

Methadone increases risk of death in first 4 weeks of treatment for opioid dependence compared to buprenorphine

Patients who start treatment for dependence on opioids are five times as likely to die in the first 4 weeks when they are prescribed the most commonly used treatment, methadone, than if taking buprenorphine, a study by researchers at the University of Bristol, King's College London and the National Drug and Alcohol Research Centre at UNSW in Australia has found (Kimber et al, 2015).

The study reviewed the records of 32 033 patients who had started treatment with methadone or buprenorphine between 2001 and 2010. Patients who started treatment with buprenorphine were less likely to die from any cause, including drug-related causes, in the first 4 weeks of treatment. However, after 4 weeks there was little difference in risk of death between methadone and buprenorphine.

Around 50 000 Australians (and over 100 000 people in the UK) currently receive opioid pharmacotherapy treatment for dependence on heroin or other opioids. Around two thirds of these are being treated with methadone with the remainder on buprenorphine, according to figures from the Australian Institute of Health and Welfare.

Buprenorphine is considered to be safer as it is less likely to

cause respiratory depression, but patients are more likely to drop out of treatment than those taking methadone. Both treatments are endorsed by the World Health Organization.

Dr Jo Kimber, one of the study's lead author's and a researcher at the National Drug and Alcohol Research Centre UNSW and King's College London, said: 'Clinicians providing opioid substitution treatment face an important dilemma: which is more likely to reduce patient risk, buprenorphine or methadone?'

She added: 'Our data suggests at least at the beginning of treatment for heroin use that buprenorphine has clear benefits over methadone in reducing mortality risk.'

Professor Matthew Hickman, Professor in Public Health and Epidemiology at the University of Bristol, said: 'One way to reduce risks might be to commence treatment on buprenorphine for the first 4 weeks and then switch to methadone at a later stage.'

Professor Louisa Degenhardt at the National Drug and Alcohol Research Centre and one of the study's authors, added: 'The findings support a stepped approach to treatment. Opioid substitution therapy is proven to be a cost effective and safe treatment for opioid dependence. It not only reduces risk of death but also involvement in crime and imprisonment.'

Kimber J, Larney S, Hickman M, Randall D, Degenhardt L (2015) Mortality risk of opioid substitution therapy with methadone versus buprenorphine: a retrospective cohort study. *Lancet Psychiatry* (doi: 10.1016/S2215-0366(15)00366-1)

Determining risk factors for development of epilepsy in childhood brain tumour survivors

Seizures are common during and after treatment for a primary brain tumour. A team from Boston has described the incidence of and risk factors for seizures in long-term survivors of paediatric brain tumours (Ullrich et al, 2015).

A retrospective, longitudinal study reviewed all consecutive patients during a 12-month period who were at least 2 years post initial diagnosis of a brain tumour. Data collection included age at diagnosis, length of follow-up, extent of initial resection, tumour histology, and treatment modalities.

For patients who had experienced seizures at any time, the timing and frequency of seizures, seizure semiology, electroencephalography results, and anticonvulsant use were recorded.

Dr Nicole Ullrich, Boston Children's Hospital, Boston, MA



analyses and logistic regression were performed to assess risk factors.

The cohort included 298 patients (140 female). Average duration of follow-up was 7.6 years. Initial surgical resection was gross-total in 109 patients, and subtotal for 143. Twenty-nine patients underwent biopsy alone and 17 had no surgical intervention. Most frequent diagnoses were low grade glioma, medulloblastoma and ependymoma. Other treatments included cranial irradiation ($n=163$) and chemotherapy ($n=127$). Tumour

recurrence occurred in 92 patients (30%).

Seventy-one patients had seizures (24%). Ongoing seizures at the time of most recent follow-up were present in 42 patients. Risk factors for sei-

zures included tumour location, tumour histology, tumour recurrence, and incomplete resection at time of initial presentation.

These data may help identify and manage patients at highest risk for seizures as well as identifying patients for potential treatment trials with antiepileptogenic agents.

Lead author Dr Nicole Ullrich commented: 'This information will allow clinicians to understand better who needs to stay on antiseizure medications and who might be able to come off sooner. As some patients will require chemotherapy after surgery and some antiseizure medications can interact with chemotherapy, this will be crucial to management.'

Ullrich NJ, Pomeroy SL, Kapur K, Manley PE, Goumnerova LC, Loddenkemper T (2015) Incidence, risk factors, and longitudinal outcome of seizures in long-term survivors of pediatric brain tumors. *Epilepsia* (doi: 10.1111/epi.13112)

Success of cancer treatment almost doubles when patients are informed about disease

Providing cancer patients with information about their disease, its treatment and its impact on work life and education, nearly doubles their chances of a positive treatment outcome (Kamau, 2015).

Research indicates that educating cancer patients helps lower uncertainty and stress, while also equipping working patients with coping strategies during treatment.

The study analysed survey data from nearly 3500 British cancer patients in employment to investigate the relationship between the frequency with which patients received information that increased their understanding of their condition, its treatment and side effects, and the likely impact on their work life and education.

A positive treatment outcome (completion of treatment with no further signs or symptoms of

cancer) was more likely in patients who receive information about the impact of cancer on work life or education (1.72 times more likely), patients who receive information about the type of cancer (1.99 times more likely) and patients who receive information before a cancer-related operation (1.90 times more likely). Conversely, patients who receive information about the side effects had worse odds of a positive treatment outcome (0.65 to 1).

The results were then corroborated with a secondary analysis of survey data from the wider sample of 6700 patients (irrespective of their current employment status), which showed that preparing patients produces nearly twice better odds of successful cancer treatment.

Interpreting the results, Dr Caroline Kamau, from the Department of Organizational

Psychology, Birkbeck, University of London, said: 'There are two main reasons why preparing patients seems to produce nearly twice better odds of successful cancer treatment. One is that patient education lowers uncertainty and the stress that comes with not knowing what to expect. Uncertainty is a known stressor that interferes with health therefore reducing it will improve the odds of successful cancer treatment.'

'The second is that preparation equips working cancer patients with knowledge about good coping strategies, including how to cope with the fatigue that comes with treatment through adjusting work load.'

Kamau C (2015) Preparing patients with cancer who work and treatment responsiveness. *BMJ Support Palliat Care* (doi: 10.1136/bmjspcare-2015-000870)

Complete record of mutations behind pulmonary arterial hypertension

Scientists investigating pulmonary arterial hypertension have compiled the most up to date and complete record of all the defects found in the genes that cause the disease (doi: 10.1002/humu.22904).

Award for COPD Patient Passport

The British Lung Foundation won first prize in the category 'information that aids decision making' for their COPD Patient Passport at the 2015 British Medical Association Patient Information Awards. The passport is designed to help patients with chronic obstructive pulmonary disease (COPD) manage their condition as effectively as possible, through enabling shared decision making with clinicians.

Even mild depression puts a burden on carers of Alzheimer's patients

Caring for a patient with Alzheimer's disease is especially burdensome for carers who suffer from depressive symptoms, according to a study from the University of Eastern Finland (pii: 0891988715598229).

Significant improvements seen in the treatment and care of patients following hip fracture

The National Hip Fracture Database is managed by the Clinical Effectiveness and Evaluation Unit of the Royal College of Physicians. Its development has been described in annual reports.

All 180 eligible hospitals in England, Wales and Northern Ireland are now regularly uploading data to this database. The latest report (Royal College of Physicians, 2015)



describes the process and outcome of care provided to 64 102 people who presented with a hip fracture in 2014; nearly 95% of all cases in England, Wales and Northern Ireland.

The sixth national report is more focused on supporting the needs of clinical teams, and is designed to work alongside interactive graphs on the National Hip Fracture Database website,

providing a wealth of tabulated data to support clinical governance meetings in individual hospitals.

Speaking on behalf of the British Geriatrics Society, Dr Adam Gordon said: 'We need to continue to use these data to improve care until all older patients have access to timely, appropriate surgery and are able to benefit from full multi-disciplinary input in the run up to and immediately following surgery.'

Royal College of Physicians (2015) *National Hip Fracture Database annual report 2015*. Royal College of Physicians, London

Mechanisms by which childhood stress can affect female fertility

Can events you endured as a child really impact your ability to have children yourself? New research from a team from Tulane University School of Public Health and Tropical Medicine, New Orleans, and Boston University School of Medicine, Boston, examines

the mechanism by which adverse experiences in childhood impact female fertility (Jacobs et al, 2015).

Dr Marni Jacobs and colleagues explore the hypothesis that negative experiences in childhood can result in menstrual cycle irregularities, which

consequently impact on fertility. They relate their hypothesis to the life-history theory, which talks of balancing the preservation of one's health and the production of offspring that will survive to reproduce themselves, and theorise that 'early life stressors may predispose an individual to adaptively suppress fertility when situations are less than optimal, leading to periods of fertility difficulties even following previous births.'

The study examined data from 774 women of reproductive age, 195 of whom were pregnant. It analysed fertility difficulties, menstrual cycle irregularities and adverse childhood experiences, through a mixture of in-person interviews and take-home questionnaires.

Following their research, the team came to the conclusion that those women who had experienced negative events at a young age – such as 'abuse, neglect, household dysfunction or parental substance abuse' – were more likely to have faced fertility difficulties and abnormal absences of menstruation lasting 3 months or more, and also took a longer time to get pregnant.

The authors concluded that the strong relation between adverse experiences and periods of amenorrhoea suggests that the effect of childhood stress on fertility may be mediated by altered functioning of the hypothalamic–pituitary–adrenal axis, manifesting as menstrual cycle disruption.

Jacobs MB, Boynton-Jarrett RD, Harville EW (2015) Adverse childhood event experiences, fertility difficulties and menstrual cycle characteristics. *J Psychosom Obstet Gynaecol* **36**(2): 46–57 (doi: 10.3109/0167482X.2015.1026892)

PT and aPTT tests unnecessary in most patients

An American study sought to characterize whether requests for prothrombin time (PT) and activated partial thromboplastin time (aPTT) tests of preoperative patients are supported by evidence (Capoor et al, 2015).

Prospectively-collected patient data from 19 major teaching hospitals and eight hospital-affiliated surgical centres were evaluated. This included 1 053 472 consecutive patients – every patient admitted for elective surgery from 2009 to 2012 at all 27 settings. A subset of 682 049 patients (64.7%) had one or both tests done and history and physical records available for analysis.

Among preoperative patients, 26.2% received PT tests, and 94.3% of tests were unnecessary, given the absence of findings on history and physical records. Similarly, 23.3% of preoperative patients received aPTT tests, of which 99.9% were unnecessary.

Among patients with no history and physical records findings suggestive of bleeding risk, 6.6% of PT tests and 7.1% of aPTT tests were either a false positive or a true positive.

Use of unnecessary screening tests raises concerns for the costs of such testing and the consequences of false positive results.

Capoor MN, Stonemetz JL, Baird JC et al (2015) Prothrombin time and activated partial thromboplastin time testing: a comparative effectiveness study in a million-patient sample. *PLoS One* **10**(8): e0133317

Surgery effective for obese patients with type 2 diabetes

An open-label, randomized controlled trial was carried out at a diabetes centre in Italy, comparing 5-year outcomes from surgery with conventional medical treatment for the management of type 2 diabetes in obese patients (Mingrone et al, 2015).

Patients aged 30–60 years with a body mass index of 35 kg/m² or more and a history of type 2 diabetes lasting at least 5 years were randomly assigned to receive either medical treatment or surgery by Roux-en-Y gastric bypass or biliopancreatic diversion.

The primary end point was the rate of diabetes remission at 2 years (a glycated haemoglobin A_{1c} concentration of 6.5% or less (≤ 47.5 mmol/mol) and a fasting glucose concentration of 5.6 mmol/litre or less without active pharmacological treatment for 1 year).

Overall, 19 (50%) of the 38 surgical patients (seven of 19 in the gastric bypass group and 12 of 19 in the biliopancreatic diversion group) maintained diabetes remission at 5 years, compared with none of the 15 medically treated patients ($P=0.0007$).

Of patients who achieved 2-year remission, relapse of hyperglycaemia was recorded in eight of 15 patients in the gastric bypass group and seven of 19 patients in the biliopancreatic diversion group.

Surgical patients lost more weight than medically treated patients, but weight changes did not predict diabetes remission or relapse after surgery.

Five major complications of diabetes arose in four (27%) patients in the medical group compared with only one complication in the gastric bypass group and none in the biliopancreatic diversion group. No late complications or deaths occurred in the surgery groups.

The authors concluded that surgery is more effective than medical treatment for the long-term control of obese patients with type 2 diabetes. However, continued monitoring of glycaemic control is necessary because of potential relapse of hyperglycaemia.

Mingrone G, Panunzi S, De Gaetano A et al (2015) Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. *Lancet* **386**(9997): 964–73 (doi: 10.1016/S0140-6736(15)00075-6)

Small bites best for closing abdominal midline incisions

A prospective, multicentre, double-blind, randomized controlled trial has been undertaken at surgical and gynaecological departments in ten hospitals in the Netherlands (Deerenberg et al, 2015). This compared the large bites and small bites suture techniques for fascial closure of midline laparotomy incisions.

Patients aged 18 years or older who were scheduled to undergo elective abdominal surgery with midline laparotomy were randomly assigned to receive small tissue bites of 5 mm every 5 mm or large bites of 1 cm every 1 cm. The pri-

mary outcome was the occurrence of incisional hernia.

Between 2009, and 2012, 560 patients were randomly assigned to the large bites ($n=284$) or the small bites group ($n=276$). A total of 545 (97%) patients were included in the primary outcome analysis.

Patients in the small bites group had fascial closures sutured with more stitches than those in the large bites group, a higher ratio of suture length to wound length and a longer closure time. At 1-year follow-up, 57 (21%) of 277 patients in the large bites group and 35

(13%) of 268 patients in the small bites group had incisional hernia ($P=0.0220$). Rates of adverse events did not differ significantly between groups.

This shows that the small bites technique is more effective than the traditional large bites technique for preventing

incisional hernia in midline incisions and is not associated with a higher rate of adverse events. This should become the standard closure technique for midline incisions.

Corresponding author Dr Joris J Harlaar from Erasmus University Medical Center, commented: 'Incisional hernia is a preventable complication, but is seen in up to 35% of all open abdominal procedures and frequently requires reoperation. Our study shows that running multiple sutures with many small bites has a beneficial effect for patients.'

Dr Joris J Harlaar, Department of Surgery, Erasmus University Medical Center, Rotterdam, Netherlands



Deerenberg EB, Harlaar JJ, Steyerberg EW et al (2015) Small bites versus large bites for closure of abdominal midline incisions (STITCH): a double-blind, multicentre, randomised controlled trial. *Lancet* **386**: 1254–60 (doi: 10.1016/S0140-6736(15)00459-7)

Social factors affect survival in younger patients with leukaemia

A new study from the USA reveals that insurance status, marital status and county-level income may affect the chances of survival in young patients with acute myelogenous leukaemia (Borate et al, 2015). The findings indicate that efforts are needed to address the social factors that impact critical aspects of health in these patients.

Acute myelogenous leukaemia will affect approximately 20 830 and kill 10 460 Americans in 2015. Great progress has been made in identifying disease characteristics that cause a patient to have a higher or lower chance of cure following intense treatment, which often involves bone marrow transplantation.

Investigators at the University of Alabama at Birmingham have analysed a database with 5541 patients younger than 65 years of age to demonstrate that, in addition to age and disease char-

acteristics, other 'non-biological' patient characteristics also matter. The study is the largest to date to look at socioeconomic factors in outcomes of younger patients with acute myelogenous leukaemia.

Patients who were single or divorced, who were uninsured or were Medicaid beneficiaries, and patients who lived in areas with lower income had substantially elevated risks of dying prematurely.

Dr Uma Borate, lead author of the study and assistant professor in the UAB Division of Hematology and Oncology, said: 'We believe these three factors indicate lack of material and social support preventing young patients from successfully walking the long and difficult road towards a cure.'

Borate U, Mineishi S, Costa LJ (2015) Non-biological factors affecting survival in younger patients with acute myeloid leukemia. *Cancer* (doi: 10.1002/cncr.29436)

Gains made against malaria, but challenges remain

The WHO/UNICEF report, *Achieving the Malaria MDG Target*, outlines the tremendous gains against the disease over 15 years and underscores the need to focus renewed efforts in sub-Saharan Africa.

Significant progress has been made since 2000, when malaria was killing close to one million people per year, the majority of them young children. A global effort to rapidly scale up prevention, treatment and care led to the Millennium Development Goal of halting and reversing the incidence of malaria by 2015 being met. Annual

malaria deaths have fallen by 60% to 438 000. This equates to an estimated 6.2 million deaths averted – approximately 5.9 million of those among children under 5 years of age.

Marijke Wijnroks, Chief of Staff at the Global Fund, a partnership which supports locally run programmes to combat malaria, commented: 'This report clearly shows that we can't stop now. We must focus on areas where the disease burden is highest and people are least able to access lifesaving prevention and care, such as mosquito nets and anti-malarial medication.'

