

Digoxin increases risk of death in patients with heart problems

The largest review of all the evidence to date shows that use of digoxin is associated with an increased risk of death, particularly in patients being treated for atrial fibrillation.

Researchers from the J.W. Goethe University in Frankfurt, Germany, conducted a systematic review and meta-analysis of all studies published in peer-reviewed journals between 1993 and 2014 which looked at the effects of digoxin on death from any cause in patients with atrial fibrillation or congestive heart failure (Vamos et al, 2015).

They identified 19 relevant studies which included a total of 326 426 patients (235 047 with atrial fibrillation and 91 379 with congestive heart

failure). They found that among patients who were treated with digoxin, there was an overall 21% increased risk of death from any cause compared to patients who were not receiving this treatment.

When they looked at patients with atrial fibrillation and patients with congestive heart failure separately, digoxin was associated with a 29% and 14% increased risk of death from any cause respectively, compared to patients not receiving the drug.

Currently, the use of digoxin is recommended in guidelines from the USA and from the European Society of Cardiology for patients with heart failure or atrial fibrillation. However, the authors of this study wrote:

‘These recommendations reflect the highly unsatisfactory data basis on which to judge the supposed benefits of digoxin.’

Stefan Hohnloser, Professor of Cardiology at the university, who led the study, said: ‘Definite evidence can only come from results of randomized controlled trials. However, next to these, carefully performed meta-analyses provide the best clinical guidance and serve to generate hypotheses that need to be tested prospectively. Our analysis, together with evidence from other studies, all point in the same direction: there is harm associated with the use of digoxin.’

Professor Hohnloser said that there has only been one prospective randomized controlled trial of digoxin in 6800 patients with congestive heart failure, and none in patients with atrial

fibrillation. He concluded: ‘We need randomized controlled trials to examine the use of digoxin for both conditions and that test the drug *vs* a placebo or another, active treatment.’

Vamos M, Erath JW, Hohnloser SH (2015) Digoxin-associated mortality: a systematic review and meta-analysis of the literature. *Eur Heart J* (doi: 10.1093/eurheartj/ehv143)

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Guidelines to resolve conflicts in treating critically ill patients

Who should decide what life-prolonging medical treatments the intensive care patient should receive: the clinician or the patient’s family? The answer should almost always be ‘both’, according to a new policy statement from the American Thoracic Society (Bosslet et al, 2015).

‘Clinicians should neither simply acquiesce to treatment requests that they believe are not in a patient’s best interest, nor should they unilaterally refuse to provide treatment. Instead, if conflicts arise between clinicians and patients’ families, a fair process of dispute resolution should be undertaken, in which neither individual can unilaterally impose his or her will on the other,’ explained Dr Douglas White, Chair for Ethics in

Critical Care Medicine, associate professor in the University of Pittsburgh Department of Critical Care Medicine, and co-chair of the committee that produced these guidelines.

The statement also outlines procedures for situations when families request treatment that is truly futile, and situations in which medical urgency does not allow compliance with the longer dispute resolution process.

Bosslet GT, Pope TM, Gordon D, Rubenfeld GD et al, on behalf of The American Thoracic Society ad hoc Committee on Futile and Potentially Inappropriate Care (2015) An Official ATS/AACN/ACCP/ESICM/SCCM Policy Statement: Responding to Requests for Potentially Inappropriate Treatments in Intensive Care Units. *Am J Respir Crit Care Med* (doi: 10.1164/rccm.201505-0924ST)

Family history of breast cancer does not mean poor prognosis

Women who are diagnosed with breast cancer and have a family history of the disease face no worse a prognosis after treatment than other women with breast cancer (Eccles et al, 2015).

A team from Southampton and Oxford analysed the Prospective Outcomes in Sporadic *vs* Hereditary breast cancer (POSH) study, which included 2850 women under age 41 years who were diagnosed with breast cancer and treated in the UK. The study recorded patients’ personal characteristics, tumour characteristics, treatment, and family history of breast/ovarian cancer over a 15-year period.

The investigators found no significant differences in cancer recurrence rates after treatment for women with a history of breast cancer *vs* those without.

‘Successful treatment for breast cancer is just as likely in young patients with a family history of breast cancer, as in those without a family history,’ said Mr Ramsey Cutress, Associate Professor in Breast Surgery at the University of Southampton.

Eccles BK, Copson ER, Cutress RI et al, the POSH Study Steering Group (2015) Family history and outcome of young patients with breast cancer in the UK (POSH study). *Br J Surg* (doi: 10.1002/bjs.9816)

Expert group calls for improved diagnosis and treatment of dry eye disease

Around one in four people have dry eye disease and the incidence is increasing, specialists warned at a recent meeting. They reviewed latest developments and identified gaps in diagnosis and management to be addressed in an expert review and new global consensus to be developed over the next few years.

'Many patients with dry eye disease are currently not diagnosed,' warned Professor Harminder Dua, Professor of Ophthalmology and Visual Sciences, University of Nottingham, UK. 'This is one of the most frequent pathological conditions in ophthalmology,' he said, with a prevalence of up to 50% depending on the criteria used for diagnosis.

Dry eye disease is a progressive condi-

tion, underlining the importance of prompt diagnosis and treatment. 'If you don't do anything, dry eye disease will progress,' pointed out Kelly Nichols, Dean of the School of Optometry, University of Alabama, Birmingham, USA.

One of the challenges is the lack of clear diagnostic criteria and a simple screening test. James Wolffsohn, Deputy Executive Dean of the School of Life and Health Sciences,

Professor Harminder Dua, Professor of Ophthalmology and Visual Sciences, University of Nottingham, Nottingham



Aston University, Birmingham, UK, noted, 'We need a clear definition of dry eye disease with an unbiased physiological range adjusted for demographic factors.'

'There is huge unmet need for effective treatments for dry eye disease,' said David Sullivan, Senior Scientist at

the Schepens Eye Research Institute and Associate Professor of Ophthalmology, Harvard Medical School, Boston, USA. He noted that growing understanding of the pathophysiology of the condition, including the major role of dysfunction of the meibomian glands and increasing recognition of the role of neuronal damage in the cornea in dry eye disease, is resulting in new treatment approaches.

Professor Nichols concluded: 'Dry eye disease is a global problem. We need a clear definition of the condition and minimum gold standard diagnostic criteria. More specific treatments are needed. And we need to improve prevention and patient education.'

Susan Mayor

The meeting was convened by The Tear Film & Ocular Surface Society (TFOS; www.TearFilm.org) and sponsored by Dompé. TFOS is organising the development of the new report and consensus on dry eye disease, DEWS II.

Non-invasive test can detect cocaine use via a fingerprint

A team of researchers from the Netherlands Forensic Institute, the National Physical Laboratory, King's College London and Sheffield Hallam University, used mass spectrometry to analyse the fingerprints of patients attending drug treatment services. Testing the prints against saliva samples showed that the tests detected cocaine use equally well (doi: 10.1039/C5AN00112A).

Physical training helps women with polycystic ovary syndrome

Women with polycystic ovary syndrome often experience sexual dysfunction and low self-esteem, but this is improved by physical resistance training, such as upper body, lower body and abdominal exercises (doi: 10.1111/jsm.12909).

EpiTrack to monitor cognitive function in patients with epilepsy

EpiTrack – a tool which assesses and tracks changes in cognitive function in people with epilepsy – is now available for clinicians. To receive EpiTrack, contact UCB on medicalinformationuk@ucb.com

Most patients positive about their hospital care

A majority (84%) of respondents in the latest national survey of hospital inpatients, published by the Care Quality Commission (2015), rated their overall experience as seven or higher out of ten, with about one in four people rating it ten out of ten.

The survey is based on the replies of more than 59 000 people who stayed in one of 154 acute and specialist NHS trusts in England for at least one night during June, July or August 2014.

Over three quarters (77%) of people said they were 'always' well looked after dur-

ing their hospital stay. Eight out of ten 'always' had confidence and trust in the doctors and 78% 'always' had confidence and trust in the nurses.

However, over two fifths (42%) said there were delays with being discharged from hospital, with the majority (61%) citing the main reason for the delay as waiting for medicines. Nearly one in four (23%) of those who experienced delays waited for longer than 4 hours.

Of those who had an operation or procedure, one in ten said they did not understand

the explanation given by staff of how their operation went.

Professor Edward Baker, Deputy Chief Inspector of Hospitals at the Care Quality Commission, said: 'Despite the pressures facing the NHS, many patients are reporting positive experiences about their care. I strongly urge senior staff to review their results to see where improvements can be made as every patient deserves to receive the best possible care.'

Care Quality Commission (2015) Inpatient survey 2014. www.cqc.org.uk/content/inpatient-survey-2014 (accessed 28 May 2015)

Healthy lifestyle before bowel cancer diagnosis could help to improve survival

Following lifestyle guidelines about diet, physical activity and maintaining a healthy weight is associated with an improved likelihood of survival when diagnosed with bowel cancer (Romaguera et al, 2015).

Survival rates of bowel cancer have wide variations even in people with similar tumours and receiving the same treatment. It has been suggested that lifestyle factors before and

after diagnosis of bowel cancer can influence survival.

To investigate this further, a group of researchers analysed the data of 520 000 participants from 10 countries in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study.

Lead researcher, Dr Dora Romaguera from Imperial College London and CIBER-OBN, explained: 'Current advice given to cancer survivors

about lifestyle is to follow the same lifestyle recommendations for cancer prevention. Based on results of our own previous work on the EPIC cohort on cancer prevention, we wanted to see if following these recommendations were associated with the survivability of bowel cancer.'

At the start of the study, participants completed questionnaires about their medical history, diet and lifestyle. Weight



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Large but unexplained variations in paracetamol-induced liver failure among European countries

A fifty-fold between-country difference in rates of paracetamol-induced acute liver failure (ALFT) has been revealed by a study that compared patient data from seven countries at the request of the European Medicines Agency: France, Greece, Ireland, Italy, Netherlands, Portugal and the UK (Gulmez et al, 2015). This variation was even more pronounced on a per-capita basis.

The Study of Acute Liver Transplantation (SALT) identified patients with paracetamol-linked liver failure between 2005 and 2007, and compared the rate of these events per person and also per tonne of paracetamol sold in the country.

Although the average event rate

of ALFT in participating countries over 3 years was one case per 6 million inhabitants per year, the rate was highest in Ireland (one case for every 286 000 inhabitants) and lowest in Italy (one case for every 180 million people in Italy), with a 200-fold difference between these two countries.

Similar variation was seen when looking at the frequency of events for each tonne of paracetamol sold: while there was one ALFT event in Ireland for every 20.7 tonnes of paracetamol sold, there was only one for every 1074 tonnes sold in Italy.

Furthermore, paracetamol overdose represented 20% of all causes of this type of ALFT across Europe. This rose to 52% in Ireland and 28% in the

UK, but dropped to only 1% in Italy. There were no cases at all recorded in Greece. Intriguingly while France had the highest per-person use of paracetamol, it had the third-lowest ALFT rate.

'Overall, we found a six-times higher risk in Ireland and a two-fold higher risk in the UK compared to the average of the countries participating in the study,' said lead researcher Dr Sinem Ezgi Gulmez, Associate Professor of Pharmacology at the University of Bordeaux, France.

She added: 'Since we do not have event rates for overdoses not leading to liver failure, we cannot conclude anything about the rates of non-ALFT overdoses in the different countries, but indicators point to more common use of paracetamol for self-poisoning in certain countries'.

Gulmez SE, Larrey D, Pageaux G-P et al (2015) Liver transplant associated with paracetamol overdose: results from the seven-country SALT study. *Br J Clin Pharmacol* (doi: 10.1111/bcp.12635)



Dr Sinem Ezgi Gulmez, Associate Professor of Pharmacology, CIC Bordeaux CIC1401 Pharmaco-épidémiologie, Université de Bordeaux, Bordeaux, France

and height measurements were also taken. During the study period of an average of 6.4 years, 3292 participants were diagnosed with bowel cancer.

The researchers developed a scoring system based on joint guidelines from the World Cancer Research Fund and the American Institute of Cancer Research.

It was found that men who had a lifestyle score of 3 or more points out of a possible 6 were more likely to survive bowel cancer. For women, a score of 4 or above of a possible 7 was associated with increased survival; in both cases, the higher the score, the lower the risk of mortality after bowel cancer.

Owing to the study design, it has not been possible to demonstrate what would happen if these lifestyle habits were acquired after cancer diagnosis. Also, lifestyle was measured only once so it is not possible to know if lifestyle habits changed during follow up or after cancer diagnosis.

Romaguera D, Ward H, Wark PA et al (2015) Pre-diagnostic concordance with the WCRF/AICR guidelines and survival in European colorectal cancer patients: a cohort study. *BMC Medicine* 13: 107 (doi: 10.1186/s12916-015-0332-5)

Treatments for childhood cancer may increase risk of obesity

Individuals who had cancer as a child may be at increased risk of being obese as a result of the therapies they received during their youth. The study's results suggest the need for effective counselling and weight loss interventions for certain childhood cancer survivors (Wilson et al, 2015).

Previous research has shown that obesity rates are elevated in childhood cancer survivors who were exposed to cranial radiation, which is used to prevent or delay the spread of cancer to the brain. A team led by Dr Carmen Wilson and Dr Kirsten Ness of St. Jude Children's Research Hospital in Memphis, designed a study to estimate the prevalence of obesity among childhood cancer survivors and to identify the clinical and treatment-

related risks for obesity in these individuals. The study also looked for potential genetic factors that might play a role.

The study included 1996 survivors previously treated for cancer at St. Jude who had been diagnosed with cancer at least 10 years ago. The research-

Dr Kiri Ness, Epidemiology & Cancer Control, St. Jude Children's Research Hospital, Memphis, Tennessee, USA



ers found that 47% of survivors who had received cranial radiation were obese, compared with 29.4% of survivors who had not received cranial radiation.

The likelihood of obesity increased among survivors treated with cranial radiation who had also received glucocorticoids, or who were younger at the time of diagnosis. Also, certain variants in genes involved with neurons' growth, repair and connectivity were linked with obesity among survivors treated with cranial radiation. Survivors who had been treated with

chest, abdominal, or pelvic radiation were half as likely to be obese as those who did not receive these treatments.

'The ability to identify patients at increased risk may guide selection of therapeutic protocols that will maximize treatment outcomes while simultaneously minimizing the risk of long-term complications among children diagnosed with cancer,' said Dr Ness.

Wilson CL, Liu W, Yang JJ et al (2015) Genetic and clinical factors associated with obesity among adult survivors of childhood cancer: A report from the St. Jude Lifetime Cohort. *Cancer* (doi: 10.1002/cncr.29153)

Older people want more opportunities to plan their care

Older people who want to talk to health professionals about advance care planning are not always able to do so, finds a study by Musa et al (2015).

Thirteen general practices sent out surveys to potential participants aged 65 years or older. There were no additional inclusion or exclusion criteria for participants. Of the 5375 (34%) community-dwelling older peoples, 1823 returned questionnaires.

More than a third of respondents said that they would be interested in discussing advance care plans with a health professional. However, only 17% of respondents had prepared an advance care plan, and only

5% had been actively offered the opportunity to talk about it with a health professional.

Corresponding author Dr Irfana Musa, of Leicester Royal Infirmary, said: 'With the population growing older and living longer, we are treating many more conditions such as dementia, in which an individual's decision-making ability becomes impaired. Advance care planning can help people think ahead and also inform others of their wishes in anticipation of a time when they cannot communicate themselves.'

Musa I, Seymour J, Narayanasamy MJ, Wada T, Conroy S (2015) A survey of older peoples' attitudes towards advance care planning. *Age Ageing* 44(3): 371-6 (doi: 10.1093/ageing/afv041)

NICE guidance to help NHS staff deal with violence from patients

The National Institute for Health and Care Excellence (NICE) has updated its guideline on the management of violent and aggressive behaviour in people with mental health problems when they are being treated in the NHS and across all health and social care provider organizations.

The updated guideline aims to help safeguard NHS and health and social care staff and patients by preventing violent situations and offering clear guidance on managing them safely if needed.

Physical restraint should only be used as a last resort, once all other methods of preventing or calming the situation have failed. However, if restraint is the only course of action available, the guideline includes clear recommendations on how it should be done to ensure the safety of both staff and the individual.

Between 2013 and 2014 there were 68 683 assaults reported against NHS staff in England. The majority of these – 69% – occurred in mental health or learning disability settings and include incidents involving the families or carers of service users as well as service users themselves.

Professor Tim Kendall, director of the National Collaborating Centre for Mental Health and facilitator of the group that developed the guideline, said: 'This guidance represents a major step forward for people with mental health problems, especially in institutional settings, but also in the community and across health and social care.'

National Institute for Health and Care Excellence (2015) The short-term management of violent and physically threatening behaviour in mental health, health and community settings. www.nice.org.uk/guidance/NG10 (accessed 29 May 2015)