

## Survivors of childhood brain tumours have lasting cognitive and socioeconomic burdens

Survivors of childhood brain tumours who received radiotherapy and were very young at the time of diagnosis may experience cognitive and socioeconomic burdens decades after treatment (<https://doi.org/10.1002/cncr.32186>). Interventions such as cognitive therapies and educational and occupational services may be needed to mitigate such long-term effects.

A total of 181 survivors of paediatric low-grade glioma were compared with 105 siblings of cancer survivors. Survivors were a median age of 8 years at the time of diagnosis and a median age of 40 years at assessment.

Overall, survivors treated with surgery plus radiotherapy at the site of the tumour had lower estimated IQ scores than survivors treated with surgery only, who had lower scores than siblings. Survivors – especially those treated with surgery plus radiotherapy – were less educated and earned lower incomes than siblings.

## Pear-shaped is better for postmenopausal women, even if they are normal weight

Postmenopausal women who are 'apple' rather than 'pear' shaped are at greater risk of cardiovascular disease, even if they have a normal, healthy body mass index (<https://doi.org/10.1093/eurheartj/ehz391>).

This study involved 2683 women postmenopausal women with normal body mass index (18.5 to less than 25 kg/m<sup>2</sup>) who were part of the Women's Health Initiative in the USA. They did not have cardiovascular disease initially but, during a median of nearly 18 years' follow up, 291 cases of cardiovascular disease occurred.

The highest risk of cardiovascular disease occurred in women who had the highest percentage of fat around their middle and the lowest percentage of leg fat – more than three-fold increased risk compared to women at the opposite extreme.

## Increased risk of developing Crohn's disease or ulcerative colitis while being treated with anti-TNF $\alpha$

While anti-tumour necrosis factor-alpha (TNF $\alpha$ ) agents have revolutionised management of chronic inflammatory diseases, paradoxically, they may provoke development of new autoimmune diseases.

A nationwide cohort study examined whether there is an increased risk of developing Crohn's disease and ulcerative colitis while under treatment with anti-TNF $\alpha$  agents for diseases other than inflammatory bowel disease (Korzenik et al, 2019). This was based on data from Danish health registries of all patients who had received at least one dose of an anti-TNF $\alpha$  agent for non-inflammatory bowel disease indications (rheumatoid arthritis, psoriasis or psoriatic arthritis, ankylosing spondylitis, others).

In total 17 018 individuals with autoimmune diseases were exposed to anti-TNF $\alpha$  (the vast majority had infliximab, etanercept or adalimumab), and 63 308 individuals were not. Patients treated with etanercept had an increased risk of being diagnosed with Crohn's



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disease or ulcerative colitis while under treatment (adjusted hazard ratio 2.0 and 2.0 respectively). The corresponding hazard ratios for infliximab were 1.3 and 1.0, and for adalimumab 1.2 and 0.6. This finding has relevance to clinical care and insights into common mechanisms of the pathophysiology of these diseases.

Discussing the findings, lead author Dr Joshua Korzenik, of Brigham and Women's Hospital, Boston, Massachusetts, said:

'This association may be clinically important for those who develop inflammatory bowel disease in this context. Given the wide use of these drug and etanercept in particular, the population affected may be large, despite the relative rarity of the event.'

Korzenik J, Larsen MD, Nielsen J, Kjeldsen J, Nørgård BM. Increased risk of developing Crohn's disease or ulcerative colitis in 17 018 patients while under treatment with anti-TNF $\alpha$  agents, particularly etanercept, for autoimmune diseases other than inflammatory bowel disease. *Aliment Pharmacol Ther.* 2019 Aug;50(3):289–294. <https://doi.org/10.1111/apt.15370>

## Antidepressant treatment and brain connectivity: searching for new targets to treat depression

Nearly 50% of patients do not respond to antidepressant medications or have side effects rendering them unable to continue treatment. Mechanistic studies might help identify pathways through which treatments exert their effects. Two studies looked at the effects of antidepressant treatment on neural connectivity, the relationship with symptom improvement, and whether these effects were reproducible (Wang et al, 2019).

Two double-blind, placebo-controlled trials of serotonin and noradrenaline reuptake inhibitors were carried out in adults with persistent depressive disorder, with magnetic resonance imaging scans taken before and after treatment. One was a 10-week trial of duloxetine (30–120 mg daily) and the other was a 12-week trial of desvenlafaxine (50–100 mg daily). The authors examined the effect of treatment on whole-brain functional connectivity, and

correlations between change in functional connectivity and improvement in symptoms of depression and pain symptom severity.

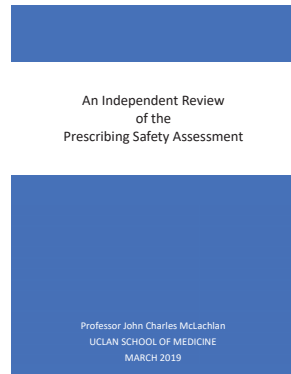
In both studies, antidepressants decreased functional connectivity compared with placebo within a thalamo-cortico-periaqueductal network that has previously been associated with the experience of pain. Within the active drug groups, reductions in functional connectivity in this network correlated with improvements in depressive symptom severity. The thalamo-cortico-periaqueductal network could be a new, potentially important target for antidepressant therapeutics.

Wang Y, Bernanke J, Peterson BS et al. The association between antidepressant treatment and brain connectivity in two double-blind, placebo-controlled clinical trials: a treatment mechanism study. *Lancet Psychiatry.* 2019 Aug;6(8):667–674. [https://doi.org/10.1016/S2215-0366\(19\)30179-8](https://doi.org/10.1016/S2215-0366(19)30179-8)

## Independent review says Prescribing Safety Assessment will 'contribute to patient safety'

An independent review of the Prescribing Safety Assessment ([https://www.bps.ac.uk/getmedia/8028ab78-0e36-4e11-a2d8-9da39f4833e8/PSA-Independent-Review-Report-\(public\).pdf.aspx](https://www.bps.ac.uk/getmedia/8028ab78-0e36-4e11-a2d8-9da39f4833e8/PSA-Independent-Review-Report-(public).pdf.aspx)) has found that it increases the attention paid by students and faculty to accurate prescribing, and allows students to demonstrate competencies in the safe and effective use of medicines. According to the report's author, the assessment will contribute to patient safety and reduce harm in the years to come.

The Prescribing Safety Assessment is an online assessment of competency in the safe and effective prescribing of medicines, taken by final-year medical students and by overseas graduates coming to the UK to work as foundation year 1 doctors. This assessment has



been compulsory for all new doctors since 2016.

The review, conducted by Professor John McLachlan, Professor of Medical Education in the School of Medicine at the University of Central Lancashire, found that the processes underlying the assessment's development, standard setting and delivery are of a high standard, and comparable with other national level tests.

Professor Jenny Higham, Co-Chair of the Prescribing Safety Assessment Executive, Chair of the Medical Schools Council and member of the Medical Schools Council Assessment Board, said: 'We are delighted that students have reported the positive educational impact the Prescribing Safety Assessment has had on their prescribing knowledge. This review confirms its strength as an assessment.'

## Mental Health Act Code of Practice not being used as intended, finds Care Quality Commission

The Mental Health Act Code of Practice is not being used as it was intended because of a lack of awareness and understanding of the statutory guidance among providers and staff, finds a report by the Care Quality Commission ([https://www.cqc.org.uk/sites/default/files/20190625\\_mhacop-report.pdf](https://www.cqc.org.uk/sites/default/files/20190625_mhacop-report.pdf)).

The Code of Practice helps those working in services to interpret and apply the legislation to decision making in day-to-day practice and to provide safeguards for involving and protecting people in mental health services. It also includes guiding principles that should always be considered when decisions are being made about care, support or treatment in services that detain patients under the Mental Health Act.

However, the Care Quality Commission found that providers lack understanding about how to promote, apply and report on the guiding principles as set out in the Code of Practice. The report recommended that the Department of Health and Social Care takes a lead in:

- Developing standardized resources, support and training for patients, carers and staff so that they understand how the Code applies to individuals, practice, services and local partnerships
- Promoting the use of the guiding principles to improve practice and enable meaningful engagement with families and carers
- Making sure that the Code gives clear and consistent guidance on providers' governance arrangements
- Improving the usability of and access to the Code, taking into account the way the Code is intended to be used in practical situations between patients and their care team.

Dr Paul Lelliott, Deputy Chief Inspector of Hospitals (lead for mental health), at the Care Quality Commission, said: 'We'd like to see more work undertaken to raise awareness of the Code's guiding principles and to improve its usability. This might include using digital technology to make the content of the Code easier to access by patients, carers and clinicians.'

## Burden of multidrug-resistant tuberculosis in England

Research from Public Health England (<https://doi.org/10.5588/ijtld.18.0399>) has found that the number of prevalent cases of multidrug-resistant tuberculosis is higher than incident cases, and increases over time, so a focus on prevalent cases enables better planning for services to support patients.

## Adults with type 2 diabetes face high risk of dying from cancer

Cancer has overtaken cardiovascular disease as the most common cause of death in Scottish adults with type 2 diabetes (<https://doi.org/10.1111/jdi.13067>). The authors suggest that where cardiovascular risk factors are being treated aggressively, cancer takes on a greater importance in the cause of death.

## Around 1.8 million fewer adult smokers in England in 2018 than 7 years ago

The number of adult cigarette smokers in England has dropped by around 1.8 million from 7.7 million (19.8%) in 2011 to 5.9 million (14.4%) in 2018, shows official figures from the *Statistics on Smoking, England: 2019* report (<https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-smoking/statistics-on-smoking-england-2019>). The prevalence of adult smokers throughout the UK was 14.7%.

56th ERA-EDTA Congress Budapest, Hungary, 13–16 June

**Vitamin D after kidney transplant: no benefits beyond fracture risk**

High-dose vitamin D3 (cholecalciferol) lowers the risk of fractures in kidney transplant recipients, but has no effect on extra-skeletal complications. This is the conclusion of the prospective, multicentre, double-blind, controlled VITALE trial, presented as a late-breaking abstract at ERA-EDTA.

VITALE randomized 536 adult renal transplant recipients with serum 25(OH)-vitamin D levels <30 ng/ml 12–48 months after transplant to high-dose (100 000 IU) or low-dose (12 000 IU) cholecalciferol every 2 weeks for 2 months, then monthly for 22 months.

There was no difference in primary composite outcome (diabetes, major adverse cardiac events, de novo cancer and death) between high-dose and low-dose groups, nor any difference in infections, acute rejection or graft loss.

The incidence of fractures was significantly lower in the high-dose group (4% vs 1%,  $P=0.02$ ). High-dose cholecalciferol was well tolerated, with no between-group differences in new-onset hypercalcaemia or hyperphosphataemia, changes in urinary calcium:creatinine ratio, or development of valvular calcification.

**New biomarker predicts acute kidney injury in cardiac patients**

Dickkopf-related protein 3 (DKK3), an indicator of renal tubular stress, helps to identify patients at risk of acute kidney injury after cardiac surgery, according to a study presented during ERA-EDTA 2019 and simultaneously published in the *Lancet* (Schunk et al, 2019).

‘Urinary DKK3 can significantly improve the prediction of acute kidney injury beyond the established clinical models and available biomarkers. Measurement of urinary DKK3 might therefore represent a personalised medicine approach in patients having cardiac surgery,’ commented investigator Professor Danilo Fliser, from the Saarland University Medical Center and Saarland University Faculty of Medicine, Homburg, Germany.

In 733 consecutive patients undergoing elective cardiac surgery, urinary concentrations of DKK3:creatinine >471 pg/mg were associated with significantly higher risk of acute kidney injury (odds ratio 1.65, 95% confidence interval 1.10–2.47,  $P=0.015$ ), independent of baseline kidney function. Compared with clinical and other laboratory measurements, urinary concentrations of DKK3:creatinine



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significantly improved acute kidney injury prediction (net reclassification improvement 0.32, 95% confidence interval 0.23–0.42,  $P<0.0001$ ).

The study concluded that preoperative urinary DKK3 might help identify patients in whom preventive treatment strategies are effective.

Similarly, in a validation cohort of 216 patients enrolled in the prospective RenalRIP trial, compared with DKK3:creatinine concentrations of  $\leq 471$  pg/mg, preoperative concentrations >471 pg/mg were associated with

a significantly greater risk of acute kidney injury (odds ratio 1.94, 95% confidence interval 1.08–3.47,  $P=0.026$ ), persistent renal dysfunction (odds ratio 6.67, 1.67–26.61,  $P=0.0072$ ) and dialysis dependency (odds ratio 13.57, 1.50–122.77,  $P=0.020$ ) after 90 days.

Schunk SJ, Zarbock A, Meersch M et al. Association between urinary dickkopf-3, acute kidney injury, and subsequent loss of kidney function in patients undergoing cardiac surgery: an observational cohort study. *Lancet*. 2019 Jun 12. pii: S0140-6736(19)30769-X. [https://doi.org/10.1016/S0140-6736\(19\)30769-X](https://doi.org/10.1016/S0140-6736(19)30769-X)

**UK Kidney Week 2019 Brighton, 3–5 June**

**Spot urinary sodium poorly estimates 24-hour sodium excretion**

Current equations should be used with caution when estimating 24-hour sodium excretion in patients who are hypertensive, according to a UK study presented during UK Kidney Week and published in the *American Journal of Hypertension* (<https://doi.org/10.1093/ajh/hpz104>).

Urinary sodium excretion over 24 hours is thought to reflect sodium ingestion over the same period. However, since 24-hour collections are often impractical, spot urinary measurements

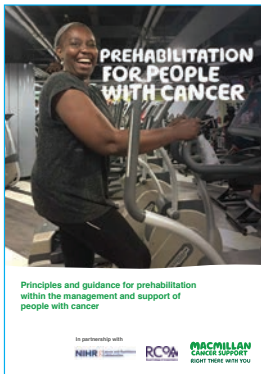
are used to estimate 24-hour excretion using the Kawasaki (INTERSALT) and Tanaka formulas.

The researchers compared spot and 24-hour urinary concentrations in 77 patients, who had matched and complete 24-hour and spot urine and serum biochemistry, and who were managed at a hospital hypertension clinic. Spot urine tests poorly estimated 24-hour excretion, and 24-hour urine was also not a reliable measure of sodium intake in that 24-hour period.

The 24-hour and spot sodium concentrations correlated moderately ( $r=0.4633$ ,  $P<0.0001$ ), and 24-hour and spot sodium:creatinine ratios correlated weakly ( $r=0.2625$ ,  $P=0.0194$ ). The 24-hour and spot fractional excretion of sodium results showed a weak negative correlation ( $r=-0.222$ ,  $P=ns$ ). The 24-hour sodium excretion and the Kawasaki-derived spot urine sodium excretion correlated moderately ( $r=0.3118$ ,  $P=0.0052$ ).

Sue Lyon

## Report emphasizes benefits of prehabilitation for patients before receiving treatment for cancer



A new report from Macmillan Cancer Support, the Royal College of Anaesthetists and the National Institute for Health Research Cancer and Nutrition Collaboration calls for integrated action on

- Prehabilitation should underpin the whole cancer pathway and should be adopted for all people with cancer
- Treatments should be led by cancer multidisciplinary teams which should include those delivering prehabilitation
- All people with cancer should have a co-developed personalized prehabilitation care plan as part of their overall care
- Education in nutrition, exercise, psychology and behavioural change should be integrated into health and care professional training
- Implementation and effectiveness of prehabilitation should be audited and reported according to recognized standards.

Professor Mike Grocott, Royal College of Anaesthetists' council member and joint project leader, commented: 'My patients tell me how prehabilitation offers them the opportunity to take control of their own care. We all see the improved resilience that prehabilitation brings, not only enabling more rapid recovery following treatment, but on occasions opening the possibility of receiving treatments that were previously out of reach.'

He added: 'The potential value of long-term behavioural change and the positive health impact this change may deliver is enticing to all involved – patients and professionals alike.'

psychological support, physical activity and nutrition for people with cancer (<https://www.macmillan.org.uk/assets/prehabilitation-guidance-for-people-with-cancer.pdf>).

Of the 1.8 million people in the UK living with cancer 70% are also living with one or more other long-term health conditions. *Prehabilitation for people with cancer* develops principles and guidance together with an action plan. The report sets out how NHS organizations across the UK can replicate the pioneering work already taking place in some trusts. The report recommendations include:

- Interventions targeted at improving physical and/or mental health should start as early as possible and in advance of any cancer treatment

## Frequency, clinical features and implications of cardiac arrest in people with takotsubo syndrome

An international team of researchers reviewed the records of patients with cardiac arrest and known heart rhythm from the International Takotsubo Registry (Gili et al, 2019). The main outcomes were 60-day and 5-year mortality. In addition, predictors of mortality and predictors of cardiac arrest during the acute takotsubo syndrome phase were assessed.

Of 2098 patients, 103 patients with cardiac arrest and known heart rhythm during cardiac arrest were included. Compared with patients without cardiac arrest, cardiac arrest patients were more likely to be younger, male, and have apical takotsubo syndrome, atrial fibrillation and neurological comorbidities, among others.

In all, 57.1% of patients with cardiac arrest at admission had ventricular fibrillation or

tachycardia, while 73.7% of patients with cardiac arrest in the acute phase had asystole or pulseless electrical activity. In the acute phase, cardiac arrest occurred less frequently in women and more frequently in patients with atrial fibrillation, ST-segment elevation and higher C-reactive protein level on admission.

The team concluded that cardiac arrest is relatively frequent in patients with takotsubo syndrome and is associated with higher short- and long-term mortality. Clinical and electrocardiographic parameters independently predicted mortality after cardiac arrest.

Gili S, Cammann VL, Schlossbauer SA et al. Cardiac arrest in takotsubo syndrome: results from the InterTAK Registry. *Eur Heart J*. 2019 Jul 1;40(26):2142–2151. <https://doi.org/10.1093/eurheartj/ehz170>

## HIV infection and incidence of cardiovascular diseases

An analysis of information from a large health insurance database reveals that people living with HIV have an elevated risk of developing cardiovascular disease, particularly heart failure and stroke (Alonso et al, 2019). The findings indicate that increased efforts to protect patients' cardiovascular health are needed.

Researchers analysed information on 19 798 people living with HIV and 59 302 age- and sex-matched uninfected individuals who were followed for an average of 20 months. People living with HIV had 3.2 times higher risk of heart failure and 2.7 times higher risk of having a stroke.

The association of HIV infection with cardiovascular disease was especially strong for persons younger than 50 years of age and those without a prior history of cardiovascular disease. People living with HIV did not have an increased risk of peripheral artery disease and only moderately increased risk of heart attack or atrial fibrillation.

'Our findings reinforce the importance of primary prevention of cardiovascular disease through control of risk factors such as high blood pressure or smoking in persons living with HIV,' said lead author Dr Alvaro Alonso, of Emory University, Atlanta.

The authors also noted that additional research needs to evaluate whether specific screening strategies for identification of subclinical cardiovascular disease, including atrial fibrillation, are needed in people living with HIV. With the ageing of the HIV population, developing interventions for cardiovascular health promotion and cardiovascular disease prevention is imperative.

Alonso A, Barnes AE, Guest JL, Shah A, Shao IY, Marconi V. HIV infection and incidence of cardiovascular diseases: an analysis of a large healthcare database. *J Am Heart Assoc*. 2019 Jul 16;8(14):e012241. <https://doi.org/10.1161/JAHA.119.012241>