

## Delaying meal times delays the circadian rhythm of blood glucose

Delaying meal times delays the circadian rhythm of glucose in the blood. The findings could help to alleviate symptoms of shift work or jet lag (<https://doi.org/10.1016/j.cub.2017.04.059>).

Researchers examined the impact of altering meal times on the circadian rhythms of ten volunteers. Volunteers were given three meals. In the first phase of the study, the first meal was given 30 minutes after waking with later meals at subsequent 5-hour intervals, while in the second phase each meal was delayed by 5 hours after waking.

Postponing meal times by 5 hours delayed rhythms of blood glucose levels by the same time frame, but did not affect insulin or triglyceride levels in the blood, indicating that blood glucose rhythms can be governed by separate circadian clocks. Researchers indicated that people who struggle with circadian rhythm disorders, including shift workers, might consider timed meals to help resynchronize their body clocks.

## Autism alone does not increase risk of violent offending

A study exploring a possible link between autism and violent offending has found that a diagnosis of autism alone does not increase the risk of violent offending (<https://doi.org/10.1016/j.jaac.2017.03.011>).

An increased risk was found among individuals with both autism and co-occurring conditions such as attention-deficit/hyperactivity disorder or conduct disorder. However, the presence of an autism diagnosis among those with these conditions seems to reduce the risk of violent offending, compared to having these conditions without autism.

Dr Dheeraj Rai, Consultant Senior Lecturer in Psychiatry at the University of Bristol, said: 'These findings are important for autism services, which often focus on providing a diagnosis of autism, rather than the identification of, and support for, the conditions that commonly occur alongside it.'

## Mental health services for children and adolescents across Europe need improvement

A study of child and adolescent mental health care, part of the 5-year MILESTONE project which aims to improve transitions for young people from child and adolescent mental health services to adult mental health services across Europe, has found that provision needs to be improved across the whole of the EU (Signorini et al, 2017).

The team of academics examined characteristics of national child and adolescent mental services across the EU, including legal aspects of adolescent care. Child psychiatrists and national child psychiatry associations in each country completed an online survey which covered issues such as availability of services, inpatient beds, clinicians and organizations, and delivery of specific services and treatments. The study found substantial improvements were needed across the board from planning to monitoring, and delivery.

The number of public services varies considerably across the EU, from just two each in Malta and Luxembourg to 939 in the UK. The number of public child and adolescent mental health services relative to the target population ranged from 12.9 per 100 000 young people in Finland to 0.5 per 100 000 young people in Bulgaria. On

average young people constitute a fifth of the general population of Europe. In several countries, specific subgroups of children and adolescents had poor access to specialized mental health services dedicated to them, e.g. refugees, orphans and minority groups. The heterogeneity of resource allocation did not seem to match epidemiological burden.

Professor Swaran Singh of Warwick Medical School, University of Warwick, said: 'In all 28 countries we found that resource allocation was not evenly spread to effectively deal with need.'

He added: 'Our survey provides important information for the evaluation and planning of child and adolescent mental health services in Europe. It highlights areas of concern: poor service planning and the paucity of standardized outcome assessments for service provision or performance, scarce or variable involvement of service users and their families, and the scarcity of interdisciplinary child and adolescent mental health services and adult mental health services.'

Signorini G, Singh SP, Boricevic-Marsanic V et al; MILESTONE Consortium (2017) Architecture and functioning of child and adolescent mental health services: a 28-country survey in Europe. *Lancet Psychiatry* [https://doi.org/10.1016/S2215-0366\(17\)30127-X](https://doi.org/10.1016/S2215-0366(17)30127-X)

## Validation of clinical decision rules for computed tomography imaging of children with head injuries

A prospective observational study analysed the use of three clinical decision rules in 20 137 children and adolescents (aged <18 years) with head injuries of any severity who presented to the emergency departments of ten Australian and New Zealand hospitals (Babl et al, 2017).

The study looked at the diagnostic accuracy of these rules (PECARN, CATCH and CHALICE) in predicting each rule-specific outcome measure (clinically important traumatic brain injury, need for neurological intervention, and clinically significant intracranial injury respectively).

For each calculation the authors used rule-specific predictor variables in populations that satisfied inclusion and exclusion criteria for each rule (validation cohort). In a secondary analysis, the authors compiled a comparison cohort of patients with mild head

injuries (Glasgow Coma Scale score 13–15) and calculated accuracy using rule-specific predictor variables for the standardized outcome of clinically important traumatic brain injury. In this comparison cohort of 18 913 patients with mild injuries, sensitivities for clinically important traumatic brain injury were similar.

The sensitivities of the three clinical decision rules for head injuries in children were high when used as designed. The findings are an important starting point for clinicians considering introducing one of the rules.

Babl FE, Borland ML, Phillips N et al; Paediatric Research in Emergency Departments International Collaborative (PREDICT) (2017) Accuracy of PECARN, CATCH, and CHALICE head injury decision rules in children: a prospective cohort study. *Lancet* **389**(10087): 2393–2402. [https://doi.org/10.1016/S0140-6736\(17\)30555-X](https://doi.org/10.1016/S0140-6736(17)30555-X)

## Limited radiographic progression found after 4 years' certolizumab in patients with axial spondyloarthritis

Janet Fricker

Little radiographic progression was found in patients with axial spondyloarthritis after 4 years' treatment with certolizumab pegol (Cimzia), reported the RAPID-axSpA study (van der Heijde et al, 2017). The study, presented at the annual European Congress of Rheumatology (EULAR), held 14–17 June 2017, Madrid, Spain, is the first report of 4-year imaging results for certolizumab.

'These 4-year data show that there is minimal progression in structural damage and the reduction in inflammation is sustained. This supports the good long-term clinical outcome of treatment with certolizumab in patients with axial spondyloarthritis,' said study presenter, Professor Désirée van der Heijde, from Leiden Medical Centre, The Netherlands.

Axial spondyloarthritis is sub-classified according to the presence or absence of sacroiliac joint damage on X-ray. The RAPID-axSpA study included patients both with and without radiographic evidence of sacroiliitis.

RAPID-axSpA was a phase 3 double-blind trial, which was placebo controlled out to week 23, dose blind to week 48 and then open label to week 204. Magnetic resonance imaging scans were performed at baseline, and weeks 12, 48, 96 and 204 using SPARCC scores for sacroiliac joints and Berlin scores for the spine. Spinal X-rays were available for 196 of the 315 patients treated with certolizumab.

For patients with ankylosing spondylitis, the mean change on the modified Stokes Ankylosing Spondylitis Spine Score on X-ray between baseline and week 204 was 0.98.

This, said Professor van der Heijde, represents a change of only about one unit over 4 years. Furthermore, she added, less progression was observed between weeks 96 and 204 than during the first 96 weeks of the study.

van der Heijde D, Dougados M, Landewé R et al (2017) Sustained efficacy, safety and patient-reported outcomes of certolizumab pegol in axial spondyloarthritis: 4-year outcomes from RAPID-axSpA. *Rheumatology (Oxford)* <https://doi.org/10.1093/rheumatology/kex174>

## Competitive football players have superior vision, study suggests

Mackenzie Moore

Competitive football players exhibit better visual performance than healthy, non-athletic adults according to the first comprehensive assessment of visual acuity in English Premier League players (Bennett et al, 2017).

Researchers from Liverpool John Moores University examined a range of visual functions

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in 49 elite football players from an English Premier League club and 31 intermediate players of different skill level and playing position using a Nike SPARQ sensory

station. They found that while elite and intermediate soccer players do not differ in their visual abilities, they do exhibit superior acuity-based measures of visual function and accommodative vergence than the 230 non-athlete adults assessed. These data also revealed that defensive players exhibit faster accommodative vergence than offensive players.

This function coincides with the demand on defensive players to continually and quickly shift gaze between teammates and opposing players located at near and far locations.

According to Professor Simon J Bennett, from the School of Sport and Exercise Sciences, Liverpool John Moores University, Liverpool: 'While these findings add to the growing evidence that a good level of vision could be important in dynamic invasion sports, future studies need to determine the precise nature of the relationship with on-field performance.'

Bennett SJ, Roberts JW, Strudwick AJ (2017) Visual function of English Premier League soccer players. *Science and Medicine in Football* <https://doi.org/10.1080/024733938.2017.1330552>

## MBRRACE-UK report shows decrease in stillbirth rate

The stillbirth rate in the UK reduced by almost 8% from 2013 to 2015, according to the MBRRACE-UK report ([www.npeu.ox.ac.uk/mbrrace-uk/reports](http://www.npeu.ox.ac.uk/mbrrace-uk/reports)), which focuses on rates of stillbirth and neonatal death for babies born at 24 weeks of gestation or more. In 2015 the stillbirth rate was 3.87/1000 total births, a fall from 4.20/1000 total births in 2013.

## Whole genome analysis shows genetic basis for anorexia nervosa

A large-scale, international whole-genome analysis has revealed that anorexia nervosa is associated with genetic anomalies on chromosome 12 (<https://doi.org/10.1176/appi.ajp.2017.16121402>). The significant locus lies in a region associated with type 1 diabetes and autoimmune disorders, as well as insulin metabolism.

## Additional insulin injection could protect people with type 1 diabetes against heart disease

A small preliminary trial found that one additional insulin injection 3 hours after eating may protect people with type 1 diabetes from cardiovascular disease (<https://doi.org/10.1177/1479164117698918>). Participants had normal levels of blood sugar, fat and inflammatory markers in the blood post-injection compared to raised levels when the injection was not given.

54th Congress of the ERA-EDTA Madrid, Spain, 3–6 June

**No cardiovascular benefit from vitamin D in dialysis patients**

Active vitamin D does not prevent cardiovascular disease in haemodialysis patients with normal levels of parathyroid hormone, according to the prospective, randomized J-DAVID trial (Oshohi et al, 2017). On intention-to-treat analysis, cardiovascular risk was slightly, although not significantly, higher in patients receiving vitamin D ( $P=0.127$ ).

The study included 972 patients from 108 sites in Japan, randomized to either oral alfacalcidol (starting dose 0.5 µg/day) or no treatment for 48 months. All patients were able to receive other standard care including phosphate binders and cinacalcet.

Activation of vitamin D by the kidney is severely impaired in patients with end-stage renal disease. Observational studies had shown that vitamin D receptor activators were associated with lower all-cause and cardiovascular mortality in dialysis patients regardless of serum parathyroid hormone.

Oshohi T, Inaba M, Nishizawa Y et al (2017) Active vitamin D in the prevention of cardiovascular events in haemodialysis patients: the Japan Dialysis Active Vitamin D (J-DAVID) trial. Abstract 3404. European Renal Association-European Dialysis and Transplant Association (ERA-EDTA), Madrid, Spain, 3–6 June

**Home-based exercise cuts hospital admissions in patients on haemodialysis**

A simple low-intensity walking programme reduces short- and long-term risks of hospitalization in haemodialysis patients, with greater benefits for patients who continue to adhere to their programme. These are the results of the EXCITE clinical trial (Mallamaci et al, 2017). Previously reported results of the study had shown that the home exercise programme also improved patients' physical performance and quality of life (Manfredini et al, 2017). Lead investigator Professor Francesca Mallamaci, from the Bianchi-Melacrino-Morelli Hospital, Reggio Calabria, Italy, commented: 'Patients with the highest adherence had the lowest risk of hospitalization.'

The multicentre Italian trial randomized 296 haemodialysis patients to either usual activity (control) or home-based walking exercise, scheduled according to baseline performance for 6 months. The risk of hospitalization fell significantly in the exercise arm compared to control (hazard ratio 0.46, 95% confidence interval 0.22–0.97,  $P=0.04$ ). This benefit was confirmed at 36-month follow up, with a risk reduction in hospital admissions of 29% (hazard ratio 0.71, 95% confidence interval 0.50–1.003,  $P=0.05$ ).

Risk of hospitalization up to 6 months was lowest in patients with high adherence, defined as >60% exercise sessions completed (hazard



Professor Francesca Mallamaci, Director, UO Complex of Nephrology, Dialysis and Transplantation, Bianchi-Melacrino-Morelli Hospital, Reggio Calabria, Italy

ratio 0.55, 95% confidence interval 0.35–0.87,  $P=0.01$  vs control). In patients with low adherence, risk was similar to that of controls. There was no significant difference in mortality between the exercise and control groups during 36 months' follow up.

Mallamaci F, Manfredini F, Baggetta R et al (2017) A personalized walking exercise program reduces the risk of hospitalization in dialysis patients. Abstract 3410. European Renal Association-European Dialysis and Transplant Association (ERA-EDTA), Madrid, Spain, 3–6 June

Manfredini F, Mallamaci F, D'Arrigo G et al (2017) Exercise in patients on dialysis: a multicenter, randomized clinical trial. *J Am Soc Nephrol* 28(4): 1259–1268. <https://doi.org/10.1681/ASN.2016030378>

**Consider first-line rituximab in steroid-dependent nephrotic syndrome**

In children with steroid-dependent nephrotic syndrome, rituximab is more effective than tacrolimus in maintaining disease remission and minimizing steroid exposure.

This is the conclusion of the RITURNS trial, a 12-month, open-label, single-centre study (Basu et al, 2017), including 120 children with steroid-dependent nephrotic syndrome in Kolkata, India. Patients were randomized to either tacrolimus plus tapering doses of alternate-day prednisolone, or to a single

rituximab course and 4 weeks' alternate-day prednisolone.

Compared with tacrolimus, rituximab resulted in significantly higher 12-month relapse-free survival (90% vs 63.3%,  $P<0.001$ ), lower cumulative prednisolone intake (25.8±27.8 mg/kg/year vs 86.3±58.0 mg/kg/year,  $P<0.001$ ), better growth and better estimated glomerular filtration rate. Both regimens were well tolerated and adverse events comparable.

Investigator Professor Franz Schaefer, from the Center for Pediatrics and

Adolescent Medicine, Heidelberg University Hospital, Heidelberg, Germany, concluded: 'Given its excellent tolerability and lacking nephrotoxicity, rituximab may be considered as first-line steroid-sparing therapy in children with steroid-dependent nephrotic syndrome.'

Basu B, Roy BN, Sandler A et al (2017) Superior efficacy of rituximab v. tacrolimus in pediatric steroid dependent nephrotic syndrome (RITURNS trial). Presented during ERA-EDTA 2017. Abstract 3413. European Renal Association-European Dialysis and Transplant Association (ERA-EDTA), Madrid, Spain, 3–6 June

## American Society of Clinical Oncology Chicago, Illinois, 2–6 June

## Abiraterone acetate: new standard of care in prostate cancer

Adding abiraterone acetate (Zytiga) to androgen-deprivation therapy for men with locally advanced hormone sensitive prostate cancer significantly increased overall survival, found the LATITUDE trial (Fizazi et al, 2017).

'In my opinion, this finding supports the fact that adding abiraterone and prednisone to castration should now be considered as the new standard of care for these men with high-risk, newly diagnosed metastatic prostate cancer,' said study presenter Dr Karim Fizazi, from University Paris-Sud, France.

Abiraterone, currently used for patients with metastatic prostate cancer that worsened despite androgen-deprivation therapy, blocks androgen production by inhibiting CYP17, an enzyme expressed in testicular, adrenal and prostate tumour tissue.

In the phase 3 trial, 1199 men with newly diagnosed, high-risk, hormone-sensitive metastatic prostate cancer were randomized to receive androgen-deprivation therapy plus abiraterone and prednisone ( $n=597$ ) or androgen-deprivation therapy plus placebo ( $n=602$ ). The study was conducted across 235 sites in 34 countries.

The median overall survival with androgen-deprivation therapy and placebo was 34.7 months, but was not yet reached in



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the abiraterone group (hazard ratio 0.62, 95% confidence interval 0.51–0.76,  $P<0.0001$ ). The median radiographic progression-free survival in the abiraterone arm was 33.0 months *vs* 14.8 months in the control arm. Several severe side effects were more common with abiraterone acetate and prednisone than placebo including high blood pressure (20% *vs* 10%), low potassium (10.4% *vs* 1.3%), and liver enzyme abnormalities (5.5% *vs* 1.3%).

Fizazi K, Tran N, Fein L et al; LATITUDE Investigators (2017) Abiraterone plus prednisone in metastatic, castration-sensitive prostate cancer. *N Engl J Med* <https://doi.org/10.1056/NEJMoa1704174>

## Pregnancy safe after breast cancer

Pregnancy does not increase the chances of breast cancer returning, found a retrospective multicentre study of over 1200 women who had had breast cancer.

'Our findings confirm that pregnancy after breast cancer should not be discouraged, even for women with ER-positive cancer,' said presenter Dr Matteo Lambertini, from the Institut Jules Bordet, Brussels, Belgium.

The study enrolled women under the age of 50 years when diagnosed with non-metastatic breast cancer before 2007. Of the participants 333 became pregnant and 874 did not. Each woman who became pregnant was matched to three women with similar tumour and treatment characteristics who did not become pregnant.

After a median follow up of 10 years there was no difference in disease-free survival between women who became pregnant and those who did not, for both ER positive and ER negative patients.

Survivors of ER-negative breast cancer who became pregnant had a 43% lower chance of dying than those who did not become pregnant. 'Pregnancy could be a protective factor for patients with ER-negative breast cancer ... but we need more research into this,' said Dr Lambertini.

## Selective internal radiation therapy reduces side effects in Asian Pacific and European patients with advanced hepatocellular carcinoma

Advanced or inoperable hepatocellular carcinoma patients treated with selective internal radiation therapy had better tumour responses and significantly fewer adverse events than patients treated with sorafenib, found an Asian Pacific study.

For the SIRveNIB study, 360 patients with hepatocellular carcinoma were randomized 1:1 to receive assessment for selective internal radiation therapy ( $n=182$ ) or sorafenib ( $n=178$ ). Selective internal radiation therapy involves

Y-90 resin microspheres (emitting beta radiation) delivered via the hepatic artery.

The median overall survival (primary endpoint) was 8.84 months for patients receiving selective internal radiation therapy *vs* 10.02 months for sorafenib (hazard ratio 1.12;  $P=0.360$ ). Serious adverse events were significantly less for selective internal radiation therapy than sorafenib ( $P=0.0091$ ) and patients who received selective internal radiation therapy showed higher tumour response rates  $P<0.001$ .

Notably, said presenter Professor Pierce Chow, from the National Cancer Centre, Singapore, SIRveNIB findings mirror the French SARAH study reported in April. 'French patients get hepatocellular carcinoma from alcohol and hepatitis C, while Asian Pacific patients get hepatocellular carcinoma from hepatitis B. This shows selective internal radiation therapy can be effective across a whole range of primary hepatocellular carcinoma patients,' said Professor Chow.

Janet Fricker