

Use of antipsychotics increases risk of pneumonia in people with Alzheimer's disease

Teams from Finland and Sweden have performed a cohort study of over 60 000 people with Alzheimer's disease and a matched group of people without Alzheimer's disease (Tolppanen et al, 2016).

They found that antipsychotic use was associated with a higher pneumonia risk (adjusted hazard ratio 2.01, 95% confidence interval 1.90–2.13) in those with Alzheimer's disease and somewhat higher risk in the non-Alzheimer's disease cohort (adjusted hazard ratio 3.43, 95% confidence interval 2.99–3.93).

With observational data the authors cannot fully rule out a shared causality between pneumonia and antipsychotic use, but the risk–benefit balance should be considered when antipsychotics are prescribed.

Tolppanen AM, Koponen M, Tanskanen A et al (2016) Antipsychotic use and risk of hospitalisation or death due to pneumonia in persons with and without Alzheimer's disease. *Chest* (doi: 10.1016/j.chest.2016.06.004)

Psychosocial issues important in weight management programmes for severely obese adolescents

Tackling issues such as low self-esteem, depression, anxiety and poor social relationships could be key when dealing with severe adolescent obesity (doi: 10.1016/j.jadohealth.2016.06.014).

SHINE is an established tier 3 (delivered by specialist providers) weight management programme, targeted at children with more complex, severe obesity. SHINE's psychosocial intervention method, which addresses emotional issues which may impede weight loss, has proved successful when working with 10–17-year-olds.

Lower severity trauma patients could be more likely to die after 2–3 weeks

A new study has shown that lower severity trauma patients could be more likely to die after 2–3 weeks (Mirkes et al, 2016).

Using data from the largest trauma database in Europe, the Trauma Audit and Research Network (TARN) database, Dr Evgeny Mirkes, Professor Tim Coats, Professor Jeremy Levesley and Professor Alexander Gorban used 165 559 trauma cases to conduct the research, among them 19 289 cases with unknown outcome.

The problem of multiphase mortality is well-known in trauma study. For the whole TARN dataset, the team found that the coefficient of mortality decreases monotonically over time. However, for lower severities, the coefficient of mortality is a non-monotonic function which may have maxima at the second and third

Professor Tim Coats, Professor of Emergency Medicine, University of Leicester, Leicester



weeks. This means that while the probability of dying for all trauma cases consistently decreases over time, there are peaks in the probability of death for those with less severe trauma who remain in hospital at around 14 days and 21 days after admission.

Handling missing data is one of the main tasks in data pre-processing, especially in large public service datasets. In health care, the problems with data are not their size, but their quality. As human inspection at this scale is impossible, there is a need for intelligent tools for accuracy and believability control.

Discussing the implications of the findings for clinicians, Professor Tim Coats, Professor of Emergency Medicine in the Emergency Medicine Academic Group, University of Leicester, Leicester, said: 'Analysis of "big data" in health care can give clinicians new information about their patients – showing "what" happens, but not "why". This analysis in major trauma shows new patterns, and we now need to look into the cause. Finding things that we don't understand is exciting for researchers as it creates new questions for further study.'

Mirkes EM, Coats TJ, Levesley J, Gorban AN (2016) Handling missing data in large healthcare dataset: A case study of unknown trauma outcomes. *Comput Biol Med* 75: 203–16 (doi: 10.1016/j.compbmed.2016.06.004)

Epilepsy surgery found safe and cost-effective

French researchers have compared the cost-effectiveness of resective surgery and medical therapy in adult patients with partial intractable epilepsy (Picot et al, 2016).

The prospective controlled cohort of patients with surgically remediable and medically intractable partial epilepsy was followed over 5 years in 15 French centres. Effectiveness was defined as 1 year without a seizure, based on the International League Against Epilepsy (ILAE) classification. Clinical outcomes and direct costs were compared between surgical and medical groups.

Among the 289 enrolled surgery candidates, 207 were operable – 119 in the surgical group and 88 in the medical group. The proportion of patients completely seizure-free during the

last 12 months (ILAE class 1) was 69.0% in the operated group and 12.3% in the medical group during the second year ($P<0.001$), and it was respectively 76.8% and 21% during the fifth year ($P<0.001$).

Direct costs became significantly lower in the surgical group the third year after surgery, as a result of reduced use of antiepileptic drugs.

The authors concluded that resective surgery for epilepsy is cost-effective in the medium term, and should be considered earlier in the development of epilepsy.

Picot MC, Jaussent A, Neveu D et al (2016) Cost-effectiveness analysis of epilepsy surgery in a controlled cohort of adult patients with intractable partial epilepsy: A 5-year follow-up study. *Epilepsia* (doi: 10.1111/epi.13492)

Risk of liver, colon and kidney cancer increased in patients with polycystic kidney disease

A nationwide cohort study was carried out in Taiwan to establish the risk of cancer in patients with polycystic kidney disease without either chronic kidney disease or end-stage renal disease (Yu et al, 2016).

From inpatient claims of the Taiwan National Health Insurance Research Database, patients aged 20 years and older, and diagnosed with polycystic kidney disease between January 1998 and December 2010, were included in the polycystic kidney disease cohort. Patients with a history of cancer, chronic kidney disease or end-stage renal disease were excluded. The control group matched patients aged older than 20 years with no history of polycystic kidney disease or cancer who were randomly selected from the National Health Insurance Research Database, giving a total of 4346 patients in each group.

The overall incidence of cancer was higher in the polycystic kidney disease cohort than in the control cohort (20.1 [95% confidence interval 18.3–21.9] per 1000 person-years *vs* 10.9 [95% confidence interval 10.1–11.8] per 1000 person-years; crude hazard ratio 1.77 [95% confidence interval 1.52–2.07]; hazard ratio adjusted for age, sex, frequency of medical visits, and comorbidities was 1.83 [95% confidence interval 1.57–2.15]).

The specific risks (adjusted subhazard ratios) were significantly higher in the polycystic kidney disease cohort than in the non-polycystic kidney disease cohort for liver cancer (1.49, 95% confidence interval 1.04–2.13, $P=0.030$), colon cancer (1.63, 95% confidence interval 1.15–2.30, $P=0.006$) and kidney cancer (2.45, 95% confidence interval 1.29–4.65, $P=0.006$).

Commenting on the findings, Dr Tung-Min Yu from the Graduate Institute of Clinical Medical Science and School of Medicine, China Medical University, Taichung, Taiwan, said: 'Evidence indicates that the dysregulation of mTOR [mechanistic target of rapamycin] is involved in a variety of diseases including cancer. Polycystic kidney disease is the most common inherited cystic renal disease worldwide. Remarkably high levels of mTOR activity were observed in patients with autosomal dominant polycystic kidney disease. We supposed that patients with polycystic kidney disease should have an associated increased risk of cancers; nevertheless, evidence in humans was previously lacking.'

Yu TM, Chuang YW, Yu MC et al (2016) Risk of cancer in patients with polycystic kidney disease: a propensity-score matched analysis of a nationwide, population-based cohort study. *Lancet Oncol* (doi: 10.1016/S1470-2045(16)30250-9)

Patient factors affect how long a hip replacement will last

The National Joint Registry's 13th Annual Report highlights that patient factors have a significant bearing on how long the implant will last, with younger patients having an increased risk of revision than their older counterparts. Moreover, the data reveal that a patient from a younger age group is more likely to be revised irrespective of gender, with the youngest group having the worst predicted outcomes in terms of the risk of subsequent revision.

The National Joint Registry records performance data for hip, knee, ankle, shoulder and elbow joint replacements in England, Wales, Northern Ireland and the Isle of Man, and input into it is mandatory for all hospitals.

Commenting on the results of the report, National Joint Registry medical director, Mr

Martyn Porter, said: 'Revision estimates are much higher in younger patients under 55 years of age compared to patients over 75 years of age. This presumably relates to patient activity.

He added: 'Younger patients should not be denied life-changing surgery but they need to be advised that revision may be two or three times more likely at 10 years compared to less active patients.'

The full report and orthopaedic clinical activity data are available online via www.njrreports.org.uk



e-learning modules for essentials of clinical nutrition

BAPEN has updated its virtual learning environment (www.bapen.org.uk/e-learning-portal). The e-learning modules, free to all those who work in the NHS, cover the basics of disease-related malnutrition, nutrition support and nutrition-related ethics. They meet the requirements of the foundation and core medical training curricula.

Deaths from ovarian cancer decline worldwide as a result of use of oral contraceptives

Deaths from ovarian cancer fell worldwide between 2002 and 2012 and are predicted to continue to decline by 2020 (doi: 10.1093/annonc/mdw306). The researchers believe the main reason is the use of oral contraceptives and their long-term protection against ovarian cancer, but the decline in use of hormone replacement therapy and better diagnosis and treatment may also play a role.

Purinergic receptors potential new target for treating hypertension

Researchers at the University of Bristol and Afferent Pharmaceuticals have identified a potential new way of treating hypertension by reducing nervous system activity from the carotid body. When activated, this can cause blood pressure to rise uncontrollably (doi: 10.1038/nm.4173).

Monitoring prostate cancer as effective as surgery or radiotherapy for survival over 10 years

Active monitoring is as effective as surgery and radiotherapy, in terms of survival at 10 years, reports the largest study of its kind, funded by the National Institute for Health Research (Hamdy et al, 2016).

All three treatments result in similar, and very low, rates of death from prostate cancer. Surgery and radiotherapy reduce the risk of cancer progression over time compared with active monitoring, but cause more unpleasant side effects.

Chief investigator Professor Freddie Hamdy from the University of Oxford, said: 'treating the disease [prostate cancer] radically, when found, reduces the number of men who develop spread of prostate cancer, but we do not know yet whether this will make a difference to them living longer or better, and we have been unable to determine reliably which disease is lethal, and which can be left alone.'

Hamdy FC, Donovan JL, Lane JA et al; ProtecT Study Group (2016) 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. *N Engl J Med* (doi: 10.1056/NEJMoa1606220)

Scalpel-bougie cricothyroidotomy most efficient for obtaining emergency front of neck access

A cross-specialty working group of ear, nose and throat surgeons and anaesthetists recommends the scalpel-bougie cricothyroidotomy technique as the most efficient and reliable method of obtaining emergency front of neck access to the trachea in a situation where the patient's airway is blocked and routine methods fail (Pracy et al, 2016).

Without this rescue technique, which involves placing a tube into the windpipe using a scalpel and a small guide, many of these patients would die.

The working group recommends that, based on the most recent Difficult Airway Society guidelines, a scalpel-bougie cricothyroidotomy will be the quickest and most appropriate technique to access the airway and allow oxygenation when 'can't intubate, can't oxygenate' occurs. The group acknowledges, however, that variable training has been devoted to this technique in anaesthesia or surgery, and stresses that clinicians charged with the provision of the airway should choose the most appropriate technique based on their own experience and clinical judgement.

Dr Richard Marks, Chair of the Working Group and Council Member of the Royal College of Anaesthetists, said: 'Although "can't intubate, can't oxygenate" events are fortunately very rare, anaesthetists and surgeons have a

responsibility to make themselves familiar with emergency airway procedures including scalpel-bougie cricothyroidotomy. We believe there is a good opportunity here for anaesthetists and surgeons to work even more effectively together to tighten emergency protocols and improve training to ensure that patients with breathing problems are offered the best chance of survival during these life-threatening events.'

Pracy JP, Brennan L, Cook TM et al (2016) Surgical intervention during a Can't Intubate Can't Oxygenate (CICO) event: Emergency Front-of-neck Airway (FONA)? *Clin Otolaryngol* (doi: 10.1111/coa.12669)

Dr Richard Marks, Chair of the Working Group and Council Member of the Royal College of Anaesthetists



Single inhaler triple therapy effective in patients with COPD

TRILOGY was a randomized, parallel group, double-blind, active-controlled study done in 159 sites across 14 countries, carried out to assess the efficacy of a single-inhaler combination of an extra fine formulation of beclometasone dipropionate, formoterol fumarate, and glycopyrronium bromide (triple therapy) in patients with chronic obstructive pulmonary disease (COPD) compared with beclometasone dipropionate and formoterol fumarate (dual therapy) treatment (Singh et al, 2016).

The three co-primary endpoints were pre-dose forced expiratory volume in 1 second (FEV₁), 2-hour post-dose FEV₁, and transition dyspnoea index focal score, all measured at week 26 in the intention-

to-treat population (all patients who were randomly assigned and received at least one dose of study drug and had at least one post-baseline efficacy assessment).

Between March 2014, and January 2016, 1368 patients received either triple ($n=687$) or dual therapy ($n=681$). At week 26, triple therapy improved pre-dose FEV₁ by 0.081 litres (95% confidence interval 0.052–0.109, $P<0.001$) and 2-hour post-dose FEV₁ by 0.117 litres (95% confidence interval 0.086–0.147, $P<0.001$) compared with dual therapy. Mean transition dyspnoea index focal scores at week 26 were 1.71 for triple therapy and 1.50 for dual therapy, with a difference of 0.21 (95% confidence interval –0.08–0.51, $P=0.160$).

Adverse events were reported by 368 (54%) patients with triple therapy and 379 (56%) with dual therapy. One serious treatment-related adverse event occurred (atrial fibrillation) in a patient in the triple therapy group.

The authors believe that these results provide evidence for the clinical benefits of stepping up patients with COPD from an inhaled corticosteroid/long-acting β_2 -agonist combination treatment to triple therapy using a single inhaler.

Singh D, Papi A, Corradi M et al (2016) Single inhaler triple therapy versus inhaled corticosteroid plus long-acting β_2 -agonist therapy for chronic obstructive pulmonary disease (TRILOGY): a double-blind, parallel group, randomised controlled trial. *Lancet* **388**(10048): 963–73 (doi: 10.1016/S0140-6736(16)31354-X)

Closing the gaps in psoriasis care

Susan Mayor

Many patients with moderate to severe psoriasis are currently not treated with systemic therapy despite this being recommended by evidence-based guidelines, warned specialists attending the *Values in Psoriasis Care: From Patients to Payers* meeting in Hamburg, Germany.

A survey of 391 dermatologists in North American and Europe estimated that only one in five (19.5%) patients with moderate to severe psoriasis were treated with conventional oral therapy and a similar proportion (19.6%) with biologics (van de Kerkhof et al, 2015). A related survey of psoriasis patients found that over 80% of those with greater than four palms of body surface area affected were receiving no treatment or topical treatment only (Lebwohl et al, 2014).

‘Undertreatment is very common,’ warned Professor Matthias Augustin, from the University Medical Center Hamburg-Eppendorf. The survey found reasons for not initiating or maintaining systemic therapy included long-term safety concerns, tolerability, convenience of use and the cost of biologics. ‘But the chronic patient burden of psoriasis can result in irreversible cumulative life course impairment, supporting the need for early and effective intervention,’ he pointed out.

Growing recognition that psoriasis is a systemic inflammatory disorder further underlines the need for effective treatment. ‘In

the past, we perceived psoriasis as only a skin disease but we now recognise it is a complex systemic disease,’ said Professor Diamant Thaci, Comprehensive Center Inflammation Medicine, University of Lubeck. He suggested that optimized, integrated management of psoriasis clinics is important to improve the value to patients and health systems.

‘We need to match therapy with the patient’s needs,’ agreed Professor Kristian Reich, from Dermatologikum Hamburg. The survey found that physicians were particularly focused on the location and size of skin lesions, with 53% giving this as their top priority in selecting treatment. However, for patients the top priority was itching, with 38% giving this as their key concern (Lebwohl et al, 2014; van de Kerkhof et al, 2015).

Lebwohl MG, Bachelez H, Barker J et al (2014) Patient perspectives in the management of psoriasis: Results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey. *J Am Acad Dermatol* **70**(5): 871–81.e1-30 (doi: 10.1016/j.jaad.2013.12.018)

van de Kerkhof PC, Reich K, Kavanaugh A et al (2015) Physician perspectives in the management of psoriasis and psoriatic arthritis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis survey. *J Eur Acad Dermatol Venereol* **29**(10): 2002–10 (doi: 10.1111/jdv.13150)

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Lack of sleep and untreated depression may increase risk of developing Alzheimer’s disease

Depression and sleeplessness have long been considered symptoms of Alzheimer’s disease. An American study (Burke et al, 2016) indicates that whether in combination with genetic risk factors or on their own, untreated depression and lack of sleep may lead to the onset of Alzheimer’s disease dementia later in life.

‘Previous research has attempted to explore the relationship between depression, sleep disturbance and Alzheimer’s disease. Our research is significant in that it is the first to find an increased risk of Alzheimer’s disease caused by insomnia and depression independently, as well as in combination

with genetic risk factors,’ said Dr Shanna L Burke, assistant professor of social work at the Robert Stempel College of Public Health & Social Work, Florida International University, Miami, Florida.

Although treating the genetic risk factors for Alzheimer’s disease is not yet possible, these findings suggest that alleviating depression and sleep disturbance may decrease the chances of a person developing the disease.

Burke SL, Maramaldi P, Cadet T, Kukull W (2016) Associations between depression, sleep disturbance, and apolipoprotein E in the development of Alzheimer’s disease: dementia. *Int Psychogeriatr* **28**(9): 1409–24 (doi: 10.1017/S1041610216000405)

Many adolescent girls with leukaemia not screened for pregnancy before chemotherapy

A new study indicates that adolescent females with acute leukaemia have low rates of pregnancy screening before receiving chemotherapy that can cause birth defects (doi: 10.1002/cnrc.30225).

Researchers compared pregnancy screening patterns among adolescents with acute leukaemia with adolescents with an emergency room visit who received computed tomography scans of the abdomen or pelvis. (Emergency medicine has pregnancy screening protocols for adolescents because of the teratogenic risks of radiation.)

Among 35 650 patient admissions of females aged 10–18 years with newly diagnosed leukaemia or emergency room admissions with abdominal or pelvic scans, the proportion of visits with an appropriately timed pregnancy test was 35%, 64% and 58% in acute lymphoblastic leukaemia, acute myeloid leukaemia and emergency room groups respectively. There was substantial variation in pregnancy screening patterns between hospitals.

Wide-ranging renal and cardiovascular risks from atrial fibrillation

Interventions aimed at reducing outcomes beyond stroke are warranted in patients with atrial fibrillation, according to a new meta-analysis (doi: 10.1136/bmj.i4482).

Atrial fibrillation was associated with an increased risk of all-cause mortality, cardiovascular mortality, major cardiovascular event, stroke, ischaemic stroke, ischaemic heart disease, sudden cardiac death, heart failure, chronic kidney disease and peripheral arterial disease but not haemorrhagic stroke. The highest absolute risk increase was for heart failure.