

New gene for idiopathic pulmonary fibrosis

An international team of researchers has identified AKAP13 as a susceptibility gene for idiopathic pulmonary fibrosis ([https://doi.org/10.1016/S2213-2600\(17\)30387-9](https://doi.org/10.1016/S2213-2600(17)30387-9)). They undertook a genome-wide association study in patients with idiopathic pulmonary fibrosis of European ancestry and matched controls, and a follow-up of associated genetic variants in independent datasets of patients with idiopathic pulmonary fibrosis and controls from two independent American samples.

They analysed over 2700 people with idiopathic pulmonary fibrosis and 8500 people without and found that people with idiopathic pulmonary fibrosis are more likely to have changes in AKAP13.

Author Professor Gisli Jenkins, from the University of Nottingham, said: 'What is really exciting about these studies is that this gene affects a pathway that can be targeted by drugs currently in development, opening the door to precision medicine in idiopathic pulmonary fibrosis.'

Future trials in advanced breast cancer should include premenopausal women

In new guidelines for treating advanced breast cancer, an expert panel at the Advanced Breast Cancer Fourth International Consensus Conference, Lisbon, Portugal, said that the majority of clinical trials for hormone-dependent advanced breast cancer either explicitly exclude premenopausal women, or deter them by means of unnecessarily restrictive inclusion criteria.

The panel has called for future trials to be designed to enable both pre- and postmenopausal women to be enrolled. Professor Fatima Cardoso, Director of the Breast Unit of the Champalimaud Cancer Centre in Lisbon, Portugal, said: 'Not only are younger women denied the opportunity to take part in clinical trials, but clinicians lack the evidence on how best to treat these patients who have advanced breast cancer with limited therapies available.'

Understanding the numbers and reasons for emergency readmission to hospital

Admissions to hospital and delayed transfers of care are well monitored and understood, but information about the number of people being readmitted to hospital for unplanned follow-up treatment is less widely available.

Healthwatch England has published *What happens when people leave hospital and other care settings?* (www.healthwatch.co.uk/resource/what-happens-when-people-leave-hospital-and-other-care-settings). This sets out what Healthwatch England has heard about people's experiences of leaving hospital over the last 2 years. It follows a 2016 report by the House of Commons Public Administration and Constitutional Affairs Committee which said the government and NHS need to improve their understanding of this particular dataset.

Healthwatch England asked 125 NHS hospital trusts in England for their data on emergency readmissions for each financial year since 2012/13. Of these trusts, 92 (73%) responded either in full or in part to the request and 72 provided the full day-by-day breakdown of their data for each of the 5 years.

For 2016–17 529 318 emergency readmissions were reported by 84 hospital trusts. The top line figures from 2012–13 to 2016–17 show that:

- The number of emergency readmissions has risen over the last 5 years by 22.8%, from 372 805 to 457 880
- The number of emergency readmissions within 24 hours of discharge has risen by 29.2%, from 49 529 to 63 964

- The number of readmissions within 48 hours has risen by 27%, from 77 927 to 98 955
- Readmissions within 48 hours account for more than 1 in 5 (21.61%) of the total.

The analysis is not meant to suggest that clinicians should keep people in hospital for longer, and Healthwatch England acknowledges that emergency readmissions are not just the responsibility of the NHS. The purpose of this work is to highlight how current emergency readmissions data can help hospital trusts' boards, managers and clinicians identify risk and learn from occasions when things do go wrong. It also outlines how data collection could be improved.



Validating a risk score to predict risk and stratify adult contacts of tuberculosis index cases

An international group developed a score to predict risk of tuberculosis in adult contacts of tuberculosis index cases, using patients in Peru. They identified index case, contact and household risk factors for tuberculosis from which to derive a score and classify contacts as low, medium, or high risk. This score was validated in a different cohort in Peru.

Risk factors for tuberculosis were body mass index, previous tuberculosis, age, sustained exposure to the index case, the index case being in a male patient, lower community household socioeconomic position, indoor

air pollution, previous tuberculosis among household members, and living in a household with a low number of windows per room.

This externally validated risk score could predict and stratify 10-year risk of developing tuberculosis in adult contacts, and could be used to prioritize tuberculosis control interventions for people most likely to benefit.

Saunders MJ, Wingfield T, Tovar MA et al (2017) A score to predict and stratify risk of tuberculosis in adult contacts of tuberculosis index cases: a prospective derivation and external validation cohort study. *Lancet Infect Dis* 17(11): 1190–1199. [https://doi.org/10.1016/S1473-3099\(17\)30447-4](https://doi.org/10.1016/S1473-3099(17)30447-4)

Centralised care improved outcomes for children with cleft lip and palate but variation still seen

Around 1000 children are born with cleft lip and/or palate in the UK each year, with many requiring long-term multidisciplinary care. A study which assessed whether the centralisation of cleft lip and palate care services improved child outcomes, 15 years after centralisation took place, found that this has improved patient outcomes but highlights that more work is needed in some areas (Ness et al, 2017).

Care for children with cleft lip and/or palate is provided by multidisciplinary teams working in 11 managed clinical networks. Cleft Care UK carried out a repeat nationwide cross-sectional survey of 5-year-olds 15 years later to evaluate the impact of this care model. The researchers collected comprehensive data on care and outcomes from 268 children with unilateral cleft lip and palate. Key findings include:

- Facial growth, appearance and speech have improved since the mid-1990s
- Oral health and hearing have not improved – 45% of children were free of dental decay in the original survey compared to 48% in the current survey
- Some children still have poor results – 17% of children had unintelligible or just-intelligible speech.

Between centres there was substantial variation in practice – for oral health prevention

measures, hearing and speech treatment – and for some outcomes, such as speech intelligibility, where the centre explained 13% of the observed variation in outcome.

Professor Andy Ness, Professor of Epidemiology in the School of Oral & Dental Sciences, University of Bristol, Bristol, said: ‘Children with cleft lip and palate in the UK are now treated by a centralised interdisciplinary service that has resulted in improved outcomes. But there is still more to do... even in outcomes that have improved up to a fifth of children still do not have good outcomes.’

Ness AR, Wills A, Mahmoud O et al (2017) Centre-level variation in treatment and outcomes and predictors of outcomes in 5-year-old children with non-syndromic unilateral cleft lip treated within a centralized service: The Cleft Care UK study. Part 6: Summary and implications. *Orthod Craniofac Res* 20 Suppl 2: 48–51. <https://doi.org/10.1111/ocr.12188>



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Vitamin D linked with better live birth rates in women undergoing assisted reproduction treatment

A review and meta-analysis, analysing data from 11 published studies that included 2700 women, shows a strong link between low vitamin D concentrations in women and lower live birth rates after assisted reproduction treatment compared to women who have the right amount of vitamin D (Chu et al, 2017).

The researchers found that live births were a third more likely to occur in women who had the right amount of vitamin D compared to women who did not. A similar result was seen with the results of pregnancy tests and clinical pregnancies. Women who had sufficient vitamin D were 34% more likely to have a positive pregnancy test and 46% more likely to achieve a clinical pregnancy than women who had deficient or insufficient concentrations of vitamin D.

They are calling for a randomized clinical trial to be carried out to investigate the potential role of vitamin D supplementation in improving live birth rates following assisted reproduction treatment.

The researchers, led by Dr Justin Chu from the University of Birmingham, caution that their findings do not mean that vitamin D supplementation necessarily improves women's chances of having a baby following assisted reproduction treatment as their research can only show an association and not that having sufficient concentrations of vitamin D actually cause the improved birth rate.

Chu J, Gallos I, Tobias A, Tan B, Eapen A, Coomarasamy A (2017) Vitamin D and assisted reproductive treatment outcome: a systematic review and meta-analysis. *Hum Reprod* <https://doi.org/10.1093/humrep/dex326>

Analysis provides reassurance on the safety of biosimilars

A new analysis of publicly available regulatory documents found no substantial differences in the reporting of safety information for biosimilars and related originators (<https://doi.org/10.1111/bcp.13454>). Overall, 55 general safety concerns were identified.

Breastfed babies less likely to have eczema as teenagers

Babies whose mothers had received support to breastfeed exclusively for a sustained period from birth have a 54% lower risk of eczema at the age of 16 years, according to a study of over 13 000 Belarusian teenagers enrolled in the PROMotion of Breastfeeding Intervention Trial (PROBIT) (<https://doi.org/10.1001/jamapediatrics.2017.4064>).

New recommendations for cardiovascular imaging in athletes

The European Association of Preventive Cardiology and European Association of Cardiovascular Imaging have released a joint position statement for cardiovascular imaging in athletes (<https://doi.org/10.1093/eurheartj/ehx532>). This focuses on the imaging modalities, providing the correct indications and the keys for appropriate interpretation of result, in the context of the athlete's sport, age, race and gender.

37th Société Internationale D'Urologie meeting Lisbon, Portugal, October 19–22

Urine-based test for bladder cancer could reduce need for cystoscopy and computed tomography scans

A urine-based test for bladder cancer has been shown to have 95% sensitivity for higher risk cancers and a negative predictive value greater than 97% according to new data. The test, launched at the 37th Société Internationale D'Urologie meeting in Lisbon, Portugal, opens the way for non-invasive testing to be incorporated into the diagnostic pathway.

'Our study demonstrates ADXBLADDER has one of the highest sensitivities and negative predictive values of any urine test for bladder cancer diagnosis,' said Mr Stuart McCracken, the study presenter and consultant urologist, from Sunderland Royal Hospital, Sunderland. ADXBLADDER uses standard ELISA (enzyme-linked immunosorbent assay) methodology to measure MCM5, a protein marker of replicating cells that are not terminally differentiated unlike normal surface epithelium cells in the bladder lumen.

In the study between August 2016 and February 2017, 577 patients attending diagnostic haematuria clinics at six UK centres underwent ADXBLADDER testing, with results then compared to

the diagnostic benchmark of combined cystoscopy, ultrasound and computed tomography scanning.

Results showed that the overall sensitivity of ADXBLADDER was 76% (high risk 92%, muscle invasive group 100%, intermediate risk 75%, low risk 50%), the overall specificity 69%, and the negative predictive value 97%. 'What's really important is ADXBLADDER achieved very good sensitivity in high risk patients and those with muscle invasive disease, where cancer is likely to spread quickly, and prognosis is much poorer,' said Mr McCracken, adding that the test is unaffected by infections, inflammation or blood in the urine.

The test, he said, is easy to use, involves ELISA technology available in most hospitals, requires just 10 ml of urine, and delivers a definitive 'yes/no' result within 3 hours.

Considering how ADXBLADDER might be integrated into current diagnostic pathways, Mr Tim Dudderidge, a urology surgeon from University Hospital Southampton suggested that for low risk patients with



Mr Stuart McCracken, Consultant Urologist, Sunderland Royal Hospital, Sunderland

invisible haematuria the test could be combined with ultrasound, and for high risk patients with visible haematuria combined with ultrasound and cystoscopy. 'This could lead to reductions in unnecessary cystoscopy and computed tomography scans,' said Mr Dudderidge.

ADXBLADDER, produced by Arquer Diagnostics, received its CE mark in October 2017 and is currently commercialized in the UK, France, Italy, Turkey and the Nordic region.

Enobosarm reduces stress urinary incontinence, finds pilot study

Enobosarm has 'profound effects' on reducing stress urinary incontinence, reported a pilot study presented as a poster.

Stress urinary incontinence is estimated to affect up to 35% of adult women. While a variety of treatments are used, no oral therapies have been approved.

Enobosarm, a selective androgen receptor modulator, is currently used for muscle wasting and osteoporosis. As the muscles of the pelvic floor are enriched with androgen receptors, selective androgen receptor modulators could increase pelvic floor muscle mass and reduce stress urinary incontinence.

In the single arm open-labelled study, 17 postmenopausal women with an average age of 60.7 years who had experienced stress urinary incontinence symptoms for more than 6 months were prescribed 3 mg enobosarm for 12 weeks.

Mean stress leaks decreased from 5.08 per day at baseline to 0.88 per day at week 12. The mean pad weight decreased 71% from 77.6g at baseline to 22.2g at 12 weeks. Women reported improved quality of life measurements in each of five study instruments. Adverse events were minimal and included headaches, nausea, fatigue, hot flashes, insomnia,

muscle weakness, acne, and mild transient elevations in liver enzymes.

'Enobosarm reduced stress incontinent episodes by more than 80%, improved quality of life and was extremely safe,' said lead author Professor Kenneth Peters, from Oakland University William Beaumont School of Medicine, Rochester, Michigan, USA.

A phase 2 trial is comparing enobosarm 1 mg and 3 mg with placebo. 'If the findings are supported in a large placebo-controlled trial, this may change management of stress incontinence and reduce the need for surgery,' said Professor Peters.

Janet Fricker

Obstructive sleep apnoea may increase risk of developing Alzheimer's disease

Biomarkers for amyloid beta (Ab) increase over time in elderly adults with obstructive sleep apnoea in proportion to the severity of obstructive sleep apnoea. Those with more apnoeas per hour had greater accumulation of brain amyloid over time (Sharma et al, 2017).

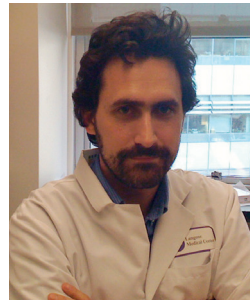
These were the findings of a study investigating the associations between obstructive sleep apnoea severity and changes in Alzheimer's disease biomarkers longitudinally, specifically whether amyloid deposits increase over time in healthy elderly participants with obstructive sleep apnoea. The study included 208 participants, aged 55–90 years, with normal cognition as measured by standardized tests and clinical evaluation.

More than half the participants had obstructive sleep apnoea, including 36.5% with mild obstructive sleep apnoea and 16.8% with moderate to severe obstructive sleep apnoea. A 2-year longitudinal study involving 104 participants found a correlation between obstructive sleep apnoea severity and a decrease in CSF Ab42 levels over time. The finding was confirmed in the subset of

participants who underwent amyloid positron emission tomography, which showed an increase in amyloid deposits in the brain in those with obstructive sleep apnoea.

'Results from this study... may mean that age tips the known consequences of obstructive sleep apnoea ... to brain impairment,' said Dr Ricardo S Osorio, senior author and assistant professor of psychiatry at New York University School of Medicine. 'If this is the case, then the potential benefit of developing better screening tools to diagnose obstructive sleep apnoea in the elderly who are often asymptomatic is enormous.'

Sharma RA, Varga AW, Bubu OM et al (2017) Obstructive sleep apnea severity affects amyloid burden in cognitively normal elderly: a longitudinal study. *Am J Respir Crit Care Med* <https://doi.org/10.1164/rccm.201704-0704OC>



Dr Ricardo S Osorio, Assistant Professor, Center for Brain Health, Department of Psychiatry, Center of Excellence on Brain Aging, NYU Langone Medical Center, New York, USA

Worldwide cancer incidence and mortality among young adults in 2012

A population-based study has been undertaken to quantify the burden of young adult cancers worldwide (Fidler et al, 2017). Young adult cancers were defined as those occurring between the ages of 20 and 39 years because these individuals will have passed puberty and adolescence, but not yet experienced the effects of hormonal decline, immune response deterioration, or organ dysfunction associated with chronic health conditions.

A total of 975 396 new cancer cases and 358 392 cancer-associated deaths occurred among young adults worldwide in 2012, which equated to an age-standardized rate of 43.3 new cancer cases per 100 000 people per year and 15.9 cancer-associated deaths per 100 000 people per year.

The burden was disproportionately greater among women and the most common cancer types overall in terms of new cases were female breast cancer, cervical cancer, thyroid cancer, leukaemia, and colorectal cancer; in terms

of deaths, female breast cancer, liver cancer, leukaemia and cervical cancer were the main contributors.

When assessed by development level and geographical region, the cancer profile varied substantially; generally the burden of infection-associated cancers was greater in regions under transition. Cancer incidence was elevated in most developed regions compared with less developed regions (age-standardized rate 64.5 vs 46.2 cancer cases per 100 000 people per year); however, the mortality burden was three times higher in less developed regions (age-standardized rate 25.4 vs 9.2 cancer-associated deaths per 100 000 people per year), reflecting differences in cancer profiles and inferior outcomes.

Fidler MM, Gupta S, Soerjomataram I, Ferlay J, Steliarova-Foucher E, Bray F (2017) Cancer incidence and mortality among young adults aged 20–39 years worldwide in 2012: a population-based study. *Lancet Oncol* [https://doi.org/10.1016/S1470-2045\(17\)30677-0](https://doi.org/10.1016/S1470-2045(17)30677-0)

Peritoneal dialysis may be linked to lower risk of stroke

Findlay et al (2017) explored the effect of renal replacement therapy modality at initiation and cumulative dialysis exposure by time-dependent regression analysis, using transplant recipients as the reference group. The group analysed data from the Scottish Renal Registry and the Scottish Stroke Care Audit to identify stroke in all adult patients who commenced renal replacement therapy from 2005 to 2013. Incidence rate was calculated and regression analyses performed to identify variables associated with stroke.

Of the 4957 patients who began renal replacement therapy 277 patients suffered a stroke (incidence 18.6/1000 patient-years). These patients were older, had higher blood pressure and were more likely to be female and have diabetes. On time-dependent analysis, haemodialysis exposure was independently associated with increased risk of stroke (compared to transplantation). Use of peritoneal dialysis did not increase stroke risk on adjusted analysis.

Commenting on the findings, Dr Mark Findlay, Speciality Registrar and Honorary Clinical Lecturer, Queen Elizabeth University Hospital, Glasgow, said: 'Our group has an interest in the effect of dialysis on the brain and carried out this study to determine if the modality of dialysis has an influence on stroke risk – with interesting results. We believe this information is useful to both patients and clinicians and may influence their choice of dialysis modality.'

He added: 'We recognize this association of haemodialysis exposure and stroke risk requires further exploration and we are presently completing research observing the real-time effect of haemodialysis on cerebral blood flow and function.'

Findlay M, MacIsaac R, MacLeod MJ, Metcalfe W, Traynor JP, Dawson J, Mark PB (2017) Renal replacement modality and stroke risk in end-stage renal disease – a national registry study. *Nephrol Dial Transplant* <https://doi.org/10.1093/ndt/gfx291>