identified 674 900 people, aged 40 years and older, in the entire Danish population who were using statins between January 1995 and December 2010, and followed them up to the end of 2011.

They identified 1931 statin-related news stories from January 1995 onwards in the Danish newspapers, magazines, radio, television, websites and news agencies, and graded them as negative (110 stories), neutral (1090 stories) and positive (731 stories).

In addition to looking at the link from news stories to statin discontinuation, they also looked at the link with having cardiovascular disease or diabetes at the time the statins were first prescribed, the calendar year (i.e. the passing of time), statin dose, being male, living in cities, and being of non-Danish ethnicity.

During the period from 1995 to 2010 the proportion of people on statins increased from less than 1% to 11%, while early statin discontinuation increased from 6% to 18%. The number of all statin-related news stories (positive, neutral and negative) increased from 30 per year in 1995 to 400 in 2009.

In addition to the increased risk from negative news stories, the researchers found that the risk of early statin discontinuation increased per increasing calendar year (4%), increased daily dose (4%), being male (5%), living in cities (13%) and for being of non-Danish ethnicity (67%). In contrast, the risk of discontinuation decreased after exposure to positive news stories about statins (8%), and having cardiovascular disease or diabetes at the time the statins were first prescribed (27% and 9% respectively).

Professor Nordestgaard said: 'Statins represent a success story in modern medicine, and currently they are the most effective way to prevent cardiovascular disease. However, a prerequisite for this is that patients adhere to the prescribed therapy. In our study we find that close to one in six of individuals discontinue therapy at an early stage, and this represents a major problem for cardiovascular health. Our findings suggest a need to develop ways of increasing people's adherence to statin therapy during the first 6 months in particular.'

Professor Børge G Nordestgaard, Department of Clinical Biochemistry, Herlev and Gentofte Hospital, Copenhagen University Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

Nielsen SF, Nordestgaard BG (2015) Negative statin-related news stories decrease statin persistence and increase myocardial infarction and cardiovascular mortality: a nationwide prospective cohort study. *Eur Heart J* (doi: 10.1093/eurheartj/ehv641)

Tight control of psoriatic arthritis disease activity improves joint outcomes in newly diagnosed patients

An open-label multicentre randomized controlled trial enrolled adult patients (aged ≥18 years) with early psoriatic arthritis (<24 months symptom duration), who had not previously received treatment with any disease-modifying anti-rheumatic drugs. The patients came from eight secondary care rheumatology centres in the UK (Coates et al, 2015).

This was an open-label study in which patients and clinicians were aware of treatment group assignment. Clinical outcomes were recorded by a masked assessor every 12 weeks. The primary outcome was the proportion of patients achieving an American College of Rheumatology (ACR) 20% (ACR20) response at 48 weeks, analysed by intention to treat with multiple imputation for missing ACR components. Cost-effectiveness was also assessed.

A total of 206 eligible patients were enrolled and randomly assigned to receive tight control (n=101) or standard care (n=105). In the intention-to-treat population, the odds of achieving an ACR20 response at 48 weeks were higher in the tight control group than in the standard care group (odds ratio = 1·91, 95% confidence interval= 1·03–3·55; P=0·0392).

Serious adverse events were reported by 20 (10%) patients (25 events in 14 (14%) patients in the tight control group and eight events in six (6%) patients in the standard care group) during the course of the study. No unexpected serious adverse events or deaths occurred.

The authors concluded that tight control of psoriatic arthritis disease activity through a treat-to-target approach significantly improves joint outcomes for newly diagnosed patients, with no unexpected serious adverse events reported.

Coates LC, Moverley AR, McParland L et al (2015) Effect of tight control of inflammation in early psoriatic arthritis (TICOPA): a UK multicentre, open-label, randomised controlled trial. *Lancet* **386**(10012): 2489–98 (doi: 10.1016/S0140-6736(15)00347-5)

Paracetamol no benefit against flu symptoms

A randomized, double-blind, placebo-controlled trial was carried out in adults aged 18–65 years with influenza-like illness and positive influenza rapid antigen test (Jefferies et al, 2015). Treatments were 1 g paracetamol four times a day, or matching placebo, for 5 days. Pernasal swabs were taken for influenza quantitative RT-PCR at baseline and days 1, 2 and 5. Temperature and symptom scores were recorded for 5–14 days or time of resolution respectively. The primary outcome variable was area under the curve (AUC) for quantitative PCR log10 viral load from baseline to day 5.

A total of 80 participants were randomized: no one was lost to follow up, and one withdrew after 4 days. There were 22 and 24 participants who were influenza PCR-positive in placebo and in paracetamol groups respectively. Mean (standard deviation) AUC PCR log10 viral load was 4.40 (0.91) in those taking placebo and 4.64 (0.88) in those taking paracetamol; difference was −0.24, 95% confidence interval −0.78 to 0.29, P=0.36. In all participants there were no differences in symptom scores, temperature, time to resolution of illness and health status, with no interaction between randomized treatment and whether influenza was detected by PCR.

Regular paracetamol had no effect on viral shedding, temperature or clinical symptoms in patients with PCR-confirmed influenza. There remains an insufficient evidence base for paracetamol use in influenza infection.

'We initially theorized that taking paracetamol might be harmful, as the influenza virus cannot replicate as well at higher temperatures, and by reducing a person's temperature the virus may have thrived. Fortunately this was found not be the case,' said co-author Dr Irene Braithwaite.

Dr Braithwaite said it is difficult to make a recommendation for or against using paracetamol in adults with influenza or influenza-like illness based on these results. She emphasized that annual vaccination is the best protection against the influenza virus.

Jefferies S, Braithwaite I, Walker S et al; Pi Study Group (2015) Randomized controlled trial of the effect of regular paracetamol on influenza infection. *Respirology* (doi: 10.1111/resp.12685)

Breast cancer survivors' risk of developing leukaemia after treatment

Certain characteristics, including personal and family histories suggestive of inherited cancer susceptibility, may increase a breast cancer survivor's risk of developing leukaemia after undergoing chemotherapy and/or radiation (doi: 10.1002/cncr.29615). One in five of the women in the study carried an inherited mutation in a gene associated with an increased risk of breast cancer.

Slow walking speed in elderly may signal Alzheimer's disease

How fast older people walk may be related to the amount of amyloid they have built up in their brains, even if they don't yet have symptoms of Alzheimer's disease, according to a study published in *Neurology* (doi: 10.1212/WNL.0000000000002235). The study involved 128 people with an average age of 76 years who did not have dementia but were considered at high risk for developing it.

Protecting children who receive liver transplants from hepatitis B-infected donors

Prophylaxis with HBV vaccine intramuscular injections can prevent new-onset hepatitis B in children who receive liver transplants from donors who were previously infected with hepatitis B virus but had successfully cleared the virus (doi: 10.1002/lt.24372).

Erythropoietin is not neurocytoprotective

Erythropoietin in Traumatic Brain Injury (EPO-TBI) was a double-blind, placebo-controlled trial undertaken in 29 university-affiliated teaching hospitals in Australia, New Zealand, France, Germany, Finland, Ireland and Saudi Arabia (Nichol et al, 2015). Within 24 hours of brain injury, 606 patients were randomly assigned to erythropoietin (40 000 units subcutaneously) or placebo (0·9% sodium chloride subcutaneously) once per week for a maximum of three doses.

The primary outcome, assessed at 6 months, was improvement in the patients' neurological status (reduction in the proportion of patients with an Extended Glasgow Outcome Scale of 1–4 (death, vegetative state, and severe disability)).

Following moderate or severe traumatic brain injury, erythropoietin did not reduce the number of patients with severe neurological dysfunction (Extended Glasgow Outcome Scale level 1–4) or increase the incidence of lower limb deep venous thrombosis. The effect of erythropoietin on mortality remains uncertain.

Nichol A, French C, Little L et al; EPO-TBI Investigators and the ANZICS Clinical Trials Group (2015) Erythropoietin in traumatic brain injury (EPO-TBI): a double-blind randomised controlled trial. *Lancet* **386**(10012): 2499–506 (doi: 10.1016/S0140-6736(15)00386-4)

Use of antibiotics in third trimester of pregnancy increases risk of childhood wheeze

A new study has evaluated whether confounding factors could explain the suggested association between antibiotic use in pregnancy and the risk of wheeze (Popovic et al, 2015).

Although prenatal antibiotic exposure and infant wheezing can largely be explained by confounding factors, when these were accounted for, the risk associated with taking antibiotics in the third trimester of pregnancy remained.

Researchers studied more than 3500 women and their children from the NINFEA birth cohort study. They assessed maternal antibiotic use during the first and third trimester of pregnancy via self-reported information and assessed any incidence of wheeze in the child up to the age of 18 months of age using questionnaires.

Dr Maja Popovic, Department of Medical Sciences, University of Turin, Turin, Italy

They focused on several confounding factors that could explain the risk of wheeze found after antibiotic use during pregnancy. These included the mother's age and educational level, the number of siblings the child had, the mother's smoking history, paracetamol use during pregnancy, any history of asthma, and any respiratory or other infections during pregnancy.

Following statistical analysis there was no evidence of an association between antibiotic exposure in the first trimester of pregnancy and wheezing in childhood as any association identified was explained by the confounding factors. However, the excess risk of recurrent wheeze persisted after antibiotic use in the third trimester of pregnancy and could not be explained by any of the confounding factors.

Dr Maja Popovic, lead author from the University of Turin, Italy, said: 'Even the large number of confounding factors ... could not explain the risk of recurrent wheezing when mothers took antibiotics during their third trimester. This is important as recurrent wheezing ... often predicts later unfavourable respiratory outcomes.'

Popovic M, Rusconi F, Zugna D et al (2015) Prenatal exposure to antibiotics and wheezing in infancy: a birth cohort study. *Eur Respir J* (doi: 10.1183/13993003.00315-2015)

Body surface decolonization effective in reducing bacteriuria and candiduria in men but not women in intensive care units

A secondary analysis has been undertaken of a three-group, cluster-randomized trial of 43 hospitals (clusters) with patients in 74 adult intensive care units (Huang et al, 2016). The trial, REDUCE MRSA Trial (Randomized Evaluation of Decolonization *vs* Universal Clearance to Eradicate MRSA), showed that body surface decolonization reduced all-pathogen bloodstream infections.

The groups included were either meticillin-resistant *Staphylococcus aureus* screening and isolation, targeted decolonization with chlorhexidine and mupirocin, and universal decolonization with chlorhexidine and mupirocin.

Outcomes included high-level bacteriuria (≥50 000 colony forming units/ml) with any uropathogen, high-level candiduria (≥50 000 colony forming units/ml), and any bacteriuria with uropathogens.

The analysis concluded that universal decolonization of patients in the intensive care unit with once a day chlorhexidine baths and short-course nasal mupirocin could be a potential preventive strategy in male patients because it significantly decreases candiduria and any bacteriuria, but not for women.

Huang SS, Septimus E, Hayden MK et al; Agency for Healthcare Research and Quality (AHRQ) DEcIDE Network and Healthcare-Associated Infections Program, and the CDC Prevention Epicenters Program (2016) Effect of body surface decolonisation on bacteriuria and candiduria in intensive care units: an analysis of a cluster-randomised trial. *Lancet Infect Dis* **16**(1): 70–9 (doi: 10.1016/S1473-3099(15)00238-8)

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ENDEAVOR: carfilzomib superior to bortezomib in relapsed and refractory multiple myeloma

In relapsed or refractory multiple myeloma progression-free survival was significantly better for patients randomized to carfilzomib (Kyprolis) and dexamethasone than bortezomib (Velcade) and dexamethasone, concluded the ENDEAVOR study presented at ASH and published simultaneously in *The Lancet Oncology* (Dimopoulos et al, 2015).

'Taken together, the results from the ENDEAVOR study suggest an important role for carfilzomib-based regimens for patients with relapsed or refractory multiple myeloma,' wrote Dr Meletios Dimopoulos, from the National and Kapodistrian University of Athens, Greece, and co-authors.

Carfilzomib, the first irreversible proteasome inhibitor, was approved by the European Medicines Agency in November 2015 for use in combination with lenalidomide and dexamethasone to treat adults with multiple myeloma who have received at least one prior therapy. Irreversibility of binding, it is believed, offers more sustained target enzyme inhibition and protein build-up and cell death.

In the phase 3 study, 929 patients with relapsed multiple myeloma, and up to three prior lines of therapy, were randomized 1:1 to intravenous carfilzomib and oral dexamethasone (Kd, n=464) or intravenous bortezomib and oral dexamethasone (Vd, n=465). Cycles were repeated until disease progression or unacceptable toxicity.

Median progression-free survival was 18.7 months for the Kd group *vs* 9.4 months for the Vd group (hazard ratio = 0.53; 95% confidence interval = 0.44–0.65; P<0.001), and median overall survival was 24.3 months in the Vd arm, but had yet to be reached in the Kd arm (hazard ratio = 0.79; P=0.066).

In a sub-group analysis (Chng et al, 2015) the investigators assessed the cytogenetic risk status of ENDEAVOR study patients with fluorescence in situ hybridization.

Results show carfilzomib benefits persisted for high-risk patients, with median progression-free survival 8.8 months for Kd *vs* 6 months for Vd (hazard ratio = 0.646, 95% confidence interval = 0.453–0.921). Overall response rates in high-risk groups were 72.2% for carfilzomib and 58.4% for bortezomib.

On the back of ENDEAVOR, Amgen has submitted for variation to the Marketing Authorization Application to expand the indication to carfilzomib in combination with dexamethasone for multiple myeloma patients who have received just one prior therapy.

Chng W, Goldschmidt H, Dimopoulos M et al (2015) Dexamethasone in Patients with Relapsed Multiple Myeloma Based on Cytogenetic Risk Status: subgroup Analysis from the Phase 3 Study Endeavor. Abstract 30

Dimopoulos M, Moreau P, Palumbo A et al (2015) Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR: a randomised, phase 3, open label, multicentre study. *Lancet Oncol* (doi: 10.1016/S1470-2045(15)00464-7)

Blinatumomab shows efficacy for wider group of ALL patients

Blinatumomab has the potential to be used in patients with acute lymphocytic leukaemia (ALL) and minimal residual disease, reports a phase 2 study presented at ASH (Gökbuget et al, 2015).

Blinatumomab is a first-in-class bispecific T-cell engager (or BiTE) approved for patients with relapsed or refractory Philadelphia chromosome-negative (Ph-) ALL of B-cell lineage. Patients with persistent/recurrent minimal residual disease after first-line induction and consolidation have a higher risk of relapse and shorter survival than those with a complete minimal residual disease response.

Dr Nicola Gökbuget, Goethe University, Frankfurt, Germany

Investigators evaluated long-term outcomes for blinatumomab in 116 patients with B-cell precursor ALL and minimal residual disease >10^3 after more than three intensive chemotherapy treatments. Subjects were given blinatumomab 15 µg/m^2/day by continuous intravenous infusion for 4 weeks, followed by a 2-week break (one cycle). Minimal residual disease responders in cycle 1 received up to three additional cycles or underwent haematopoietic stem cell transplants.

'Nearly all patients with persistent or recurrent minimal residual disease relapse despite continued chemotherapy,' said Dr Nicola Gökbuget, the study presenter from Goethe University, Frankfurt, Germany. The treatment need for this population, she added, is to achieve molecular complete response and avoid haematological relapse.

A complete minimal residual disease response was achieved in 80% of patients, with 67% remaining in continuous remission until transplant. Overall survival was 36.5 months. 'In relapsed ALL the median survival is around 6 months, and a third had prior relapses, so this is very favourable,' said Dr Gökbuget.

Gökbuget N, Dombret H, Bonifacio M et al (2015) Long-Term Outcomes after Blinatumomab Treatment: Follow-up of a Phase 2 Study in Patients (Pts) with Minimal Residual Disease (MRD) Positive B-Cell Precursor Acute Lymphoblastic Leukemia (ALL). Abstract 680

Janet Fricker