

## Women with migraines have higher risk of cardiovascular disease and mortality

Women diagnosed with migraines have a slightly increased risk of developing cardiovascular diseases, such as heart attacks and strokes, and are somewhat more likely to die from these conditions than women who do not have migraine, according to findings of a study of 115 541 women aged 25–42 years (doi: 10.1136/bmj.i2610).

## Telehealth interventions not ‘magic bullet’

A UK-wide study has concluded that while telehealth could provide some benefit to some patients, it is not a simple answer to a complex problem (Salisbury et al, 2016a).

The Healthlines study, of 641 adults with a high risk of heart disease or strokes, evaluated the effectiveness and cost-effectiveness of a new telehealth service. The Healthlines Service involved participants receiving regular phone calls from a health advisor. The service led to a modest improvement in overall cardiovascular risk for a minority of participants, but had no impact on average risk.

The service has also been used to support patients with depression (Salisbury et al, 2016b). Participants reported small improvements in depression and anxiety, better access to support and advice, greater satisfaction with the support they received, and improvements in self-management.

Lead author Professor Salisbury commented: ‘While a telehealth intervention such as this can be beneficial to some patients, it is not the magic bullet that some policy-makers seem to think it is.’

Salisbury C, O’Cathain A, Thomas C et al (2016a) Telehealth for patients at high risk of cardiovascular disease: pragmatic randomised controlled trial. *BMJ* **353**: i2647 (doi: 10.1136/bmj.i2647)

Salisbury C, O’Cathain A, Edwards L et al (2016b) Effectiveness of an integrated telehealth service for patients with depression: a pragmatic randomised controlled trial of a complex intervention. *Lancet Psychiatry* **3**(6): 515–25 (doi: 10.1016/S2215-0366(16)00083-3)

## Smoking cessation treatments: safety and efficacy in patients with and without neuropsychiatric disorders

A randomized controlled study has compared the relative neuropsychiatric safety risk and efficacy of varenicline and bupropion with nicotine patch and placebo in smokers with and without psychiatric disorders (Anthenelli et al, 2016).

A randomized, double-blind, triple-dummy, placebo-controlled and active-controlled (nicotine patch 21 mg per day with taper) trial of varenicline (1 mg twice a day) and bupropion (150 mg twice a day) for 12 weeks with 12-week non-treatment follow-up done at 140 centres (clinical trial centres, academic centres and outpatient clinics) in 16 countries.

Professor Robert M Anthenelli, Professor and Executive Vice Chair, Department of Psychiatry, University of California, San Diego, California



Participants were motivated-to-quit smokers with and without psychiatric disorders who received brief cessation counselling at each visit. The primary endpoint was the incidence of a composite measure of moderate and severe neuropsychiatric adverse events. The main efficacy endpoint was biochemically confirmed continuous abstinence for weeks 9–12.

The study did not show a significant increase in neuropsychiatric adverse events attributable to varenicline or bupropion relative to nicotine patch or placebo. Varenicline was more effective than placebo, nicotine patch and bupropion in helping smokers achieve abstinence, whereas bupropion and nicotine patch were more effective than placebo.

Commenting on the results, Professor Robert M Anthenelli from the Department of Psychiatry, University of California, San Diego, California, said: ‘This large multinational trial provides further evidence that varenicline and bupropion – alongside nicotine replacement therapy – can be used safely by psychiatrically stable smokers.’

Anthenelli RM, Benowitz NL, West R et al (2016) Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *Lancet* **387**(10037): 2507–20 (doi: 10.1016/S0140-6736(16)30272-0)

## New biomarker-based bleeding risk score for patients with atrial fibrillation

The benefit of oral anticoagulation in patients with atrial fibrillation is based on a balance between reduction in ischaemic stroke and increase in major bleeding. A new biomarker-based risk score was developed to improve the prognostication of major bleeding in patients with atrial fibrillation.

The ABC-bleeding score (age, biomarkers, and clinical history) was developed and internally validated in 14 537 patients with atrial fibrillation randomized to apixaban *vs* warfarin in the ARISTOTLE trial and was externally validated in 8468 patients with atrial fibrillation randomized to dabigatran *vs* warfarin in the RE-LY trial (Hijazi et al, 2016).

The most important predictors for major bleeding were the concentrations of the biomarkers growth differentiation factor-15, high-sensitivity cardiac troponin T and haemoglobin, age, and previous bleeding.

The authors concluded that the ABC-bleeding score performed better than HAS-BLED and ORBIT scores and should be useful as decision support on anticoagulation treatment in patients with atrial fibrillation.

Hijazi Z, Oldgren J, Lindbäck J et al; ARISTOTLE and RE-LY Investigators (2016) The novel biomarker-based ABC (age, biomarkers, clinical history)-bleeding risk score for patients with atrial fibrillation: a derivation and validation study. *Lancet* **387**(10035): 2302–11 (doi: 10.1016/S0140-6736(16)00741-8)

American Society of Clinical Oncology Chicago, USA, 3–7 June

## Combination chemotherapy improves survival in patients with resected pancreatic cancer

Adjuvant combination chemotherapy with gemcitabine plus capecitabine significantly improves 5-year survival in patients with resected pancreatic cancer, according to a large phase III trial.

The European Study Group for Pancreatic Cancer 4 trial randomized 732 patients with early-stage pancreatic ductal adenocarcinoma to six 4-week cycles of gemcitabine alone or gemcitabine plus oral capecitabine for 24 weeks, starting within 12 weeks of surgery.

Results from the open-label study showed higher median overall survival with combination chemotherapy compared to gemcitabine alone (28.0 months *vs* 25.5 months, hazard ratio 0.82,  $P=0.032$ ). The estimated 5-year survival rate was 28.5% *vs* 16.3% in the two groups.

‘The difference in median survival may seem modest, but the improvement in long-term survival is substantial for this cancer,’ said lead author Dr John Neoptolemos, from the Cancer Research UK Liverpool Cancer Trials Unit, University of Liverpool, Liverpool.

He added: ‘These findings are significant because they show that those patients who can undergo surgery have a fighting chance of surviving this cancer with the combination of two commonly used chemotherapies.’

The trial patients are representative of real-world pancreatic cancer patients.

A large proportion had unfavourable prognostic factors, including locally advanced or aggressive disease, large tumour size or incomplete tumour removal during surgery.

As expected there was slightly more toxicity with the combination regimen but this was manageable. Severe diarrhoea was slightly more common with the combination regimen than with monotherapy (5% *vs* 2%) and hand-foot syndrome was also more common (7% *vs* 0%).

‘Adjuvant gemcitabine/capecitabine is the new standard of care for resected pancreatic cancer,’ Dr Neoptolemos concluded.

**Dr John Neoptolemos, Cancer Research UK Liverpool Cancer Trials Unit, University of Liverpool, Liverpool**



## Ten years of hormone therapy reduces breast cancer recurrence

Postmenopausal women with early breast cancer have a 34% lower risk of recurrence with prolonged hormonal therapy with aromatase inhibitors for 10 years, reported a large randomized phase III study.

The MA.17R trial included 1918 postmenopausal women who had been treated with 5 years of one of three aromatase inhibitors either as initial treatment after surgery for early breast cancer or after tamoxifen. They were randomized to an additional 5 years of letrozole (2.5 mg once daily) or placebo.

Results showed a significantly lower risk of recurrence at 5 years: 95% of women treated with letrozole were free from recurrence compared to 91% of the placebo group (hazard ratio 0.66,  $P=0.01$ ). The annual incidence of contralateral breast cancer was also lower and 5-year overall survival was similar for both groups (93% *vs* 94%).

‘Women with early-stage hormone-receptor positive breast cancer face an indefinite risk of relapse,’ said lead author Dr Paul Goss, from Massachusetts General Hospital, Boston, USA. ‘This study ... confirms that prolonging aromatase inhibitor therapy can further reduce the risk of breast cancer recurrences.’

## Similar survival with once- and twice-daily radiotherapy in SCLC

Once-daily radiotherapy achieves similar overall survival as twice-daily treatment in patients with small cell lung cancer (SCLC), shows a large randomized trial. Standard treatment for SCLC is chemotherapy plus thoracic radiotherapy and studies have suggested that twice-daily radiotherapy improves outcomes compared to once-daily radiotherapy.

CONVERT (Concurrent ONce trial Versus twice-daily RadioTherapy) randomized 547 patients with SCLC to concurrent twice-daily radiotherapy (45 Gy

in 30 twice-daily fractions over 3 weeks) or concurrent once-daily radiotherapy (66 Gy in 33 once-daily fractions over 6.5 weeks). Both regimens started on day 22 of the first cycle of chemotherapy.

Results showed similar 2-year survival at 2 years with once-daily radiotherapy (51%) as with twice-daily treatment (56%) (hazard ratio 1.17, 95% confidence interval 0.95–1.45,  $P=0.15$ ). Median overall survival was 25 months with once-daily radiotherapy and 30 months with twice-daily radiotherapy.

Toxicity rates were similar, although there was slightly more grade 3/4 neutropenia with twice-daily radiotherapy. There was no difference in grade 3/4 oesophagitis and grade 3/4 acute radiation pneumonitis was rare.

Reporting the findings, Professor Corinne Favre-Finn, Professor of Thoracic Radiation Oncology, Institute of Cancer Sciences, University of Manchester, said: ‘The results of CONVERT support the use of either once-daily or twice-daily radiotherapy.’

Susan Mayor

UK Kidney Week Birmingham, 7–10 June

**Routine assessment reveals unmet need in older dialysis patients**

A study of routine assessment by a specialist renal geriatric integration nurse included 34 haemodialysis patients (mean age 80.3 ± 5.2 years) and 24 peritoneal dialysis patients (mean age 77.8 ± 6.1 years). Before geriatric assessment, 9% of haemodialysis and 4% of peritoneal dialysis patients were known to have cognitive impairment and 18% of haemodialysis and 37% of peritoneal dialysis patients were known to have falls.

On assessment, 79% of haemodialysis patients and 58.3% of peritoneal dialysis patients had moderate to severe frailty, 26% of haemodialysis patients and 17% of peritoneal dialysis patients had cognitive impairment, and 62% of haemodialysis patients and 45% of peritoneal dialysis patients had scores indicating cognitive deficit.

Following assessment, 50% of haemodialysis and 50% of peritoneal dialysis patients were referred to community teams, including the memory clinic, falls clinic, social services, physiotherapy/dietitian and the renal counsellor.

Bartholomew C (2016) Outcomes from introducing routine geriatric assessment for patients on dialysis. Abstract O013

**Is there a ‘weekend effect’ for deceased-donor kidney transplants?**

An analysis of deceased-donor kidney transplants in England between 2003 and 2013 found no association between weekend transplantation and increased risks of 30-day mortality, 1-year mortality or rehospitalization within 1 year.

The study included 11 459 deceased-donor kidney-alone transplants: 13.8% performed on Monday, 15.1% on Tuesday, 16.0% on Wednesday, 14.9% on Thursday, 16.7% on Friday, 13.0% on Saturday and 10.6% on Sunday. There was no significant difference between transplantation performed at the weekend (Friday–Sunday) or on a weekday for 30-day mortality (1.1% vs 1.2%, *P*=0.778) or 1-year mortality (3.9% vs 3.8%, *P*=0.640).

Results were similar when defining the weekend as Saturday–Sunday for both 30-day mortality (1.1% vs 1.2% on weekdays, *P*=0.774) and 1-year mortality (3.7% vs 3.9% on weekdays, *P*=0.658). There was no difference in rehospitalization within 1 year in both weekend models compared to weekday transplantation.

Presenting the study, Dr Ben Anderson, Renal Registrar in the Department of Nephrology, Queen Elizabeth Hospital, Birmingham, said: ‘These results are very reassuring for our patients, but before drawing any firm conclusions, potential confounders

should be investigated. Transplantation is a 7-day, consultant-led service in most centres. Recipients are very extensively worked up, and significant comorbidities preclude surgery.

Evidence from the USA shows that the kidney discard rate is significantly higher at the weekends (Mohan et al, 2016) and this higher threshold for transplantation – if it exists in England – may mitigate any weekend effect and warrants further investigation.’



Dr Ben Anderson, Renal Registrar, Department of Nephrology, Queen Elizabeth Hospital, Birmingham

Anderson B (2016) Outcomes after kidney transplantation comparing weekend versus weekday procedures: results from a population-based cohort analysis across England (2003–2013). Abstract O003  
Mohan S, Foley K, Chiles MC et al (2016) The weekend effect alters the procurement and discard rates of deceased donor kidneys in the United States. *Kidney Int* 90(1): 157–63 (doi: 10.1016/j.kint.2016.03.007)

**Medications review lightens pill burden for haemodialysis patients**

A multidisciplinary medication review decreased the number of daily medications by one quarter in nearly two-thirds of haemodialysis patients, and reduced costs without needing further resources.

Before the start, researchers surveyed patients to confirm that they wished to reduce their pill burden. The team assessed 100 patients’ medications between August 2015 and January 2016, and agreed options for trial discontinuation, e.g. withdrawal of diuretics, proton-pump inhibitors and statins, and reduction in

phosphate binders. Changes were agreed with each patient, who received advice about possible symptom recurrence, and the revised medication list was shared with the patient’s GP.

Before the review, the average daily pill burden per patient was 11 (3–16), which fell after review in 64% of patients. Average reduction was 24% – the largest was 70% (13 pills) in one patient – and the total number of daily pills discontinued was 188. There were no reported adverse events and no patient restarted a discontinued

medication. The average saving was £316/patient/year (£13–£1224), and total projected annual saving was £20244.

Dr Wendy Baird, Ulster Hospital, Belfast, concluded: ‘The results ... far exceeded our target of 10% pill reduction in 50% of patients. We ensured that physicians, pharmacists and GPs were all on board, but key to success was to involve patients by asking their opinion on their pill burden before starting the review.’

Baird W (2016) Less is more. Abstract O004

Sue Lyon

## Bacteriophage cocktail shows significant promise for *Clostridium difficile* infections

A new study, funded by AmpliPhi Biosciences, has confirmed the therapeutic potential of bacteriophage combinations to treat highly infectious *Clostridium difficile* infections while retaining a healthy gut (Nale et al, 2016).

Bacteriophage combinations significantly reduce growth of *C. difficile* cells and proliferation in complex models, while preventing the destruction of beneficial bacteria seen with traditional antibiotic treatment.

*C. difficile* infection causes approximately 39% of cases of antibiotic-associated diarrhoea in the western world. Ten per cent of patients who have *C. difficile* infections die because of a lack of effective therapies.

Specific phage combinations caused complete destruction of *C. difficile* and prevented the appearance of resistant bacteria, while complex models showed that oral delivery of optimized phage combinations resulted in reduced *C. difficile* spread at 36 hours post-infection.

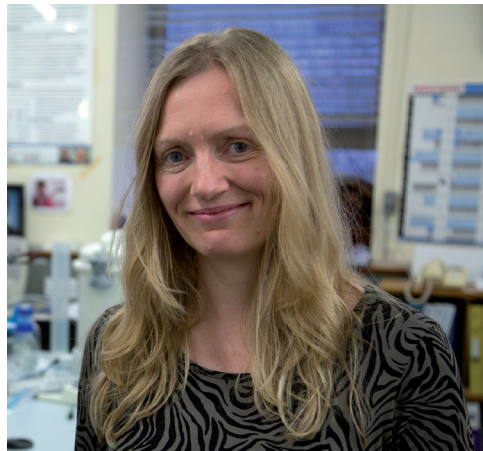
The phage combination was also able to kill 12 of the 13 *C. difficile* variants that are most prevalent in the UK, and were effective against emerging variants that are increasingly causing concern in the UK, the USA and more widely. The phage combination also reduced or completely prevented regrowth of *C. difficile* compared to treatment with individual phages.

‘Our data support the therapeutic potential of phage combinations to treat *C.*

*difficile* infections,’ said Professor Clokie. ‘In particular, combinations of phages optimized in the laboratory setting were shown to be effective in the treatment of *C. difficile* in animals. Further refinements to our bacteriophage cocktails can be explored to maximize phage efficacy and to target the most dominant *C. difficile* variants.’

Nale JY, Spencer J, Hargreaves KR, Buckley AM, Trzepeński P, Douce GR, Clokie MRJ (2016) Bacteriophage combinations significantly reduce *Clostridium difficile* growth in vitro and proliferation in vivo. *Antimicrob Agents Chemother* **60**: 968–81 (doi: 10.1128/AAC.01774-15)

Professor Martha Clokie, Professor of Microbiology, Department of Infection, Immunity and Inflammation, University of Leicester, Leicester



## Do drugs warning of disturbed sleep actually make patients sleep less well?

Medicines that carry warnings about sleep disturbances do not seem to contribute to the amount of sleep disturbances in the general population, according to new ‘real world’ research (Lehnic et al, 2016).

To investigate whether drugs labelled as sleep disturbing in patient information leaflets actually lead to more sleep disorders Anna-Therese Lehnic, of the University of Duisburg-Essen in Germany, and her colleagues analysed information on 4221 individuals aged 45–75 years.

Interviews revealed no clear links between drugs labelled as sleep disturbing with problems related to sleep. ‘We found that

drugs labelled as sleep disturbing do not contribute strongly to the high frequency of sleep disturbances in the general population. Moreover, the intake of several sleep disturbing drugs at the same time barely led to more sleep disturbances at night,’ said Lehnic.

The findings suggest that investigators may need to more carefully report side effects in clinical trials, and emphasizes the value of real world research into the safety of medicines.

Lehnic AT, Kowall B, Kuß O et al (2016) Do patients with intake of drugs labelled as sleep disturbing really sleep worse? A population based assessment from the Heinz Nixdorf Recall Study. *Br J Clin Pharmacol* (doi: 10.1111/bcp.13015)

## Singing improves speech of people with Parkinson’s disease

A systematic review has found that singing benefits the speech of people with Parkinson’s disease (Barnish et al, 2016).

Most studies supported the idea that singing helps the speech of people with Parkinson’s disease. However, more studies are required to assess whether this benefit can lead to functional communication as opposed to just physical speech features in people with Parkinson’s disease.

Co-author Rachel Atkinson, an adult neurological specialist speech and language therapist at St Helier Hospital in London, said: ‘This review reminds us as a profession to think outside the box and encourage community activities in addition to traditional clinic-based therapy to facilitate broader social activity and participation for our client groups.’

Barnish J, Atkinson RA, Barran SM, Barnish MS (2016) Potential benefit of singing for people with Parkinson’s disease: a systematic review. *J Parkinsons Dis* (doi: 10.3233/JPD-160837)

## New digital centre to help improve mental health care

A new centre for digital innovation could transform the way mental health care is delivered. The Centre for Translational Informatics is led by King’s College London’s Institute of Psychiatry, Psychology & Neuroscience and South London and Maudsley NHS Foundation Trust.

It brings together advances in analytics, software development and implementation to drive forward improvements in the way that mental health is treated.

Innovations include the use of virtual reality to assess thought, emotions and behaviour in patients with psychosis, eating disorders and mood disorders, and using wearable and smartphone technology to improve quality of life and revolutionize mental health-care delivery.