Ovary removal may increase the risk of colorectal cancer

A cohort study in Sweden has examined the risk of developing colorectal cancer after oophorectomy for benign indications (Segelman et al, 2016). Of 195 973 women who had undergone oophorectomy, 3150 (1·6%) were diagnosed with colorectal cancer at a later date (median follow-up 18 years).

Colorectal cancer risk was increased after oophorectomy compared with that in the general population. The risk was lower for younger age at oophorectomy and the risk was highest 1–4 years after oophorectomy.

Dr Josefin Segelman, lead author, from the Department of Surgery, Ersta Hospital, Stockholm, Sweden, commented: 'This emphasizes that prophylactic resection of normal ovaries should be reserved for women with a clear indication.'

Segelman J, Lindström L, Frisell J, Lu Y (2016) Population-based analysis of colorectal cancer risk after oophorectomy. *Br J Surg* **103**: 908–15 (doi: 10.1002/bjs.10143)

Decision makers for critically ill patients hold overly optimistic expectations

A mixed-methods study comprising quantitative surveys and qualitative interviews was conducted in four intensive care units involving 229 surrogate decision makers and 99 physicians caring for patients at high risk of death (White et al, 2016).

Among critically ill patients, discordant expectations about prognosis were common between patients' physicians and surrogate decision makers and were related to misunderstandings by surrogates about physicians' assessments of patients' prognoses and differences in beliefs about patients' prognoses.

White DB, Ernecoff N, Buddadhumaruk P et al (2016) Prevalence of and factors related to discordance about prognosis between physicians and surrogate decision makers of critically ill patients. *JAMA* **315**(19): 2086–94 (doi: 10.1001/jama.2016.5351)

Risk of diabetes from glucocorticoids used to treat rheumatoid arthritis quantified for first time

Glucocorticoid (or steroid) therapy, prescribed to around half of patients with rheumatoid arthritis, is a known risk factor for developing diabetes. An international cohort study has determined how the risk of diabetes increases in patients with rheumatoid arthritis in relation to the dosage, duration and timing of steroids (Movahedi et al, 2016).

The researchers looked at the records of 21 962 patients with rheumatoid arthritis in the UK and a further 12 657 records held in the USA, and compared rates of new-onset diabetes in those who were prescribed glucocorticoids to those who did not receive glucocorticoids. Results also took into account patients' body mass index and smoking status, as well as their disease severity.

Information on the dosage and timing of glucocorticoid use was extracted. In the UK database diabetes mellitus was defined using Read codes, at least two prescriptions for oral antidiabetic medication, or abnormal blood test results, and in the American database it was defined through patient self-reports. Data were analysed using time-dependent Cox models and a novel weighted cumulative dose model that accounts for dosage, duration and timing of treatment.

A range of conventional statistical models consistently confirmed increases in risk with the glucocorticoid dosage and duration. Use of glucocorticoids was associated with one new case of diabetes for every 150–200 people treated per year, but within this group, risk was affected by the dose only in the most recent 6 months. Each increase of 5 mg prednisolone per day carried a 25–30% increase in diabetes, although a dose of less than 5 mg was not associated with any measurable risk of diabetes compared to no treatment.

Dr Will Dixon, Director, Arthritis Research UK Centre for Epidemiology, University of Manchester and Honorary Consultant Rheumatologist, Salford Royal NHS Foundation Trust, Salford

Dr Will Dixon, Director of the Arthritis Research UK Centre for Epidemiology at The University of Manchester and Honorary Consultant Rheumatologist at Salford Royal NHS Foundation Trust, led the study. He said: 'Doctors treating people with arthritis have to make a decision how best to prescribe glucocorticoids by balancing the benefits against the risks. However, until now, no studies have considered how the risk changes with the dose and duration of treatment. This research provides important evidence for doctors to make this decision.'

The research does not advocate that people stop using glucocorticoids as they have been used effectively since 1948 to treat flare-ups in joint pain and for longer periods at a low dose to help people who do not respond to other treatments.

Dr Dixon said: 'This research shows that low doses of steroids (below 5 mg/day) do not increase the risk of diabetes. However, there is an increased risk of acquiring diabetes for people who use them for long periods or at high doses which can now be quantified.'

He concluded: 'It is well established that glucocorticoid therapy can lead to an increased risk of diabetes. However, the magnitude of this risk is poorly quantified, in part because the risk is dependent on the dose and duration of treatment. Clinicians therefore cannot adequately consider the benefits and harms of treatment, nor discuss these with patients to allow an informed shared decision. Our work, for the first time, has quantified the risk of diabetes for various doses and durations of glucocorticoid therapy to fill this important gap.'

Movahedi M, Beauchamp ME, Abrahamowicz M, Ray DW, Michaud K, Pedro S, Dixon WG (2016) Risk of incident diabetes mellitus associated with the dosage and duration of oral glucocorticoid therapy in patients with rheumatoid arthritis. *Arthritis Rheumatol* **68**(5): 1089–98 (doi: 10.1002/art.39537)

Recognition and management of acute kidney injury: a multinational cross-sectional study

Epidemiological data for acute kidney injury are scarce, especially in low- and lower-middle-income countries. A multinational cross-sectional study assessed regional differences in acute kidney injury recognition, management and outcomes (Mehta et al, 2016).

Dr Ravindra L Mehta, Professor of Clinical Medicine, Division of Nephrology, Department of Medicine, University of California, San Diego

A total of 322 physicians from 289 centres in 72 countries collected prospective data for paediatric and adult patients with confirmed acute kidney injury in hospital and non-hospital settings who met criteria for acute kidney injury. Signs and symptoms at presentation, comorbidities, risk factors for acute kidney injury, and process-of-care data were obtained at the start of acute kidney injury, and need for dialysis, renal recovery, and mortality recorded at 7 days, and at hospital discharge or death, whichever came earlier. Countries were classified as high-income countries, upper-middle-income countries, and combined low- and lower-middle-income countries according to their 2014 gross national income per person.

Data were collected from 4018 patients. Dehydration was the most frequent cause of acute kidney injury in low- and lower-middle-income countries and hypotension the most frequent cause in high-income countries. Mortality at 7 days was higher in low- and lower-middle-income countries than in high-income countries and upper-middle-income countries.

Commenting on the findings, Dr Ravindra L Mehta from the University of California, San Diego, said: 'Our study shows that the risk factors and causes of acute kidney injury are similar worldwide, however, there are differences in recognition, management and outcomes of acute kidney injury in different health settings for both community and hospital-acquired acute kidney injury that are influenced by the economic conditions in the different countries. A concerted effort is needed to raise awareness of acute kidney injury worldwide and implement strategies to eliminate preventable deaths from this devastating disease.'

Mehta RL, Burdmann EA, Cerdá J et al (2016) Recognition and management of acute kidney injury in the International Society of Nephrology 0by25 Global Snapshot: a multinational cross-sectional study. *Lancet* **387**(10032): 2017–25 (doi: 10.1016/S0140-6736(16)30240-9)

Blood pressure positively associated with risk of developing vascular dementia

To assess age-specific associations between blood pressure and risk of vascular dementia, researchers related blood pressure to time to physician-diagnosed vascular dementia (Emdin et al, 2016) in 4.28 million people who were free of known vascular disease and dementia, identified from electronic primary care health records. They also looked at links between blood pressure and dementia in a prospective population-based group of patients who had had incident transient ischaemic attack and stroke.

For a median follow-up of 7.0 years, 11 114 initial presentations of vascular dementia were seen in the primary care cohort after exclusion of the first 4 years of follow-up. The association between usual systolic blood pressure and risk of vascular dementia decreased with age. In the population-based cohort, prior systolic blood pressure predicted 5-year risk of dementia with no evidence of negative association at older ages.

The team concluded that blood pressure is positively associated with risk of vascular dementia, irrespective of preceding transient ischaemic attack or stroke.

Emdin CA, Rothwell PM, Salimi-Khorshidi G et al (2016) Blood pressure and risk of vascular dementia: evidence from a primary care registry and a cohort study of transient ischemic attack and stroke. *Stroke* **47**: 1429–35 (doi: 10.1161/STROKEAHA.116.012658)

Pertussis vaccination in pregnancy is safe

Researchers analysed health outcomes of 1759 births and compared 1109 cases in which the mother was immunized with the tetanus-diphtheria-acellular pertussis vaccine to 650 where the mother was not vaccinated with this vaccine. They concluded that the vaccine is safe for both mothers and infants (doi: 10.1080/21645515.2016.1157241).

Medical error is the third leading cause of death in the USA

A new analysis has found that medical error is the third leading cause of death in the USA after heart disease and cancer (doi: 10.1136/bmj.i2139). The authors say that death certificates in the USA have no facility for acknowledging medical error, and call for better reporting to help understand the scale of the problem and how to tackle it.

Failure to publish radiotherapy trial results

Although the publication of results of clinical trials carried out in the USA within 12 months of completion has been mandatory since 2007, a high number of phase III radiotherapy trials did not do so, according to research presented at the ESTRO 35 conference. An analysis of 802 trials with a primary completion date of before 1 January 2013 showed that 655, or 81.7%, did not publish even a summary result.

53rd ERA-EDTA Congress Vienna, Austria, 21–24 May

Chronic kidney disease may remit in one in five patients in primary care

Chronic kidney disease (CKD) may prove transitory and simple clinical variables can predict remission, found a prospective study in people with stage 3 CKD (estimated glomerular filtration rate (eGFR) 30–59%) (Shardlow et al, 2016).

Demographics, medical history and blood samples were collected at baseline, year 1 and year 5. CKD remission was defined as both eGFR >60 ml/min/1.73m^2 and urinary albumin:creatinine ratio <3 mg/mmol (average of three values) at year 5 visit.

Of 1484 patients, 247 (16.6%) died before year 5 and four (0.3%) reached end-stage kidney disease. By year 5, 336 (22.6%) patients were in remission and CKD progressed in 308 (20.7%). Significant remission predictors were higher eGFR, lower age, lower urinary albumin:creatinine ratio and increased eGFR at 1 year.

Dr Adam Shardlow commented: 'We propose that a definition of CKD remission be agreed ... to elucidate the incidence and determinants of CKD remission in other populations.'

Shardlow A, Fluck RJ, McIntyre CW, Taal MW (2016) CKD remission in a prospective cohort of people with CKD stage 3 recruited from primary care. Presentation MO032

Early-start renal replacement therapy improves survival in critical illness

In critically ill patients with acute kidney injury, early initiation of renal replacement therapy significantly improves 90-day survival, according to the ELAIN randomized trial (Zarbock et al, 2016).

Dr Alexander Zarbock, Max-Planck Institute for Molecular Biomedicine, Department of Vascular Cell Biology, Westphalian Wilhelm's University of Münster, Münster

The single-centre study included 231 critically ill adults with acute kidney injury admitted to a German university hospital between August 2013 and June 2015. Patients were randomized to either early-start renal replacement therapy at stage 2 acute kidney injury (creatinine 2.0–2.9 times baseline, urine output <0.5 ml/kg/h ≥12 hours) or late-start at stage 3 (creatinine 3 times baseline or increase ≥353.6 µmol/litre or renal replacement therapy, and urinary output <0.3 ml/kg/hr ≥24 hours or anuria ≥12 hours).

Renal replacement therapy was started in all patients in the early group (n=112) and 108 (90.8%) of the late group (n=119). Early-start renal replacement therapy significantly improved 90-day survival (60.7% *vs* 45.3% for late-start; hazard ratio 0.66, 95% confidence interval 0.45–0.97; P=0.03), and more early-start patients recovered renal function by day 90 (53.6% *vs* 38.7%; odds ratio 1.83, 95% confidence interval 1.08–3.09; P=0.02).

A recent multicentre randomized controlled trial (doi: 10.1056/NEJMoa1603017) found no significant difference in mortality between early- and late-start renal replacement therapy. Commenting during ERA-EDTA 2016, Dr Alexander Zarbock from the Max-Planck Institute for Molecular Biomedicine, Westphalian Wilhelm's University of Münster, Münster, Germany, said: 'That study used different cut-offs for early *vs* late start, and nearly half of late-start patients did not need renal replacement therapy compared to only a few in our study, which indicates that early renal replacement therapy is associated with better outcomes in patients who really need it.'

Zarbock A, Kellum JA, Schmidt C et al (2016) Effect of early vs delayed initiation of renal replacement therapy on mortality in critically ill patients with acute kidney injury: The ELAIN randomized clinical trial. *JAMA* **315**(20): 2190–9 (doi: 10.1001/jama.2016.5828)

A potassium-rich diet protects the kidneys

In people with preserved kidney function, higher potassium intake is associated with slower decline in renal function and lower risk of end-stage kidney disease, concluded a 15-year retrospective study of 901 adults attending the outpatient clinic at a Dutch tertiary care hospital between 1998 and 1999 (van Noordeene et al, 2016).

'Accumulating evidence indicates that higher potassium intake decreases blood pressure and cardiovascular risk, independent of sodium intake, but it has been unclear if higher potassium intake also protects the kidneys,' said lead author Dr Nicky van Noordeene, from Amsterdam, Netherlands.

All patients had estimated glomerular filtration rate (eGFR) >60 ml/min/1.73m^2, 29% had microalbuminuria and 16% macroalbuminuria. Potassium and sodium excretion were assessed by testing 10 421 24-hour urine samples, routinely collected over a median of 12.7 years.

Compared with low potassium intake (excretion <60 mmol/day), higher intake (excretion >80 mmol/day) was associated with a significantly lower risk of all predefined outcomes: renal replacement therapy, >60% eGFR decline and >30% eGFR decline. Higher sodium:potassium ratio was associated with a trend towards a lower risk of >60% eGFR decline and renal replacement therapy, but only reached significance for >30% eGFR decline.

van Noordenne ND, Olde Engberink RHG, Van Den Hoek TC, et al (2016) Associations of 15-year average potassium intake with long-term renal outcome in outpatient clinical setting. Presentation SO023

Sue Lyon

Lowering dose of alteplase reduces risk of bleeding and improves survival rates from ischaemic stroke

Thrombolytic therapy with intravenous alteplase (recombinant tissue-type plasminogen activator) at a dose of 0.9 mg/kg of body weight is an effective treatment for acute ischaemic stroke, despite increasing the risk of intracerebral haemorrhage. However, an open label study showed that a dose of 0.6 mg/kg resulted in equivalent outcomes (Anderson et al, 2016). The Enhanced Control of Hypertension and Thrombolysis Stroke Study (ENCHANTED) was designed to compare low-dose with standard-dose intravenous alteplase in patients with acute ischaemic stroke.

In an international, multicentre, prospective, randomized, open-label trial with blinded outcome evaluation, two doses of intravenous alteplase were compared in patients with an acute ischaemic stroke who were eligible for thrombolytic therapy; administration of the drug was commenced within 4.5 hours after the onset of the stroke.

Patients with elevated systolic blood pressure (range 150–220 mmHg) could also be randomly assigned to early and intensive lowering of blood pressure (target systolic blood pressure <140 mmHg within 1 hour) or conventional guideline-directed management of blood pressure (target systolic blood pressure <180 mmHg) with the use of locally available intravenous agents.

Of 3310 patients, 63% of whom were Asian, with acute ischaemic stroke who were eligible for thrombolysis reperfusion therapy, a dose of alteplase of 0.6 mg/kg was not shown to be non-inferior to the standard dose of 0.9 mg/kg with respect to the primary outcome of death and disability at 90 days. Fewer patients treated with low-dose alteplase than with standard-dose alteplase (1% *vs* 2%) had the secondary outcome of symptomatic intracerebral haemorrhage.

Professor Craig Anderson, Professor of Stroke Medicine and Clinical Neuroscience, The George Institute for Global Health, University of Sydney, Sydney, Australia, said: 'At the moment you could have a stroke but end up dying from a bleed in the brain. It's largely unpredictable as to who will respond and who is at risk with alteplase.

He added: 'What we have shown is that if we reduce the dose level, we maintain most of the clot-busting benefits of the higher dose but with significantly less major bleeds and improved survival rates. On a global scale, this approach could save the lives of many tens of thousands of people.'

Anderson CS, Robinson T, Lindley RI et al; ENCHANTED Investigators and Coordinators (2016) Low-dose versus standard-dose intravenous alteplase in acute ischemic stroke. *N Engl J Med* (doi: 10.1056/NEJMoa1515510)

No link found between patient satisfaction and appointment waiting times

A new survey challenges the accepted thinking that links long waits to patient dissatisfaction (Dimovska et al, 2016).

Consecutive patients who attended the oral and maxillofacial outpatient department at Southampton University Hospital NHS Foundation Trust over a 7-day period were given a questionnaire to complete before and after their consultation. It included questions with Likert scale responses on environmental, procedural and interactive aspects of the visit, and a 16-point scale to rank their priorities.

Questionnaires were completed by 187 patients (77%). No association was found between expected (P=0.93) or actual (P=0.41) waiting times, and 90% of patients were satisfied with their visit. Seeing the doctor, having confidence in the treatment plan, being listened to, and the ability of the doctor to recognize their personal needs, were ranked as important.

Lead author Dr Eleonora Dimovska explained: 'Clearly, the interaction between the doctor and patient is valued highly and associated with satisfaction, while waiting times are not.'

Dimovska EOF, Sharma S, Trebble TM (2016) Evaluation of patients' attitudes to their care during oral and maxillofacial surgical outpatient consultations: the importance of waiting times and quality of interaction between patient and doctor. *Br J Oral Maxillofac Surg* (doi: 10.1016/j.bjoms.2016.02.022)

Consensus recognizes metabolic surgery as treatment for type 2 diabetes

Metabolic, or weight loss, surgery quickly and dramatically improves blood glucose control. However, until now it has not been included in clinical practice guidelines as a treatment option for people with diabetes.

In a joint statement endorsed by 45 international professional organizations, diabetes clinicians and researchers are urging that metabolic surgery be recommended or considered as a treatment option for certain people with diabetes, including people who are mildly obese and fail to respond to conventional treatment (Rubino et al, 2016).

The new guidelines emerged from the Second Diabetes Surgery Summit, an international consensus conference held in London in September 2015, and jointly organized with the American Diabetes Association, International Diabetes Federation, Diabetes UK, Chinese Diabetes Society, and Diabetes India. The goal of the summit was to develop global guidelines to inform clinicians and policy makers about the benefits and limitations of metabolic surgery for type 2 diabetes.

'Surgery represents a radical departure from conventional approaches to diabetes. The new guidelines introduce, both conceptually and practically, one of the biggest changes for diabetes care in modern times,' said Professor Francesco Rubino, Professor of Metabolic and Bariatric Surgery at King's College London and co-director of the summit.

'This change is supported by documented clinical efficacy and by the evidence of an important role of the gut in metabolic regulation, which makes it an appropriate target for anti-diabetes interventions,' he added.

Rubino F, Nathan DM, Eckel RH et al on behalf of the Delegates of the 2nd Diabetes Surgery Summit (2016) Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement by international diabetes organizations. *Diabetes Care* **39**(6): 861–77 (doi: 10.2337/dc16-0236)