

Identifying genes which affect survival from sepsis

Mortality rates for sepsis remain high at about 20–30%, and the incidence of sepsis is rising. A genome-wide association study has been undertaken to identify genetic variants that

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influence sepsis survival (Rautanen et al, 2015).

The study was performed in three independent cohorts of white adult patients admitted to intensive care units with sepsis, severe sepsis or septic shock (as defined by the International Consensus Criteria) as a result of pneumonia or intra-abdominal infection (cohorts 1–3, $n=2534$ patients). The primary outcome was 28-day survival.

Results for the cohort of patients with sepsis caused by pneumonia were combined in a meta-analysis of 1553 patients from all three cohorts, of whom 359 died within 28 days of admission to the intensive care unit. The most significantly associated single nucleotide polymorphisms were geno-

typed in a further 538 white patients with sepsis caused by pneumonia (cohort 4), of whom 106 died.

Common variants in the *FER* gene were strongly associated with survival ($P=5.6 \times 10^8$) from sepsis caused by pneumonia. Mortality was 9.5% in patients carrying the CC genotype, 15.2% in those carrying the TC genotype, and 25.3% in those carrying the TT genotype.

The study identified variants in the *FER* gene that associate with a reduced risk of death from sepsis as a result of pneu-

monia. Because many of the functions of *FER* and its associated biological pathways are important in host defence, this suggests potential novel targets for therapy or prevention and candidates for the development of biomarkers for risk stratification.

Rautanen A, Mills TC, Gordon AC et al, for the ESICM/ECCRN GenOSept Investigators (2015) Genome-wide association study of survival from sepsis due to pneumonia: an observational cohort study. *Lancet Respir Med* 3(1): 53–60 (doi: 10.1016/S2213-2600(14)70290-5)

Should patients with end-stage renal disease have daily dialysis?

Patients with end-stage renal disease are dialysed three times per week for about 4 hours each time. Observational studies have associated long dialysis intervals with an excess risk of mortality and cardiovascular disease hospitalizations.

Alternate day dialysis is an appealing possibility to reduce the cardiovascular burden of long dialysis intervals. However, the actual impact of alternate day haemodialysis and of frequent haemodialysis in general on survival remains unknown.

On the other hand some studies have suggested that daily dialysis might improve left ventricular mass and health-related quality of life.

Professor Carmine Zoccali from the Department of Clinical Epidemiology and Pathophysiology of Hypertension and Renal Diseases, Ospedali Riuniti, Reggio Calabria, Italy and colleagues reviewed the evidence (Zoccali et al, 2015). They concluded that whenever and wherever possible more frequent dialysis regimens should be proactively applied, starting with the alternate day approach, in problematic patients.

Zoccali C, Dounousi E, ElHafeez SA, Tripepi G, Mallamaci F (2015) Should we extend the application of more frequent dialysis schedules? A 'yes' and a hopeful 'no'. *Nephrol Dial Transplant* 30: 29–32 (doi: 10.1093/ndt/gfu373)

Increased life satisfaction predicts reduced bone loss

A study was carried out in Finland to determine whether and how global life satisfaction is associated with bone mineral density and bone loss (Rauma et al, 2014).

A total of 2167 women from a cohort of Finnish women born from 1932–41 were included in the cross-sectional and 1147 women in the 10-year longitudinal part of the study.

Participants responded to a postal enquiry and underwent femoral bone mineral density densitometry in 1999 (baseline) and 2009 (follow up). During the follow up, their life satisfaction was repeatedly measured using a four-item scale. Self-reported data on health, lifestyle and medication were used to adjust the multivariate linear regression models.

Mean (standard deviation) femoral bone mineral density decreased over the 10-year follow up from 880 (125)

mg/cm² to 846 (122) mg/cm². In the multivariate model, life satisfaction ($P=0.028$) and its improvement ($P=0.001$) predicted reduced bone loss, whereas hospitalization as a result of depression predicted increased bone loss ($B = -0.523$ annual % change, standard error = 0.212, $P=0.014$). These effects were independent of each other.

Global life satisfaction is an easily assessed measure. This should be taken into account when effects of ageing and prevention of osteoporosis are considered in postmenopausal women as well as when planning health promotion.

Rauma PH, Koivumaa-Honkanen H, Williams LJ, Tuppurainen MT, Kröger HP, Honkanen RJ (2014) Life satisfaction and bone mineral density among postmenopausal Women: Cross-Sectional and Longitudinal Associations. *Psychosom Med* 76(9): 709–15 (doi: 10.1097/PSY.0000000000000114)

Heart failure patients with higher blood sugar levels have greater risk of early death

A large study from a team in Canada suggests that people who arrive at emergency departments with acute heart failure should have their blood sugar levels checked on arrival (Sud et al, 2015). This simple measure could identify patients at high risk of early death, further hospitalizations, or development of more health problems, such as diabetes.

Dr Douglas Lee, Associate Professor of Medicine, ICES Central, Toronto, Ontario



The study found that even if someone arrives at hospital with no prior diagnosis of diabetes and with blood sugar levels that could be considered 'normal', if their levels are above 6.1 mmol/litre they are at higher risk of developing diabetes and early death.

Researchers analysed outcomes for 16524 people who arrived at emergency departments in Ontario, Canada, with acute heart failure between 2004 and 2007. The patients were aged between 70 and 85 years old and 56% (9275) of them did not have pre-existing diabetes. Their outcomes were compared with a reference group of patients whose blood glucose levels ranged between 3.9 and 6.1 mmol/litre.

Patients without pre-existing diabetes had a risk of death within 30 days from any cause that was 26% higher than the

reference group if their blood glucose levels were between 6.1 and 7.8 mmol/litre, rising to 50% higher if levels exceeded 11.1 mmol/litre.

Their risk of death from cardiovascular causes was also increased, rising to 64% higher for levels of 9.4–11.1 mmol/litre.

Associate Professor of Medicine from the Institute for Clinical Evaluative Sciences, Dr Douglas Lee, who led the research, commented: 'Although diabetes is a known risk factor for developing heart failure, this is the first time that it has been shown that heart failure predisposes people to developing diabetes.'

Sud M, Wang X, Austin PC et al (2015) Presentation blood glucose and death, hospitalization, and future diabetes risk in patients with acute heart failure syndromes. *Eur Heart J* (doi: 10.1093/eurheartj/ehu462)

Backlog of applications for Deprivation of Liberty Safeguards

A report by the Care Quality Commission highlights a sharp increase in the number of applications for Deprivation of Liberty Safeguards. At the end of September 2014, there were 19429 applications where the outcome was still not decided, compared with 359 at the end of 2013/14.

Care booklet produced for hip fracture patients

'My Hip Fracture Care' booklet is designed to help patients, families and carers understand what is likely to happen while hip fracture patients are in hospital, and after they are discharged. The booklet can be downloaded from www.nhfd.co.uk/20/hipfractureR.nsf/vwcontent/patients2015

Two-in-one critical care ventilator now available

The V680 ventilator from Philips offers both invasive and non-invasive ventilation. Customised technology also ensures the smooth transition between invasive and non-invasive ventilation modes and streamlines workflow while providing patient comfort.

Lower mortality rates among Asian and Hispanic patients with systemic lupus erythematosus

Researchers from Brigham and Women's Hospital in Boston, Massachusetts have found that Asian and Hispanic patients with systemic lupus erythematosus have lower mortality rates than black, white or native Americans with the disease (Gomez-Puerta et al, 2015).

Researchers reviewed Medicaid claims that were filed between 2000 and 2006. The team identified individuals with lupus, aged 18–65 years, who were enrolled for three or more months and had three or more claims for lupus. Lupus

nephritis was determined by two or more claims for glomerulonephritis, proteinuria or renal failure.

Of 42221 lupus patients, 8191 had lupus nephritis. The ethnic breakdown of these patients was 40% black, 38% white, 15% Hispanic, 5% Asian, and 2% native American. The annual mortality rate for those with lupus per 1000 person-years was highest in native Americans (27.52), blacks (24.13) and whites (20.17). Hispanic and Asian lupus patients had lower mortality than black, white or native American patients even

after adjusting for demographic and clinical factors.

Lead author Dr Jose A Gomez-Puerta concluded: 'Understanding the variation of death among the races is important to determine how best to treat individual patients, modify risk factors, and ultimately improve survival for those with lupus.'

Gomez-Puerta JA, Barbhuiya M, Guan H, Feldman C, Alarcón GS, Costenbader KH (2015) Racial/ethnic variation in all-cause mortality among U.S. Medicaid recipients with systemic lupus erythematosus: an Hispanic and Asian paradox. *Arthr Rheumatol* (doi: 10.1002/art.38981)

Low-cost home modifications reduce injuries from falls

A single-blind, cluster-randomized controlled trial of households from New Zealand was performed to test the safety benefits of home modifications, including handrails for outside steps and internal stairs, grab rails for bathrooms, outside lighting, edging for outside steps, and slip-resistant surfacing for outside areas such as decks and porches (Keall et al, 2015).

Households were randomly assigned by electronic coin toss

to either immediate home modifications (treatment group) or a 3-year wait before modifications (control group). Household members in the treatment group could not be masked to their assigned status because modifications were made to their homes.

The primary outcome was the rate of falls at home per person per year that needed medical treatment, derived from administrative data for insurance claims. Coders who

were unaware of the random allocation analysed text descriptions of injuries and coded injuries as all falls and injuries most likely to be affected by the home modifications tested.

To account for clustering at the household level, all injuries from falls at home per person-year were analysed with a negative binomial generalized linear model with generalized estimating equations.

Of 842 households recruited, 436 ($n=950$ individual



Dr Michael Keall, Research Associate Professor, University of Otago, Wellington

occupants) were randomly assigned to the treatment group and 406 ($n=898$ occupants) were allocated to the control group. After a median observation period of 1148 days (interquartile range 1085–1263), the crude rate of fall injuries per person per year was 0.061 in the treatment group and 0.072 in the control group (relative rate 0.86, 95% confidence interval 0.66–1.12).

Results showed an estimated 26% reduction in the rate of injuries caused by falls at home per year in those houses where modifications had been made.

For injuries judged to be most relevant to the modifications, a 39% annual reduction in injuries was found.

Lead author Dr Michael Keall commented: 'In view of the large injury burden posed by falls at home, the results of the study have important implications for the design of effective prevention programmes focused on the home environment.'

Keall MD, Pierse N, Howden-Chapman P, Cunningham C, Cunningham M, Guria J, Baker MG (2015) Home modifications to reduce injuries from falls in the Home Injury Prevention Intervention (HIPI) study: a cluster-randomised controlled trial. *Lancet* **385**(9964): 231–8 (doi: 10.1016/S0140-6736(14)61006-0)

Lung cancer predicted to become leading cause of cancer death among European women in 2015

Death rates from lung cancer will exceed those for breast cancer for the first time among European women in 2015, according to the latest predictions from researchers in Italy and Switzerland (Malvezzi et al, 2015). They predict that although the actual number of deaths from all cancers in the European Union will continue to rise as a result of the growing populations and numbers of elderly people, the rate of cancer deaths will continue to decline overall, with some notable exceptions: lung cancer in women and pancreatic cancer in both sexes.

In women, the predicted age standardized rate of deaths from lung cancer will increase by 9% from 2009 to 14.24 per 100 000 of the population, while the death rates from breast cancer are predicted to be 14.22 per 100 000, which

represents a fall of 10.2% since 2009. However, the total number of deaths will remain slightly higher for breast cancer (90 800) than for lung (87 500).

Professor Carlo La Vecchia, professor at the Faculty of Medicine, University of Milan, Italy, one of the study authors, said: 'We still have to be cautious about the lung cancer rates in women since these are predictions. ... However, the 2015 predictions confirm our projections on long-term trends made 2 years ago that lung cancer death rates would overtake breast cancer in women around 2015.'

Professor Carlo La Vecchia, Faculty of Medicine, University of Milan, Italy



The overall death rate for lung cancer among women is being driven by women in the UK and Poland, with predicted rates of 21 and 17 per 100 000 in the UK and Poland respectively. These rates are

more than double those in Spain, which has a lung cancer death rate among women of just over eight per 100 000.

'UK and Polish women, particularly UK women, have long had much higher lung cancer rates than most other European countries... [because] British women started smoking during the Second World War, while in most other EU countries women started to smoke after 1968,' explained Professor La Vecchia.

The study predicts a total of 1 359 100 deaths from cancer in the 28 member states of the EU in 2015 (766 200 men and 592 900 women), corresponding to an age standardized rate of 138.4 per 100 000 men and 83.9 per 100 000 women. This represents a fall of 7.5% and 6% in men and women respectively since 2009.

Malvezzi M, Bertuccio P, Rosso T, Rota M, Levi F, La Vecchia C, Negri E (2015) European cancer mortality predictions for the year 2015: does lung cancer have the highest death rate in EU women? *Ann Oncol* (doi: 10.1093/annonc/mdv001)

Insufficient funding and structural barriers affect integration of mental health policy

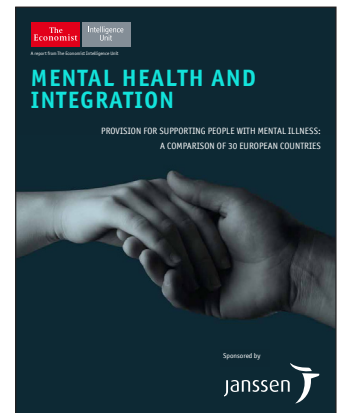
Access to health care, social services and employment opportunities for people with severe mental illness in the UK is falling short when compared to some other European countries, according to new research from the Economist Intelligence Unit (2015), commissioned and funded by Janssen.

The UK findings of the Mental Health Integration Index benchmarks the UK against 30 European countries based on their commitment to integrating people with severe mental illness into society.

In four key categories the UK is placed second overall in the Index. But while the UK finished first in the provision

of a stable family environment and governance, including human rights issues and efforts to combat stigma, it came eighth in the access to healthcare and social services category and ninth in the employment opportunities category.

The report identifies five areas on which many European



countries need to focus to provide better integration of people living with mental illness into society:

1. Obtaining better data in all areas of medical and service provision and outcomes
2. Backing up mental health policies with appropriate funding
3. Finishing the now decades-old task of deinstitutionalisation
4. Focusing on the hard task of providing integrated, community-based services
5. Including integrated employment services provision.

'This research highlights that finding gainful employment is a significant challenge for people suffering with severe mental ill health,' commented Professor Martin Knapp, Director of the Personal Social Services Research Unit at the London School of Economics.

He added: 'This is likely to be further exacerbated by the limited access to health care and social services, which means that despite positive efforts to integrate people with severe mental illness into society, more needs to be done to realize this.'

The Economist Intelligence Unit (2015) Mental Health And Integration Provision For Supporting People With Mental Illness: A Comparison Of 30 European Countries. www.mentalhealthintegration.co.uk/media/whitepaper/EIU-Janssen_Mental_Health.pdf (accessed 28 January 2015)

Cohort study finds health of babies born after infertility treatment improved over past 20 years

The last two decades has seen a steady improvement in the health outcomes of children born after assisted reproduction, with fewer babies being born preterm, with low birth weight, stillborn or dying within the first year of life.

These findings come from the largest study to date to investigate the health of assisted reproduction babies over time; data from more than 92 000 children in Denmark, Finland, Norway and Sweden were analysed for the study (Henningsen et al, 2015).

Dr Anna-Karina Aaris Henningsen, from the Fertility Clinic at the Rigshospitalet, University of Copenhagen, Denmark, and her colleagues analysed the outcomes of 62 379 singletons and 29 758 twins born between 1988 and 2007 in the four Nordic countries. They compared

them with control groups of 362 215 spontaneously conceived singletons and 122 763 spontaneously conceived twins born in the same countries in the same period.

From 1989 to 2002 the proportion of assisted reproduction twins in the four countries remained stable at around 23%, but it started to decline after that and by 2007 it was only 11.6% overall.

This decline was reflected in the health outcomes for assisted reproduction babies. The rate for preterm (babies born before 37 weeks gestation) singletons and twins fell from 27.9% in 1988–92 to 12.8% in 2003–7 in Sweden, and it decreased from a similar figure in Denmark, Finland and Norway to 21.1%, 17.8% and 21% respectively in 2003–7.

'During the 20-year period of our study, we observed a remark-

able decline in the risk of being born preterm or very preterm,' said Dr Henningsen. 'The proportion of single assisted reproduction babies born with a low or very low birth weight – less than 2500 g or 1500 g respectively – also decreased. The rates for stillbirths and death during the first year declined among both singletons and twins, and fewer assisted reproduction twins were stillborn or died during the first year compared with spontaneously conceived twins.'

Dr Henningsen said that other factors also contributed to the improvement in the health of assisted reproduction babies over the past 20 years: 'We have improved both the technical skills in the laboratory and the clinical skills of the doctors and also perform milder ovarian stimulation.'

Henningsen AA, Gissler M, Skjaerven R et al (2015) Trends in perinatal health after assisted reproduction: a Nordic study from the CoNARTaS group. *Hum Reprod* (doi: 10.1093/humrep/deu345)



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