

Ketamine fails to prevent postoperative delirium

Mackenzie Moore

According to results from an international randomized controlled trial evaluating the clinical effects of ketamine, clinicians should rethink its use in subanaesthetic doses during surgery ([https://doi.org/10.1016/S0140-6736\(17\)31467-8](https://doi.org/10.1016/S0140-6736(17)31467-8)).

Patients were randomly allocated to one of three groups to receive placebo (normal saline), low dose ketamine (0.5 mg/kg), or high dose ketamine (1.0 mg/kg) after induction of anaesthesia but before surgical incision. There was no difference in delirium incidence between patients in the combined ketamine groups and the placebo group. Older patients receiving ketamine during and after surgery were also more likely to experience hallucinations and nightmares.

Predictive model may help forecast migraines

Mackenzie Moore

A new, simple forecasting model based on measuring the frequency or perceived frequency of stressful events may help predict future occurrence of migraine attacks for chronic migraine sufferers (Houle et al, 2017).

'We know that certain people are at greater risk of having an attack over other people, but within a person, we have not been able to predict increased risk for an attack with any level of accuracy,' said lead author Dr Tim Houle. 'This study demonstrates that it is quite possible to forecast the occurrence of a headache attack within an individual headache sufferer.'

When refined, this model could allow preemptive treatment of headache or migraine attacks in at-risk individuals, thereby avoiding pain or disability.

Houle TT, Turner DP, Golding AN, Porter JAH, Martin VT, Penzien DB, Tegeler CH (2017) Forecasting individual headache attacks: Development of a multivariable prediction model for persons with episodic migraine. *Headache* 57(7): 1041–1050. <https://doi.org/10.1111/head.13137>

Researchers investigate link between air pollution and type 2 diabetes

Mackenzie Moore

In one of the largest cross-sectional studies of air pollution and diabetes, an interdisciplinary team of researchers from the University of Leicester, University of East Anglia and EarthSense investigated associations between air pollution and the rise in the number of cases of type 2 diabetes (O'Donovan et al, 2017). Exposure to traffic-related air pollutants is known to cause insulin resistance, a hallmark of type 2 diabetes, and observational evidence has been applied to better understand a potential link.

Scientists collected data from 10 443 participants in three diabetes screening studies in Leicestershire. Included in the exposure, outcome and confounder assessment were estimates of outdoor nitrogen dioxide and particulate matter concentrations, the number of cases of type 2 diabetes, the impact of demographic factors (age, sex, ethnicity, smoking, area social deprivation, urban or rural location), lifestyle factors (body mass index and physical activity), and the prevalence of neighbourhood green space.

Dr Gary O'Donovan, lead researcher, noted that 'high air pollution and low physical activity are two of the leading causes of disease and premature death in middle and high-income countries.'

'Like most cities in the UK, Leicester has only a handful of air quality monitors. The UN has estimated that two thirds of world's population will be living in cities by 2050 and our cities must become better, healthier places in which to live,' he continued. 'Cities like Copenhagen in Denmark and Medellín in Colombia are doing a much better job of measuring air pollution and facilitating active transport than most cities in the UK.'

The 3-year exposure investigation revealed that while nitrogen dioxide and particulate matter concentrations were associated with type 2 diabetes in unadjusted models, there was no statistically significant association after adjustment for demographic factors (odds 1.08, 95% confidence interval 0.91–1.29). The odds of type 2 diabetes was 1.10 (95% confidence interval 0.92–1.32) after further adjustment for lifestyle factors and 0.91 (95% confidence interval 0.72–1.16) after yet further adjustment for neighbourhood green

space. With no evidence of exposure definition bias, the authors concluded that demographic factors seemed to explain the association between air pollution and type 2 diabetes.

'While original results suggested an association between air pollution and associated particulates and type 2 diabetes, when the effects of lifestyle and demographic factors were considered, and given the limited size of the sample, evidence for direct association with air pollution was inconclusive', said Professor Roland Leigh, Technical Director of EarthSense and Director of Enterprise at the University of Leicester's Institute for Space and Earth Observation, and co-author of the study.

Professor Leigh added: 'We will, however, continue to apply cutting-edge air quality research to unpick potentially connected long-term exposure factors.'

The authors call for high-quality longitudinal studies to improve researchers' understanding of the association.

O'Donovan G, Chudasama Y, Grocock S et al (2017) The association between air pollution and type 2 diabetes in a large cross-sectional study in Leicester: The CHAMPIONS Study. *Environ Int* 104: 41–47. <https://doi.org/10.1016/j.envint.2017.03.027>

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Palliative care referrals still low in hospitalized patients with end-stage liver disease in the USA

Mackenzie Moore

One of the largest nationwide studies of palliative care referral for hospitalized patients with end-stage liver disease shows that although the rate of referral in the United States of America is low, it has been steadily rising (Rush et al, 2017). The study also reveals that certain socioeconomic and ethnic barriers may hinder access to palliative care services.

Researchers in Canada and the USA analysed data from the 2006–2012 National Inpatient Sample to investigate trends in palliative care access for patients with end-stage liver disease across the USA. This database, which contains approximately 20% of all inpatient hospitalizations from 46 of the 50 states, revealed that out of 39 349 patients, palliative care consultations were performed for only 4.5% of them. Further analysis revealed a marked increase in palliative care referral, from 0.97% in 2006 to 7.1% in 2012. Additionally,



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data showed that individuals who were ethnically Hispanic or of lower socioeconomic status were linked with lower rates of palliative care referrals.

Dr Mayur Brahmania, lead researcher, prompts focus on the overall low referral rate rather than its increase. He also notes that there has traditionally been very little guidance for the use of palliative care for end-stage liver disease, particularly given the variable course of

the disease and lack of symptom recognition. ‘We feel early concurrent palliative care could significantly improve the quality of life for patients with end-stage liver disease, and practitioners providing this care must find ways to integrate palliative care with the possibility of life-prolonging therapy.’

Rush B, Walley KR, Celi LA, Rajoriya N, Brahmania M (2017) Palliative care access for hospitalized patients with end stage liver disease across the United States. *Hepatology* <https://doi.org/10.1002/hep.29297>

Working long hours increases the risk of developing atrial fibrillation

People who work long hours have an increased risk of developing atrial fibrillation, according to a study of nearly 85 500 men and women (Kivimäki et al, 2017).

The study showed that, compared to people who worked a normal week of between 35–40 hours, those who worked 55 hours or more were approximately 40% more likely to develop atrial fibrillation during the following 10 years. For every 1000 people in the study, an extra 5.2 cases of atrial fibrillation occurred among those working long hours during the 10-year follow-up.

The team from the Individual-Participant-Data Meta-analysis in Working Populations (IPD-Work) Consortium analysed data from 85 494 men and women from the UK, Denmark, Sweden and Finland who took part in one of eight studies in these countries.

During the 10-year follow-up period, there were 1061 new cases of atrial fibrillation. This gave an incidence rate of 12.4 per 1000 people in the study, but among the 4484 people working 55 hours or more, the incidence was 17.6 per 1000.

‘Those who worked long hours had a 1.4 times higher risk of developing atrial fibrillation, even after we had adjusted for factors that could affect the risk, such as age, sex, socioeconomic status, obesity, leisure time physical activity, smoking and risky alcohol use,’ said lead author Professor Mika Kivimäki, director of the Whitehall II Study, from the Department of Epidemiology at University College London.

Kivimäki M, Nyberg ST, Batty GD et al (2017) Long working hours as a risk factor for atrial fibrillation: a multi-cohort study. *Eur Heart J* <https://doi.org/10.1093/eurheartj/ehx324>

Outcomes substantially improved following metal-on-metal hip revision

Outcomes following metal-on-metal hip revision surgery performed for abnormal reactions to metal are now similar to the outcomes in patients with other types of hip replacement undergoing revision surgery, according to an analysis from the National Joint Registry (<https://doi.org/10.1302/2046-3758.67.BJR-2017-0017.R2>).

Apolipoprotein ε-4 may increase cognitive impairment linked with sleep-disordered breathing

The Multi-Ethnic Study of Atherosclerosis analysed data from 1752 participants (average age 68 years) and found that those carrying the apolipoprotein ε-4 (APOE-ε4) allele showed greater cognitive deficits with various indices of sleep-disordered breathing than those without the allele (<https://doi.org/10.1513/AnnalsATS.201701-0520C>).

Inappropriate prescription of antiplatelet drugs in older hospitalized patients

In an analysis of nearly 2200 older hospitalized patients, 959 (44%) were prescribed an antiplatelet drug (<https://doi.org/10.1111/bcp.13355>). Half of patients prescribed for primary prevention were inappropriately prescribed (52%), being mainly overprescribed (74%). Inappropriate underprescription was also seen in secondary prevention (31%).

Mediterranean diet helps prevent colorectal cancer

High intakes of fruit and fish and cutting back on soft drinks is the best combination to avoid colorectal cancer, reported Fliss Isakov et al (2017).

For the case-controlled study, investigators asked 808 people aged between 40 and 70 years undergoing screening or diagnostic colonoscopies to complete food frequency questionnaires.

The mean number of adhered Mediterranean diet components was significantly lower among people with advanced polyps compared to controls (4.5±1.9 vs 5.1±1.7, $P=0.03$). Components of the Mediterranean diet which were negatively associated with advanced polyps were low intake of soft drinks (odds ratio=0.65), high intake of fruit (odds ratio=0.66) and high intake of fish (odds ratio=0.62). Combined adherence to all three components was significantly associated with lower odds of advanced colorectal polyps (odds ratio=0.14).

Fliss Isakov N, Zilver-Sagi S, Webb M, Ivankovsky D, Margalit D, Kariv R (2017) Mediterranean diet components are negatively associated with advanced colorectal polyps in a population-based case-control study. *Ann Oncol* **28** (suppl_3): mdx262.022. <https://doi.org/10.1093/annonc/mdx262.022>

SIRT delivers overall survival benefit for colorectal cancer patients with metastatic liver disease

A post-hoc analysis of colorectal cancer patients treated with selective internal radiation therapy (SIRT) and chemotherapy for metastatic liver disease revealed increased overall survival for patients whose primary tumours originated on the right side but not for those whose tumours originated on the left (van Hazel et al, 2017).

‘These findings are good news for patients with right-sided tumours, who have a much worse prognosis and fewer treatment options,’ said presenter Dr Guy van Hazel, from the University of Western Australia.

Primary tumour location in colorectal cancer has been emerging as a predictor of response, leading to investigators exploring sidedness in the post-hoc analysis of 739 patients enrolled in the SIRFLOX and FOXFIRE Global cohorts. The SIRFLOX and FOXFIRE Global studies were designed to evaluate the efficacy of SIRT plus first-line oxaliplatin-based chemotherapy for unresectable colorectal cancer. SIRT with Y-90 resin microspheres is a minimally invasive



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treatment delivering high doses of beta radiation to inoperable liver tumours.

Median overall survival for colorectal cancer patients with right-sided tumours was 22 months for chemotherapy + SIRT vs 17.1 months for chemotherapy alone (hazard ratio 0.64, 95% confidence interval 0.46–0.89, $P=0.007$).

Median overall survival for colorectal cancer patients with left-sided tumours

was 24.6 months for chemotherapy + SIRT vs 26.6 months for chemotherapy alone (hazard ratio 1.12, 95% confidence interval 0.92–1.36, $P=0.279$).

Subject to further validation, Dr van Hazel said, this may support earlier use of SIRT for colorectal cancer patients with liver-only or liver-dominant metastases from right-sided tumours.

van Hazel G, Heinemann V, Sharma N et al (2017) Impact of primary tumour location on survival in patients with metastatic colorectal cancer receiving selective internal radiation therapy and chemotherapy as first-line therapy. *Ann Oncol* **28**(suppl3): mdx302.005. <https://doi.org/10.1093/annonc/mdx302.005>

Combination of AM0010 and FOLFOX shows promise in pancreatic cancer

AM0010 (pegilodecakin) has shown promising results in patients with advanced pancreatic ductal adenocarcinoma in an ongoing phase 1/1b clinical trial (Hecht et al, 2017).

AM0010, a long-acting PEGylated form of recombinant human interleukin-10, has shown sustained anti-tumour effects and a good safety/tolerability profile. Its enhanced half-life gives strong immune-stimulating effects that induce the activation, proliferation and survival of intra-tumoural, tumour-reactive, cytotoxic CD8+ T-cells.

Patients with advanced pancreatic ductal adenocarcinoma (who had not received prior platinum-containing regimens) were randomized to AM0010 alone ($n=22$) or AM0010 in combination with FOLFOX chemotherapy ($n=21$).

As of 1 May 2017, the AM0010 + FOLFOX regimen produced a disease control rate of 79%, an objective response rate of 16% and a complete response rate of 11%, while AM0010 alone gave a disease control rate of 53%, and objective and complete response rates of 0%. AM0010 +

FOLFOX produced 1-year survival of 47% compared to 22% for AM0010 alone.

AM0010 + FOLFOX with a modified AM0010 dose schedule (5 days on, 2 days off) gave no grade 3/4 adverse events, and the ongoing phase 3 clinical trial is using this modified dosing schedule.

Hecht JR, Naing A, Falchook G et al (2017) Immunologic and objective tumor responses to PEGylated human IL-10 (AM0010) with 5-FU/LV and oxaliplatin (FOLFOX) in metastatic pancreatic adenocarcinoma (PDAC). *Ann Oncol* **28** (suppl_3): mdx262.003. <https://doi.org/10.1093/annonc/mdx262.003>

Janet Fricker

Social support improves self-care by patients with chronic obstructive pulmonary disease

Mackenzie Moore

Individuals with chronic obstructive pulmonary disease are more active and show increased participation in pulmonary rehabilitation if they have social support.

Research conducted on 282 patients with chronic obstructive pulmonary disease with an average age of 68 years suggests that living with others and having a caregiver encourages healthy behaviour (Chen et al, 2017).

Researchers analysed the association between healthy behaviour and two kinds of social support: structural (the type of social network a person has, such as being married or living with a partner or caregiver), and functional (the support a person believes his/her social network provides). The latter was measured via a validated questionnaire.

Notable observations from the study include that patients living with others took 903 more steps each day, scored higher on the functional social support questionnaire, were more likely to receive a pneumococcal vaccination and were less likely to smoke. Additionally, individuals with a spouse or partner caregiver were 11 times more likely to

participate in pulmonary rehabilitation.

‘Patient engagement in self-care is the crux of chronic obstructive pulmonary disease management,’ said senior author Dr Huong Q Nguyen. ‘Our goal ... was to identify factors associated with self-care activities, including physical activity, quitting smoking, participating in a pulmonary rehabilitation programme, adherence to medications, and getting vaccinations.’

Dr Nguyen said that clinicians should assess whether their patients have the necessary social support to do all they can do to remain healthy: ‘When social support is lacking, the health-care team should assist patients in marshalling social support. Similarly, health and social policies should acknowledge and consider ways to support the nearly 45 million unpaid family caregivers in the United States who are responsible for the vast majority of the day-to-day care of their loved ones.’

Chen Z, Fan VS, Belza B, Pike K, Nguyen HQ (2017) Association between social support and self-care behaviors in adults with chronic obstructive pulmonary disease. *Ann Am Thorac Soc* <https://doi.org/10.1513/AnnalsATS.201701-026OC>

Willingness to face prognosis varies in patients with terminal cancer

Mackenzie Moore

A study by researchers at Chang Gung University and Soochow University in Taiwan quantifies the variation in willingness to receive their prognosis among cancer patients who are terminally ill (Hsui Chen et al, 2017).

The study of 247 terminal cancer patients tracked their knowledge of their condition and prognosis over the last 6 months. The researchers categorized prognostic awareness into four states: unknown and not wanting to know, unknown but wanting to know, inaccurate awareness, and accurate awareness.

Initially, almost 60% of patients had an accurate awareness of their prognosis and 8% were unknown and not wanting to know. Although patients’ prognostic awareness generally remained unchanged, there was a trend in increased awareness, as 82% of patients progressed to an accurate awareness just before death and 3.6% remained unknowing. By

understanding the transition probabilities and time spent in each prognostic-awareness state, clinicians can better facilitate the transition toward accurate prognostic understanding.

‘Health-care professionals should appropriately assess patients’ readiness for prognostic information, and respect patients’ reluctance to confront their poor prognosis if they are not ready to know, but sensitively coach them to cultivate their accurate prognostic awareness,’ says Dr Siew Tzuh Tang, lead researcher. ‘Since terminally ill cancer patients need time to develop an accurate awareness of their prognosis, clinicians should begin early in the disease trajectory to cultivate patients’ accurate prognostic awareness.’

Hsui Chen C, Wen FH, Hou MM et al (2017) Transitions in prognostic awareness among terminally ill cancer patients in their last 6 months of life examined by multi-state Markov Modeling. *Oncologist* <https://doi.org/10.1634/theoncologist.2017-0068>

Muscle strength linked to better cognitive function in older people

Mackenzie Moore

Greater muscle strength is associated with better cognitive function in ageing women and men, found a Finnish study (Pentikäinen et al, 2017).

The test group, comprising 388 women and men with an average age of 66 years, had their muscle strength measured using handgrip strength, three lower body exercises (including leg extension, leg flexion and leg press), and two upper body exercises (e.g. chest press and seated row).

Researchers demonstrated the association between muscle strength and cognitive function by including sum scores of upper and lower body muscle strength in the model rather than relying solely on the common measures of handgrip strength and age. Cognitive function was assessed using the CERAD neuropsychological test battery with calculated total score.

‘The findings suggest that it may be justified to go beyond the handgrip and to include the upper and lower body when measuring muscle strength, as this may better reflect the association between muscle strength and cognition,’ said lead author Heikki Pentikäinen from the University of Eastern Finland.

The association between muscle strength and cognitive function is relatively under-researched, but this study provides new insight into the link between these functions and the methodology of measuring muscle strength, and presents further evidence for the health benefits of exercise and strength training. The work was part of the population-based DR’s EXTRA study, a 4-year randomized and controlled intervention study analysing the effects of exercise and nutrition on endothelial function, atherosclerosis and cognition.

Pentikäinen H, Savonen K, Komulainen P et al (2017) Muscle strength and cognition in ageing men and women: The DR’s EXTRA study. *Eur Geriatr Med* **8**(3): 275–277. <https://doi.org/10.1016/j.eurger.2017.04.004>