Real-world data confirm long-term effectiveness of bronchial thermoplasty

A 3-year follow-up cohort study (Chupp et al, 2017) has shown that patients with severe asthma treated with bronchial thermoplasty in the real-world study achieved similar reductions in severe exacerbations, hospitalizations and emergency room visits as patients in the previous randomized, sham-controlled trial, despite having less well-controlled symptoms.

Following the last bronchial thermoplasty treatment the percentage of patients experiencing severe exacerbations decreased from 74% to 40%, the percentage of patients with a hospitalization for at least one asthma symptom decreased from 15% to 7%, the percentage of patients with emergency room visits decreased from 27% to 11%, and the percentage of patients using daily maintenance oral corticosteroid medications decreased from 19% to 10%.

Chupp G, Laviolette M, Cohn L et al, Other members of the PAS2 Study Group (2017) Long-term outcomes of bronchial thermoplasty in subjects with severe asthma: a comparison of 3-year follow-up results from two prospective multicentre studies. *Eur Respir J* **50**(2): 1700017. https://doi.org/10.1183/13993003.00017-2017

Biomarkers support strong role of food in type 2 diabetes

A Swedish study has shown that several diet and nutrient biomarkers are linked with both the risk of having type 2 diabetes and the future risk of developing diabetes (https://doi.org/10.3945/ajcn.117.152850). Measuring dietary intake is often confounded by recall and reporting bias, so biomarkers offer a more objective view.

Although the role of diet is often discussed as a preventative measure for developing type 2 diabetes, this new research provides strong support for dietary guidelines, and underlines the importance of changing diet to improve health.

The frequency of blood donation could be safely increased

New research shows that blood donors could safely give blood more frequently than is allowed at present. At the moment in the UK men can give blood every 12 weeks and women every 16 weeks. The new research demonstrates that in certain situations and for certain donors, shortening the donation interval is a viable approach for blood services to take (Di Angelantonio et al, 2017).

A parallel group, pragmatic, randomized trial recruited 45 263 whole blood donors aged 18 years or older from 25 centres across England. Men were randomly assigned to 12-week (standard) *vs* 10-week *vs* 8-week inter-donation intervals, and women were randomly assigned to 16-week (standard) *vs* 14-week *vs* 12-week intervals. Participants were not masked to their allocated intervention group. The primary outcome was the number of donations over 2 years. Secondary outcomes related to safety were quality of life, symptoms potentially related to donation, physical activity, cognitive function, haemoglobin and ferritin concentrations, and deferrals because of low haemoglobin level.

The results showed that giving blood at the shorter intervals resulted in much more blood being collected without having a major impact on the donors' quality of life, mental function or physical activity. However, more frequent donation resulted in more donation-related symptoms (e.g. tiredness, breathlessness, feeling faint, dizziness, and restless legs, especially among men), lower mean haemoglobin and ferritin concentrations, and more deferrals for low haemoglobin ($P<0{\cdot}0001$ for each) than those observed in the standard frequency groups.

The study also showed that donors who weighed above average and those with higher initial stores of iron were able to give more blood.

Senior author Professor John Danesh, from the University of Cambridge, said: 'Our data give blood services the short-term option of more frequent collection from donors if the supply falls or demand rises. We have also measured how much iron is lost after 2 years of repeated donation, and this will help towards framing the safety guidelines in countries where blood donation is more frequent than in the UK.'

The results from the trial suggest that better screening methods should be sought to detect low haemoglobin levels in potential donors. NHS Blood and Transplant and the University of Cambridge have started the COMPARE study to test different ways to measure when a donor has a low haemoglobin level and should not give blood.

Gail Miflin, NHS Blood and Transplants Medical and Research Director commented: 'We now need to review the findings in greater depth to understand which donors can safely donate more frequently without this having an adverse impact on their iron stores. The study clearly shows that some donors could donate more frequently than the current donation intervals but it also highlights that some donors should donate at longer intervals.'

These results suggest a need to use comprehensive reminders to help donors make and keep appointments, and to review the screening method used in the UK to test individuals' eligibility to donate.

Di Angelantonio E, Thompson SG, Kaptoge S et al, on behalf of the show INTERVAL Trial Group (2017) Efficiency and safety of varying the frequency of whole blood donation (INTERVAL): a randomised trial of 45 000 donors. *Lancet* http://dx.doi.org/10.1016/S0140-6736(17)31928-1

Professor John Danesh, Professor of Epidemiology and Medicine, Department of Public Health and Primary Care, School of Clinical Medicine, University of Cambridge, Cambridge

Post-traumatic stress disorder linked with increased risk of developing systemic lupus erythematosus

A study has examined whether trauma exposure and post-traumatic stress disorder are associated with increased risk of incident systemic lupus erythematosus in civilians (Roberts et al, 2017).

The association of trauma exposure and post-traumatic stress disorder symptoms with systemic lupus erythematosus incidence over 24 years of follow-up in an American longitudinal cohort of women (n=54 763). Incident systemic lupus erythematosus was ascertained by self-report and confirmed by medical record review. Post-traumatic stress disorder and trauma exposure were assessed, and women categorized as having no trauma, trauma and no post-traumatic stress disorder symptoms, subclinical or probable post-traumatic stress disorder. The researchers examined whether longitudinally assessed health risk factors (e.g. smoking, body mass index, oral contraceptive use) accounted for increased risk of developing systemic lupus erythematosus among women with *vs* without trauma exposure and post-traumatic stress disorder.

Dr Andrea L Roberts, Research Scientist, Harvard T. H. Chan School of Public Health, Department of Environmental Health, Boston, MA

Investigators found a nearly three-fold elevated risk of lupus among women with probable post-traumatic stress disorder and more than two-fold higher risk of lupus among women who had experienced any traumatic event compared with women not exposed to trauma.

'We were surprised that exposure to trauma was so strongly associated with risk of lupus – trauma was a stronger predictor of developing lupus than smoking,' said lead author Dr Andrea Roberts, Department of Environmental Health, Harvard T. H. Chan School of Public Health, Boston, MA. She added: 'Our results add to considerable scientific evidence that our mental health substantially affects our physical health, making access to mental health care even more urgent.'

Roberts AL, Malspeis S, Kubzansky LD, Feldman CH, Chang SC, Koenen KC, Costenbader KH (2017) Association of trauma and posttraumatic stress disorder with incident systemic lupus erythematosus (SLE) in a longitudinal cohort of women. *Arthritis Rheumatol* https://doi.org/10.1002/art.40222

Telemonitoring improves adherence to CPAP

Patients with obstructive sleep apnoea are more likely to use continuous positive airway pressure (CPAP) when their use is telemonitored and they receive individualized, automated messages reinforcing therapy adherence, finds a new study (Hwang et al, 2017).

The study enrolled 1455 adult patients. Usual care consisted of a 1-hour small-group class covering home sleep apnoea testing and sleep apnoea and CPAP education. After a 1-week CPAP trial in those diagnosed with obstructive sleep apnoea, usual care included a follow-up visit with a respiratory therapist who reviewed the data with patients and asked about their experience with the therapy. Those getting automated feedback received messages encouraging CPAP use by email, text or phone based on each patient's preference. Messages were sent when CPAP use dropped below 4 hours on three consecutive nights and when the patient achieved Medicare adherence. After 90 days, those in the telemonitoring arms of the trial used CPAP 36–60 minutes longer each night.

The improved adherence achieved with telemonitoring required no additional provider intervention or staffing resources, making it highly cost effective. Lead author Dr Dennis Hwang from the Kaiser Permanente, Sleep Medicine, Fontana, California, United States, said: 'While patient education is important, it appears that accountability via telemonitoring is more effective at improving therapy adherence.'

Hwang D, Chang JW, Benjafield AV et al (2017) Effect of telemedicine education and telemonitoring on CPAP adherence: The Tele-OSA Randomized Trial. *Am J Respir Crit Care Med* https://doi.org/10.1164/rccm.201703-0582OC

Long-term efficacy of nonavalent HPV vaccine demonstrated

A 6-year long-term trial in women aged between 16 and 26 years has confirmed the long-term efficacy of a vaccine against nine subtypes of HPV (human papillomavirus). It has the potential to prevent 90% of all cases of disease triggered by HPV (https://doi.org/10.1016/S0140-6736(17)31821-4).

Second Atlas of Variation in Liver Disease outlines variations in risk factors and health care

Public Health England has launched the 2nd Atlas of variation in risk factors and healthcare for liver disease in England (https://fingertips.phe.org.uk/documents/FINAL_LiverAtlas_080917_v3.pdf). This presents 39 indicators which cover the main risk factors for liver disease, aspects of health service provision and outcomes.

Oral dimethyl fumarate available for adults with moderate-to-severe chronic plaque psoriasis

Skilarence, a new oral formulation of dimethyl fumarate, is now available as a first-line induction and long-term maintenance therapy for patients with moderate-to-severe chronic plaque psoriasis. It is the first and only fumaric acid ester approved by the European Commission, providing a new option for a larger number of patients with the disease.

Avoiding severe hypoglycaemia reduces risk of death in people with type 2 diabetes

New analyses from the DEVOTE trial showing that people with type 2 diabetes who experience severe hypoglycaemia are at greater risk of death (Zinman et al, 2017). The risk was four-fold higher 15 days after an event and 2.5-fold higher any time after an episode of severe hypoglycaemia. Daily fluctuations in blood sugar levels in people with type 2 diabetes are also associated with a higher risk of death.

'Episodes of severe hypoglycaemia are not only distressing for patients and potentially dangerous, they are also associated with an increased risk of death,' said Dr Bernard Zinman of the Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, University of Toronto, Canada and member of the DEVOTE Steering Committee. 'These results highlight the importance of maintaining low variability in blood sugar levels and reducing the risk of severe hypoglycaemia when treating people with type 2 diabetes.'

Zinman B, Marso SP, Poulter NR et al, DEVOTE Study Group (2017) Day-to-day fasting glycaemic variability in DEVOTE: associations with severe hypoglycaemia and cardiovascular outcomes (DEVOTE 2). *Diabetologia* https://doi.org/10.1007/s00125-017-4423-z

Orthopaedic joint replacement register shows 'very impressive' outcomes

The latest report from the orthopaedic joint replacement register for England, Wales, Northern Ireland and the Isle of Man (National Joint Registry, 2017) highlights a record number of procedures being performed.

More joint replacements than ever before were carried out in the financial year 2016–17, with just fewer than 243 000 cases submitted to the National Joint Registry. This is a significant increase of more than 20 000 joint replacement operations recorded in the registry on the previous 1-year period.

Commenting on the data in the report, Mr Martyn Porter, the National Joint Registry's medical director and vice chairman, and consultant orthopaedic surgeon at Wrightington Hospital, Lancashire, said: 'The consistently high number of joint replacement cases submitted per year suggests continuing high levels of patient confidence and clinical performance, in what is a remarkably successful surgical intervention.

He added: 'Specifically in the case of hip replacement, today's report shows that in the vast majority of patients over the age of 75 years at the time of their operation, their hip implant will not need to be replaced again in their remaining lifetime.

Mr Porter emphasized: 'These are very impressive results and we should not lose sight of the fact that joint replacement gets patients back to their chosen lifestyle sooner, free from pain and with improved mobility.'

Analysis from this year's report continues to show the trend for increased likelihood of revision (or 're-do' surgery) associated with younger patients across all types of joint replacement procedures recorded in the registry. Younger patients may be at higher risk of revision because they are more active which may put more strain on their implants. There may also be differences between patients which could be the result of age or variations in surgery.

Mr Porter continued: 'This trend is particularly relevant given the increase in total numbers of younger patients undergoing joint replacement. If younger patients are most likely to need at least one revision surgery in their lifetime, then we must use the maturing dataset of the National Joint Registry to get the first-time surgery as right for the patient as possible.'

National Joint Registry (2017) 14th Report 2017. www.njrreports.org.uk/Portals/0/PDFdownloads/NJR%2014th%20Annual%20Report%202017.pdf (accessed 25 September 2017)

Urinary biomarkers may predict rejection and outcome of kidney transplants

MicroRNAs (miRNAs) may be useful biomarkers of rejection and allograft outcome in patients who have undergone kidney transplantation. Elevated levels of the urinary chemokine CXCL10 have been associated with acute rejection and may predict allograft failure. Millán et al (2017) examined the correlation of miRNA, CXCL10 levels and immunosuppressive drug exposure with acute rejection and graft function in kidney transplant recipients.

Eighty denovo kidney transplant recipients were recruited from four European centres. All patients received tacrolimus, mycophenolate mofetil and methylprednisolone. Expression of miR-142-3p, miR-210-3p and miR-155-5p and urinary CXCL10 levels were assessed at the 1st week and the 1st, 2nd, 3rd and 6th months post-transplantation.

Eight patients experienced acute rejection. Before and during acute rejection, these patients showed a significant increase in urinary miR-142-3p, miR-155-5p and CXCL10 levels and a decrease in miR-210-3p levels. Analysis showed that miR-155-5p and CXCL10 had excellent capacity to discriminate between rejectors and non-rejectors. miR-155-5p and CXCL10 levels correlated with glomerular filtration rate. Levels of both biomarkers normalized after recovery of graft function.

The regular early post-transplantation monitoring of urinary miR-155-5p and CXCL10 can help in the prognosis of acute rejection and graft dysfunction. Large prospective randomized multicentre trials are warranted to refine the cut-off values and validate the clinical usefulness of these biomarkers.

Millán O, Budde K, Sommerer C et al (2017) Urinary miR-155-5p and CXCL10 as prognostic and predictive biomarkers of rejection, graft outcome and treatment response in kidney transplantation. *Br J Clin Pharmacol* https://doi.org/10.1111/bcp.13399

Hard water could contribute to the development of eczema by precipitating surfactants and altering pH

Dr Simon G Danby, Sheffield Dermatology Research, Department of Infection, Immunity and Cardiovascular Disease, Faculty of Medicine, Dentistry and Health, University of Sheffield, Sheffield

A new study (Danby et al, 2017) has shown that exposing the skin to hard water damages the skin barrier and increases the sensitivity of the skin to potential irritants found in everyday wash products such as soap or washing powder.

Hard water contains high levels of calcium and magnesium ions which bind to surfactants such as sodium lauryl sulfate and sodium lauryl ether sulfate – which act as detergents or wetting agents – making them insoluble, so they precipitate onto the skin.

The skin's pH is normally acidic but hard water has high alkalinity which means it can raise the skin surface pH. A shift towards alkaline pH disturbs the skin's natural function as a physical barrier and leaves it prone to colonization by potentially pathogenic bacteria which can cause infection.

Lead author of the study, Dr Simon Danby from the University of Sheffield's Department of Infection, Immunity and Cardiovascular Disease, said: 'By damaging the skin barrier, washing with hard water may contribute to the development of eczema.

He added: 'This new study reveals the mechanism by which calcium and magnesium ions in hard water, surfactants and filaggrin interact to damage the skin barrier, unlocking new information about how exposure to hard water could potentially contribute to the development of eczema.'

Danby SG, Brown K, Wigley AM, Chittock J, Pyae PK, Flohr C, Cork MJ (2017) The effect of water hardness on surfactant deposition following washing and subsequent skin irritation in atopic dermatitis patients and healthy controls. *J Invest Dermatol* https://doi.org/10.1016/j.jid.2017.08.037

Optimum surgical treatment for chronic pancreatitis

There is much uncertainty regarding the optimal surgical treatment for chronic pancreatitis. Short-term outcomes have been found to be better after duodenum-preserving pancreatic head resection than after partial pancreatoduodenectomy. The ChroPac trial was designed to investigate long-term outcomes of patients with chronic pancreatitis 24 months after surgery (Diener et al, 2017).

This randomized, controlled, double-blind, parallel-group, superiority trial was done in 18 hospitals across Europe. Patients with chronic pancreatitis who were planned for elective surgical treatment were randomly assigned to duodenum-preserving pancreatic head resection or partial pancreatoduodenectomy. The primary endpoint was mean quality of life within 24 months after surgery.

Between September 2009, and September 2013, 250 patients were randomly assigned to duodenum-preserving pancreatic head resection (n=125) or partial pancreatoduodenectomy (n=125), of whom 226 patients (115 in the duodenum-preserving pancreatic head resection group and 111 in the partial pancreatoduodenectomy group) were analysed. No difference in quality of life was seen between the groups.

The incidence and severity of serious adverse events did not differ between the groups: 70 (64%) of 109 patients in the duodenum-preserving pancreatic head resection group and 61 (52%) of 117 patients in the partial pancreatoduodenectomy group had at least one serious adverse event, with the most common being reoperations (for reasons other than chronic pancreatitis), gastrointestinal problems and other surgical morbidity.

Previous results from single-centre trials showing superiority for duodenum-preserving pancreatic head resection were not confirmed in this multicentre setting.

Diener MK, Hüttner FJ, Kieser M et al; ChroPac Trial Group (2017) Partial pancreatoduodenectomy versus duodenum-preserving pancreatic head resection in chronic pancreatitis: the multicentre, randomised, controlled, double-blind ChroPac trial. *Lancet* **390**(10099): 1027–1037. https://doi.org/10.1016/S0140-6736(17)31960-8

Lower rates of major bleeding with dual therapy for stent placement in patients with atrial fibrillation

The results of RE-DUAL PCI (Cannon et al, 2017) showed a significant reduction in the incidence of bleeding complications in patients with non-valvular atrial fibrillation undergoing stent placement if dabigatran dual therapy (dabigatran plus clopidogrel or ticagrelor) was used instead of warfarin triple therapy (warfarin plus clopidogrel or ticagrelor and aspirin).

In this study of 2725 patients, results showed significantly lower rates of major or clinically relevant non-major bleeding events for dual therapy with dabigatran 110 mg and 150 mg twice daily when compared to triple therapy with warfarin. The reduction in risk *vs* triple therapy was 48% for dabigatran 110 mg dual therapy (absolute risk reduction 11.5%) and 28% for dabigatran 150 mg dual therapy (absolute risk reduction 5.5%), with similar rates of overall thromboembolic events.

UK trial centre lead Professor Greg Lip, Consultant Cardiologist and Professor of Cardiovascular Medicine, Birmingham University, said: 'The results from this study will give clinicians confidence when using either of the two doses of dabigatran available in the UK to reduce the risk of stroke in patients with atrial fibrillation when needed in combination with antiplatelet agents after percutaneous coronary intervention.

Professor Lip added: 'The improved safety profile and similar efficacy for both doses of dabigatran in a dual approach will give UK clinicians confidence to move away from a triple therapy regimen with warfarin and two antiplatelet agents which is our current standard of care'.

Cannon CP, Bhatt DL, Oldgren J et al, RE-DUAL PCI Steering Committee and Investigators (2017) Dual antithrombotic therapy with dabigatran after PCI in atrial fibrillation. *N Engl J Med* https://doi.org/10.1056/NEJMoa1708454