

Supplements more likely than medications to lead to death

New research shows that liver injury caused by herbals and dietary supplements increased from 7% to 20% over 10 years in an American study (Navarro et al, 2014).

Nearly half of all adult Americans consume herbal and dietary supplements, most commonly multivitamins, minerals, calcium and fish oils.

The Drug-Induced Liver Injury Network (DILIN) was set up in 2003 to track cases of liver injury caused by medications (excluding paracetamol), herbals and dietary supplements. Herbals and dietary supplements were identified as the second most common

cause of liver injury in the first DILIN report.

The present study examines hepatotoxicity caused by supplements rather than medications, enrolling 839 patients with liver injury from eight DILIN referral centres between 2004 and 2013. Liver injury cases included 45 caused by bodybuilding supplements, 85 attributed to non-bodybuilding supplements, and 709 caused by medications.

Liver injuries from herbal and dietary supplements rose to 20% during the study period. While bodybuilding supplements caused prolonged jaundice (median 91 days) in young

men, no fatalities or liver transplantations occurred. Death or liver transplantation occurred more frequently among cases of injury from non-bodybuilding supplements (13%) than from

conventional medications (3%). Liver injury from non-bodybuilding supplements was more common in middle-aged women.

Lead author Dr Victor Navarro, from Einstein Medical Center Philadelphia, commented: 'Our study group is specific to DILIN centers and therefore we cannot conclude that liver injury due to herbals and dietary supplements is on the rise in the US. Further population-based study of liver injury due to herbal products and dietary supplements is needed.'

Dr Victor Navarro, Chairman of the Department of Hepatology, Einstein Medical Center, Philadelphia



Navarro VJ, Barnhart H, Bonkovsky HL et al (2014) Liver injury from herbals and dietary supplements in the U.S. Drug-Induced Liver Injury Network. *Hepatology* **60**: 1399–408 (doi: 10.1002/hep.27317)

European project informs preparation for flu pandemic

Key results from a €1million European Commission project were presented at the Fifth ESWI Influenza Conference in Riga, Latvia.

These results will help policymakers develop more reliable plans for responding to flu epidemics, including pandemics. The world's first extensive cost-effectiveness analysis of epidemic responses has created a new approach, which will help governments avoid costly and ineffectual policies.

For the very first time, economic evidence has been established showing that vaccination programmes targeting the general population ('universal vaccination') appear more cost-effective than targeting only at-risk people or health professionals.

This challenges existing international or national recommendations to vaccinate

only 'priority' groups. If arguments against a universal vaccination include difficulties of vaccine supply, implementation of effective strategies for vaccine delivery or public acceptability, the economical factor should no longer be a barrier as this universal approach appears to be more cost-effective than targeting only at-risk groups.

Dr Sylvie Briand, Pandemic and Epidemic Disease department Director at the World Health Organization, and collaborating partner on the project, said: 'Governments must have a regularly updated plan for different scenarios that they can implement when a pandemic looms. Whilst they can't plan for everything, it is very important to define response scenarios in advance so they have a framework to work from.'

Stents safe to treat superficial femoral artery stenosis

Randomized trials have shown that routine stenting with self-expanding nitinol stents confers durable benefits in patients with superficial femoral artery disease compared to standard balloon angioplasty. A team from Germany conducted a real-world study to appraise early and midterm outcomes of routine superficial femoral artery stenting.

A total of 998 patients suffering from chronic limb ischemia were enrolled at 13 German medical centres into a prospective multicentre observational study. Twelve-month outcomes of the participants were assessed.

The median lesion length was 8cm, but there was no restriction on the length of lesion to be treated. A general mix of patients participated

in the study, but a third of patients had diabetes, and 43% were current smokers.

In all, 1050 lesions were treated. Twelve months after surgery, target lesion revascularization – the primary endpoint – was achieved in 136 (17%) of the patients. Restenosis occurred in 24% of the patients and reocclusion in 10%. These results indicate that stent use is safe and is delivering favourable outcomes at the 1-year mark.

Female gender and lesion length were independent predictors for target lesion revascularization.

Krankenbergh H, Tübler T, Sixt S et al (2014) German multicenter real-world registry of stenting for superficial femoral artery disease: clinical results and predictive factors for revascularization. *J Endovasc Ther* **21**(4): 463–71 (doi: 10.1583/13-4625R.1)

Risk of cardiovascular events increased up to 4 years after initial myocardial infarction

The UK results from the observational APOLLO study (Rapsomaniki et al, 2014) demonstrate that the risk of repeat cardiovascular events remains high for 4 years after a patient's initial myocardial infarction, despite use of secondary prevention interventions.

The study looked at data from 10854 UK heart attack patients, between April 2005 and March 2010. Two thirds ($n=7238$) remained event free in the first year following their heart attack, but 17.2% (confidence interval 16.0–18.5) went on to suffer another event including heart attack, stroke or fatal cardiovascular disease in the subsequent 3 years.

Professor Harry Hemingway, Professor of Clinical Epidemiology and Director of the Farr Institute of Health Informatics Research, London,

at University College London, commented: 'these data tell us that all patients who have had a heart attack should be considered and treated as "high risk" of subsequent events, regardless of their previous history.'

Similar data were collected

Professor Harry Hemingway,
Professor of Clinical Epidemiology
and Director of the Farr Institute of
Health Informatics Research, London



from France ($n=1757$), Sweden ($n=77\,976$) and the US ($n=53\,909$). The unadjusted risk of a subsequent hospitalization for another heart attack or a stroke or death within 3 years of the first event is different across the four countries. It was approximately one in four in Sweden and the UK, one in five in France, and one in three in the US. However, when these risks are adjusted for differences between countries in the demographics and baseline health of the study populations, the rates are similar with about one in five going on to have a subsequent event in each country.

Rapsomaniki E et al (2014) Health outcomes in patients with stable coronary artery disease following myocardial infarction; construction of a PEGASUS-TIMI-54 like population in UK linked electronic health records. Poster presented at ESC 2014; 31 August

More patients survive hip fracture because of better hospital care

The 2014 report from the National Hip Fracture Database in association with the British Geriatrics Society shows a decrease in 30-day mortality after surgery for a hip fracture equivalent to 300 saved lives a year (www.nhfd.co.uk/2014report).

Daclatasvir offers new treatment for chronic hepatitis C

Daclatasvir (Daklinza) is an oral, once-a-day pill, used in combination with other medicinal products to treat adult patients with chronic hepatitis C. In combination with other agents, it works across multiple hepatitis C genotypes, with clinical cure rates of up to 98% in patients with hepatitis C genotype 1, 89% in patients with genotype 3 and 100% in genotype 4.

Skin cancer hospital admissions rise 40% in 5 years

The number of hospital admissions for skin cancer treatment in England has increased by 41% in the space of just 5 years, according to a study conducted by researchers at Public Health England and presented at the World Congress on Cancers of the Skin in Edinburgh.

Blood test could allow individualized treatment of ovarian cancer with bevacizumab

A new blood test allowing doctors to predict which ovarian cancer patients will respond to particular types of treatment is a step closer.

The research team looked at blood samples from patients enrolled in an international trial of bevacizumab. These patients received either standard chemotherapy treatment alone or chemotherapy plus the blood vessel-targeting drug.

The findings show that two particular proteins – Ang1 and Tie2 – could be used in combination to predict patient response (Backen et al, 2014). These proteins are involved in

controlling the formation of new blood vessels. Patients with high levels of Ang1 and low levels of Tie2 were most likely to benefit from bevacizumab. Conversely, patients with high levels of both proteins did not benefit from the additional drug.

It would mean medics could see which patients could benefit from drugs such as bevacizumab in addition to conventional therapy. Others who are not going to benefit would be spared the time and side effects associated with having the drug. The test would also help to reduce the cost to the NHS.

Study co-author Professor Caroline Dive, from the Cancer Research UK Manchester Institute, said: 'Moving towards a more individualized treatment plan specific for each patient and their particular tumour is key to improving outcomes for patients while sparing those unlikely to benefit from potential side effects of therapy.'

Backen A, Renehan AG, Clamp AR et al (2014) The combination of circulating ang1 and tie2 levels predicts progression-free survival advantage in bevacizumab-treated patients with ovarian cancer. *Clin Cancer Res* 20(17): 4549–58 (doi: 10.1158/1078-0432.CCR-13-3248)

NHS 'in the dark' about full scale of hospital infections

Most NHS trusts are unaware of the full scale, cost and impact of health-care-acquired infections, such as sepsis and norovirus, a new report from the Medical Technology Group (2014) has revealed.

A total of 136 trusts responded to some extent to a Freedom of Information request asking about infection control in their trust. Of NHS trusts that responded, 58% (63 out of 108) fail to collate the total number of cases of five common infections, while around three-quarters (76%, 50 out of 66) keep no records at all of the number of associated deaths.

The vast majority (88%, 94 out of 107) of trusts that responded are completely unaware of the financial burden or operational impact of health-care-acquired infections. Just

one trust out of 68 said that it measured the total number of extra nights that patients stay in hospital as a result of infections acquired during the course of their treatment.

The report found that 58% do not collate the total number of cases of sepsis, norovirus, urinary tract infections, blood

Barbara Harpham, chair of the Medical Technology Group



infections caused by catheters, and pneumonia from ventilators (30% record some but not all them, and only 12% recorded the total number of all five).

There is also huge regional variation in the number of infection control staff per bed – from one member of staff for every 71 beds in London to one for every 161 beds in the East Midlands.

Some trusts have received instructions to reduce expenditure on infection, prevention and control in the last 5 years.

The report also found a surprisingly low number of infection control business cases have been submitted in recent years, with the majority of trusts (on average 76% over the past 5 years) failing to submit any at all. Nevertheless when they are submitted, most of them are effective.

Barbara Harpham, chair of the Medical Technology Group, said: 'There is complacency across the NHS about other health-care-acquired infections... We must also put an end to the perverse situation where NHS trusts are reimbursed when they treat patients who acquire an infection in that trust's hospital. If trusts are hit financially, it will force them to take infection control more seriously.'

With so much variability, the report calls for a more effective national strategy to combat health-care-acquired infections.

Medical Technology Group (2014) Infection Prevention and Control: Combating a Problem That Has Not Gone Away. www.mtg.org.uk/bulletins/infection-prevention-and-control-combating-problem-has-not-gone-away (accessed 26 September 2014)

Opt-out donor consent increases transplant numbers

An analysis of the organ donation protocols of 48 countries has been published (Shepherd et al, 2014).

Researchers from the University of Nottingham, the University of Stirling and Northumbria University set out to answer some of the questions about both policies. They compared 23 countries that used the opt-in system with 25 that used opt-out over a 13-year period. They found that countries with an opt-out system had a higher total number of kidneys transplanted, which the majority of people on transplant lists are waiting for.

The analysis found that opt-in organ donation systems may have a higher rate

of kidney donations from living donors, but opt-out systems have a greater overall quantity of organ transplants.

Organs from deceased donors are not the only source of organs; there are also living donors, which sometimes include relatives wanting to help ill members of their family. This study shows that the type of consent can affect deceased and living donation rates – living donations are higher in opt-in systems compared with opt-out.

Shepherd L, O'Carroll RE, Ferguson E (2014) An international comparison of deceased and living organ donation/transplant rates in opt-in and opt-out systems: a panel study. *BMC Med* 12: 131 (doi:10.1186/s12916-014-0131-4)

Genetic data could predict possible benefit of statins

Genomic data could predict whether statins will benefit a patient or not, according to new findings (Kim et al, 2014).

The study, by scientists from the Children's Hospital Oakland Research Institute, looked at data from 372 participants in the Cholesterol and Pharmacogenetics clinical trial for simvastatin.

It was possible to predict how 15% of the patients would respond to statins, and this data could help clinicians to make a decision about whether to prescribe statins for individual patients.

Differences in around 100 genes could explain 12–17% of the variation in how effectively simvastatin lowered

patients' low-density lipoprotein cholesterol levels. The genes were particularly accurate in predicting patients who responded very well or very poorly to the treatment. Some genes were involved in cholesterol metabolism, but further studies are needed to determine the function of others.

As the study only included Caucasians from a single clinical trial, further study is needed to find out whether these genes are a good indicator in other populations.

Kim K, Bolotin E, Theusch E, Huang H, Medina MW, Krauss RM (2014) Prediction of LDL cholesterol response to statin using transcriptomic and genetic variation. *Genome Biol* 15: 460 (doi:10.1186/s13059-014-0460-9)

54TH INTERSCIENCE CONFERENCE ON ANTIMICROBIAL AGENTS AND CHEMOTHERAPY; WASHINGTON DC, USA, 5–9 SEPTEMBER

Antibiotic stewardship improves patient outcomes and reduces hospital costs

Stewardship programmes not only reduce inappropriate use of antibiotics and the risk of adverse events, but also save costs – more than \$600 000 a year according to a study in a 535-bed community hospital in the USA.

Following the implementation of a hospital-wide stewardship programme, investigators at New York Hospital Queens compared rates of multi-drug resistant organisms between 2011 and 2013 and tracked total expenditure on antibiotics in 2012–13.

Rates of multi-drug resistant *Klebsiella pneumoniae* fell from 17.7% in 2011 to 10.5% in 2013, while multi-drug resistant *Acinetobacter baumannii* decreased from 43.3% to 39.5%, *Clostridium difficile*-associated diarrhoea from 18.4% to 11.4% and methicillin-resistant *Staphylococcus aureus* from 56.8% to 41.6%.

The 5147 interventions included dosage adjustment for renal function (31%), discontinuation of antibiotic treatment (21%), changes from intravenous to oral dosing

(18%), switches to another antibiotic (14%), non-renal dosage adjustments (5%), and ‘others’ (11%). The estimated total cost savings were \$660 109.

According to lead investigator Dr Nishant Prasad: ‘We believe these findings show that limiting unnecessary antibiotics improves patient safety and streamlines use of limited healthcare dollars.’

Sue Lyon

Prasad N et al (2014) Impact of antibiotic stewardship program interventions on multi-drug resistant organism resistance rates and hospital costs. Abstract K-343

Simple method can reduce norovirus spread in hospitals

Contamination of a single doorknob spreads a virus rapidly through a building, but effective cleaning can greatly reduce spread of infection. These are the findings of a study designed to test the effectiveness of disinfectant wipes containing quaternary ammonium compounds (QUATs) in reducing transmission of norovirus through contaminated surfaces or objects.

Investigators contaminated one or two commonly touched surfaces in a health-care facility with bacteriophage MS-2 (similar in shape, size and resistance to disinfectants to norovirus).

Within 2–4 hours, 40–60% of the 60–100 high-touch areas sampled were contaminated with the phage. After providing cleaning staff and employees with QUAT-containing cleaning wipes and instruction on correct use, the number of contaminated areas was reduced by ≥80% and concentration of virus by ≥99%.

‘These results show that ... a simple intervention, with hand hygiene, can greatly help to reduce exposure to viruses,’ concluded investigator Professor Charles Gerba, University of Arizona, USA.

Sue Lyon

Gerba CP (2014) Impact of a quaternary ammonium compound (QAC) disinfectant on spread of viruses in facilities. Abstract K-1722

Isavuconazole: as effective as, but better tolerated than standard antifungal therapy

The novel antifungal drug isavuconazole is as effective as voriconazole against invasive mould disease in cancer patients regardless of their malignancy status, and is associated with a lower rate of adverse effects.

The global, multicentre, double-blind, non-inferiority SECURE trial randomized 527 patients meeting European Organisation for Research and Treatment of Cancer criteria for proven/possible/probable invasive fungal disease caused by infection with *Aspergillus* spp. or other filamentous fungi to either isavuconazole or voriconazole.

Pulmonary involvement was present in 92% of patients, 84% had haematological malignancies, 65% were neutropenic and 20% had under-

gone allogeneic haematopoietic stem-cell transplantation.

The intention-to-treat population comprised 516 patients (258 per group) who received at least one dose of the study drug.

On the primary outcome, all-cause mortality at day 42 in the intention-to-treat population with uncontrolled malignancy was 21% for isavuconazole and 22% for voriconazole. In intention-to-treat patients whose malignancy was not uncontrolled, day 42 mortality was 13% for isavuconazole and 15% for voriconazole.

Significantly fewer ($P<0.05$) treatment-emergent adverse events of the eye and skin, hepatobiliary disorders, and drug-related adverse events were reported in the isavuconazole arm.

Investigator Professor Andrew Ullman, from Würzburg, Germany, commented: ‘If approved, isavuconazole has the potential to be an important new option for the treatment of these life-threatening fungal infections.’

Isavuconazole is a triazole drug with broad-spectrum in vitro antifungal activity. It is under review in Europe and the USA for the treatment of invasive aspergillosis and invasive mucormycosis.

Sue Lyon

Ullman AJ et al (2014) A Phase 3 randomized, double-blind, non-inferiority trial evaluating isavuconazole (ISA) vs. voriconazole (VRC) for the primary treatment of invasive fungal disease (IFD) caused by *Aspergillus* spp. or other filamentous fungi (SECURE): outcomes by malignancy status. Abstract M1756