Catheter ablation for atrial fibrillation in patients with heart failure

Catheter ablation for atrial fibrillation in patients with heart failure was associated with a significantly lower rate of a composite end point of death from any cause or hospitalization for worsening heart failure than was medical therapy, found a study supported by Biotronik (https://doi.org/10.1056/NEJMoa1707855).

High levels of antibiotic resistance in children's *E. coli* when prescribed common antibiotics

Escherichia coli (the most common cause of urinary tract infection) in children show high levels of resistance to many antibiotics commonly prescribed in primary care which could make these drugs ineffective as first-line treatments, warns a study (Bryce et al, 2018).

Children are frequent consumers of antibiotics worldwide – and such routine use increases the probability of antibiotic resistance in adults with urinary tract infections. Yet little is known about the prevalence of bacterial resistance in children or important risk factors.

Researchers investigated the prevalence of antibiotic resistance in urinary *E. coli* from pre-school children, and measured risk factors associated with resistant urinary *E. coli*.

They found a high prevalence of antibiotic resistance in urinary *E. coli* against several commonly prescribed antibiotics including amoxicillin, trimethoprim and co-amoxiclav. Almost one third of all *E. coli* were multidrug resistant. There was also an association between exposure to antibiotics within the previous 3 months and increased likelihood of a resistant urinary *E. coli*.

Bryce A, Costelloe C, Wootton M, Butler CC, Hay AD (2018) Comparison of risk factors for, and prevalence of, antibiotic resistance in contaminating and pathogenic urinary *Escherichia coli* in children in primary care: prospective cohort study. *J Antimicrob Chemother* https://doi.org/10.1093/jac/dkx525

Treatment for rheumatoid arthritis works less well in patients who also have symptoms of depression

Research shows that people with rheumatoid arthritis responded less well to biologics, the key treatment for many autoimmune rheumatological diseases, if they also had symptoms of depression when they started the treatment (Matcham et al, 2018). This study adds more weight to the evidence that having symptoms of depression predicts risk of poorer rheumatological outcomes.

Dr Faith Matcham, Post-doctoral Research Associate, Institute of Psychiatry, Psychology and Neuroscience, Department of Psychological Medicine, King's College London, London

The team used data from the British Society for Rheumatology Biologics Register, representing 18 421 rheumatoid arthritis patients receiving biologic treatment. Logistic regression analyses examined the relationship between baseline depressive symptoms and odds of good treatment response by 1 year. Multilevel models addressed the association between baseline depressive symptoms and disease activity outcomes over 1-year follow-up.

The findings suggested that depression symptoms at baseline contributed to approximately 30% reduced odds of good biologics treatment response 1 year later in patients with rheumatoid arthritis. Having symptoms of depression is associated with less improvement in rheumatoid arthritis disease activity over time, once on biologics.

Dr Faith Matcham, Post-doctoral Research Associate in the Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience at King's College London said: 'We found links between depression and both subjective and objective measures of disease activity. This could be the result of reduced medication adherence, which can be impacted by depressive symptoms, or there may be a biological explanation.'

She emphasized that access to the large dataset in the biologics register for rheumatoid arthritis provided sufficient statistical power to identify effect sizes which may not be able to be seen in smaller datasets.

Matcham F, Davies R, Hotopf M, Hyrich KL, Norton S, Steer S, Galloway J (2018) The relationship between depression and biologic treatment response in rheumatoid arthritis: An analysis of the British Society for Rheumatology Biologics Register. *Rheumatology (Oxford)* https://doi.org/10.1093/rheumatology/kex528

Five and 10 minute Apgar scores and risks of cerebral palsy and epilepsy

A population-based cohort study in Sweden investigated associations between Apgar score at 5 and 10 minutes and risks of childhood cerebral palsy or epilepsy, and analysed the effect of changes in Apgar scores from 5–10 minutes after birth in infants born ≥37 completed weeks (Persson et al, 2018).

Out of the 1 213 470 infants included, 1221 (0.1%) were diagnosed as having cerebral palsy and 3975 (0.3%) as having epilepsy. Compared with children with an Apgar score of 10 at 5 minutes, the adjusted hazard ratio for cerebral palsy increased steadily with decreasing Apgar score. Similar and even stronger associations were obtained between Apgar scores at 10 minutes and cerebral palsy.

Associations were smaller between Apgar scores and epilepsy, but infants with a 5-minute Apgar score of 7 or less and a 10-minute score of 8 or less had increased hazard ratios.

Hazard ratios of cerebral palsy and epilepsy were higher among infants with a 5-minute Apgar score of 7–8 and a 10-minute score of 9–10 than those with an Apgar of 9–10 at 5 and 10 minutes. Risks of cerebral palsy and epilepsy are inversely associated with 5- and 10-minute Apgar scores across the range of scores.

Persson M, Razaz N, Tedroff K, Joseph KS, Cnattingius S (2018) Five and 10 minute Apgar scores and risks of cerebral palsy and epilepsy: population based cohort study in Sweden. *BMJ* **360**: k207. https://doi.org/10.1136/bmj.k207

Analysis of outcomes of Improving Access to Psychological Therapies

Professor David M Clark, National Clinical and Informatics Advisor for IAPT, Chair of Experimental Psychology, University of Oxford, Oxford

The clinical outcomes of routine mental health services are rarely recorded or reported. An exception is the English Improving Access to Psychological Therapies (IAPT) service, which delivers psychological therapies for depression and anxiety disorders to over 537 000 patients in the UK each year. A session-by-session outcome monitoring system ensures that IAPT obtains symptom scores before and after treatment for 98% of patients.

Using β regression models, outcome data from 2014–15 were analysed and used to develop a predictive model of reliable improvement and recovery. The team then tested whether these predictors were associated with changes in service outcome between 2014–15 and 2015–16 (Clark et al, 2018).

Five service organization features predicted clinical outcomes in 2014–15. Percentage of cases with a problem descriptor, number of treatment sessions, and percentage of referrals treated were positively associated with outcome. The time waited to start treatment and percentage of appointments missed were negatively associated with outcome. Social deprivation was negatively associated with some outcomes, but the effect was partly mitigated by the organizational factors.

These analyses show that the way psychological therapy services are implemented could be important. Commenting on the findings, Professor David M Clark, National Clinical and Informatics Advisor for IAPT and Chair of Experimental Psychology, University of Oxford, Oxford, said: 'The study highlights the value of collecting and reporting patient outcomes in routine mental health services. Key ways in which the services are organized (average therapy dose, waiting times etc) influence the outcomes they achieve. Feedback of the findings to services is instrumental in improving patient benefit.'

Clark DM, Canvin L, Green J, Layard R, Pilling S, Janecka M (2018) Transparency about the outcomes of mental health services (IAPT approach): an analysis of public data. *Lancet* **391**(10121): 679–686. https://doi.org/10.1016/S0140-6736(17)32133-5

Long-term effects of glucocorticoid treatment in patients with Duchenne muscular dystrophy

Glucocorticoid treatment is recommended as a standard of care in Duchenne muscular dystrophy, but few studies have assessed the long-term benefits of this treatment. A prospective cohort study examined the long-term effects of glucocorticoids on milestone-related disease progression across the lifespan and survival in patients with Duchenne muscular dystrophy (McDonald et al, 2018).

A total of 440 male patients aged 2–28 years with Duchenne muscular dystrophy were enrolled and followed up for 10 years. The authors compared no glucocorticoid treatment or cumulative treatment duration of less than 1 month *vs* treatment of 1 year or longer with regard to progression of nine disease-related and clinically meaningful mobility and upper limb milestones.

Time to all disease progression milestone events was significantly longer in patients treated with glucocorticoids for 1 year or longer than in patients treated for less than 1 month or never treated (log-rank $P<0{\cdot}0001$). Glucocorticoid treatment for 1 year or longer was associated with increased median age at loss of mobility milestones by 2·1–4·4 years and upper limb milestones by 2·8–8·0 years compared with treatment for less than 1 month.

In patients with Duchenne muscular dystrophy, glucocorticoid treatment is associated with reduced risk of losing clinically meaningful mobility and upper limb disease progression milestones across the lifespan as well as reduced risk of death.

McDonald CM, Henricson EK, Abresch RT et al; CINRG Investigators (2018) Long-term effects of glucocorticoids on function, quality of life, and survival in patients with Duchenne muscular dystrophy: a prospective cohort study. *Lancet* **391**(10119): 451–461. https://doi.org/10.1016/S0140-6736(17)32160-8

More action needed to reduce alcohol-attributable deaths and hospitalization in Scotland

In Scotland in 2015, alcohol contributed to 3705 deaths and 41 161 people were admitted to hospital as a result of alcohol consumption (www.healthscotland.scot/health-inequalities/impact-of-ill-health/impact-of-alcohol-on-health).

Postnatal depression has lifelong impact on mother–child relations and disrupts grandmother bonding

Postnatal depression can impact the quality of relationships between mother and child into adult life, and have a negative influence on the quality of relationships between grandmothers and grandchildren (https://doi.org/10.7717/peerj.4305). Postnatal depression was found to be specifically detrimental to the relationship the mother had with the child whose birth triggered the depression.

Every minute counts for people who have had a heart attack

A study from Germany (https://doi.org/10.1093/eurheartj/ehy004) shows numbers of deaths rise steadily and rapidly the longer the time between patients' first contact with a medical professional and when they are treated in hospital with percutaneous coronary intervention, particularly for patients suffering from cardiogenic shock.

Is maternal thyroid function linked to child's educational attainment?

A prospective cohort study was undertaken using the Avon Longitudinal Study of Parents and Children cohort in the UK to determine if first trimester maternal thyroid dysfunction is a critical determinant of a child's scholastic performance and overall educational attainment (Nelson et al, 2018).

Five age-specific national curriculum assessments in 3580 children at entry stage assessment at 54 months were reviewed, increasing up to 4461 children at their final school assessment at the age of 15 years. Children of mothers with thyroid dysfunction attained an equivalent number of GCSEs and equivalent grades as children of mothers with euthyroidism.

The authors concluded that maternal thyroid dysfunction in early pregnancy does not have a clinically important association with impaired child performance at school or educational achievement.

Nelson SM, Haig C, McConnachie A et al (2018) Maternal thyroid function and child educational attainment: prospective cohort study. *BMJ* **360**: k452. https://doi.org/10.1136/bmj.k452

Induced hypothermia does not reduce mortality in patients with septic shock and respiratory failure

A randomized controlled open-label trial, which recruited patients from ten intensive care units in three countries in Europe and North America, tested the hypothesis that a reduction of core temperature to 32–34°C attenuates organ dysfunction and reduces mortality in ventilator-dependent patients with septic shock (Itenov et al, 2018).

Inclusion criteria for patients with severe sepsis or septic shock were a mean arterial pressure of less than 70 mmHg, mechanical ventilation in an intensive care unit, age at least 50 years, predicted length of stay in the intensive care unit at least 24 hours, and recruitment into the study within 6 hours of fulfilling inclusion criteria. Patients were randomly allocated to routine thermal management or 24 hours of induced hypothermia (target 32–34°C) followed by 48 hours of normothermia (36–38°C). The primary endpoint was 30-day all-cause mortality in the modified intention-to-treat population.

After recruitment of 436 of the planned 560 participants, the trial was terminated for futility. In the hypothermia group, 96 (44·2%) of 217 died within 30 days *vs* 77 (35·8%) of 215 in the routine thermal management group.

Dr Jens-Ulrik Stæhr Jensen, Senior Consultant, Department of Internal Medicine C, Respiratory Medicine Section, Herlev Gentofte Hospital, University Hospital of Copenhagen, Hellerup, Denmark

The authors concluded that among patients with septic shock and ventilator-dependent respiratory failure, induced hypothermia does not reduce mortality, and that induced hypothermia should not be used in patients with septic shock.

Author Dr Jens-Ulrik Stæhr Jensen, Senior Consultant, Department of Internal Medicine C, Respiratory Medicine Section, Herlev Gentofte Hospital, University Hospital of Copenhagen, Hellerup, Denmark, commented: 'The research group now plans to use the biobank for genomic analysis, metabolomics profile and wide scale immunological analysis to gain knowledge on central processes that are decisive for organ failure and mortality and within 18 months, to design a personalized medicine sepsis trial.'

Itenov TS, Johansen ME, Bestle M et al; Cooling and Surviving Septic Shock (CASS) Trial Collaboration (2018) Induced hypothermia in patients with septic shock and respiratory failure (CASS): a randomised, controlled, open-label trial. *Lancet Respir Med* https://doi.org/10.1016/S2213-2600(18)30004-3

Estimating costs of complications in patients with type 2 diabetes

Scientists have examined health insurance data of more than 300 000 people with diabetes in Germany and broken down the costs involved in treating various complications of the disease (Kähm et al, 2018).

'We wanted to know the extent of the associated costs that are borne by the statutory health insurance and thus by society as a whole,' said first author Katharina Kähm from the Institute of Health Economics and Health Care Management, Helmholtz Zentrum München–German Research Center for Environmental Health, Neuherberg, Germany. The researchers examined the data of 316 220 people with type 2 diabetes from 2012–2015.

Based on these data, the researchers made a detailed assessment of the costs of diabetes-related complications, calculating example costs of a man between the ages of 60 and 69 years. In the quarter in which the respective complication occurred, costs were estimated as follows:

- Eye disease (retinopathy) approximately €700 (£620)
- Blindness approximately €3000 (£2650)
- Kidney damage approximately €3400 (£3000)
- (Dialysis-dependent) renal failure approximately €23 000 (£20 300)
- Diabetic foot approximately €1300 (£1150)
- Amputation approximately €14000 (£12 350).

The study is the first of its kind to be conducted on such a large scale and in such detail, according to the authors.

The long-term aim is to improve prevention programmes. 'The results show clinical and health policy decision makers the considerable financial consequences of diabetes-related complications,' said co-author Professor Rolf Holle, adding: 'The study can thus be helpful in the planning and prioritization of new prevention and treatment programmes in the management of type 2 diabetes.'

Kähm K, Laxy M, Schneider U, Rogowski WH, Lhachimi SK, Holle R (2018) Health care costs associated with incident complications in patients with type 2 diabetes in Germany. *Diabetes Care* https://doi.org/10.2337/dc17-1763

Clot lysis time could identify heart attack patients most at risk of subsequent cardiovascular disease

Professor Rob Storey, Professor and Honorary Consultant in Cardiology, Department of Infection, Immunity and Cardiovascular Disease, University of Sheffield, Sheffield

A new blood test could provide a clue as to why some patients are at higher risk of cardiovascular disease after suffering a heart attack (Sumaya et al, 2018).

The research may help scientists to identify new targets for reducing the risk and eventually lead to more effective treatments.

The researchers, led by Professor Rob Storey from the University of Sheffield's Department of Infection, Immunity and Cardiovascular Disease, analysed blood plasma samples from more than 4300 patients with acute coronary syndrome as they were discharged from hospital.

They measured the maximum density of a clot and the time it took for the clot to break down – known as clot lysis time. After adjustment for known clinical characteristics and risk factors, the study found that patients with the longest clot lysis time had a 40% increased risk of recurrent myocardial infarction or death as a result of cardiovascular disease.

Professor Storey, who is also Academic Director and Honorary Consultant in the Cardiology and Cardiothoracic Surgery Directorate at the Sheffield Teaching Hospitals NHS Foundation Trust, said: 'We have made huge strides over the last two decades in improving prognosis following heart attacks but there is still plenty of room for further improvement.

He emphasized: 'Our findings provide exciting clues as to why some patients are at higher risk after heart attack and how we might address this with new treatments in the future.'

Sumaya W, Wallentin L, James SK et al (2018) Fibrin clot properties independently predict adverse clinical outcome following acute coronary syndrome: a PLATO substudy. *Eur Heart J* https://doi.org/10.1093/eurheartj/ehy013

Unapproved drugs sold in India pose a global threat to antibiotic resistance control

Millions of unapproved antibiotics are being sold in India each year, according to a new study (McGettigan et al, 2018). To examine the availability of antibiotics and their approval status in India, researchers analysed the regulatory records of antibiotics as well as sales data from 2007–2012. The analysis included information on fixed dose combination antibiotics and single drug formulation antibiotics on the market in India.

There were 118 different formulations of fixed dose combinations being sold in India between 2007 and 2012, compared with five in the UK and the USA. Of these, 64% were not approved by the national drugs regulator, the Central Drugs Standard Control Organisation, even though the sale of unapproved new drugs is illegal in India. In contrast to fixed dose combinations, 93% of 86 single drug formulation antibiotics on the market in India had regulatory approval.

The 118 fixed dose combination formulations gave rise to 3307 brand-named products made by 476 pharmaceutical manufacturers. Multinational companies manufactured 53 fixed dose combination formulations, 20 of which were unapproved in India. Only four were approved in the UK and the USA.

'Selling unapproved, unscrutinised antibiotics undermines measures in India to control antimicrobial resistance. Multinational companies should explain the sale of products in India that did not have the approval of their own national regulators and, in many cases, did not even have the approval of the Indian regulator,' said lead author Dr Patricia McGettigan, of Queen Mary University of London.

McGettigan P, Roderick P, Kadam A, Pollock A (2018) Threats to global antimicrobial resistance control: Centrally approved and unapproved antibiotic formulations sold in India. *Br J Clin Pharmacol* https://doi.org/10.1111/bcp.13503

Patients' perspectives on breast radiotherapy

Over the past 20 years, there have been significant advances in how radiation therapy for breast cancer is delivered. Nonetheless, many patients have fears and misconceptions about radiation therapy.

A new study (Shaverdian et al, 2018) reveals that many patients with breast cancer have worries about radiation therapy, but their actual experiences with modern breast radiation therapy are better than they expected. Most patients agreed that their initial negative impressions were unfounded.

To get a better sense of patients' views concerning modern radiation therapy, researchers surveyed 502 patients who were treated for breast cancer between 2012 and 2016. Of the 327 patients who responded to the survey, 83% underwent breast conservation therapy (defined as lumpectomy and radiation therapy).

'We wanted to look at the patients' perspective of the breast cancer radiation experience, to have tangible real-world data to guide future patients and providers in their decision making,' said lead author Dr Narek Shaverdian, of the University of California Los Angeles.

Of surveyed patients, 68% stated that they initially had little to no knowledge about radiation therapy, but 47% reported having heard frightening stories about it. Only 2% of patients felt that the negative stories they previously heard about radiation therapy were actually true. Also, 83% reported that short-term radiation side effects were less than or as expected, and 84% of patients said this about long-term side effects.

The survey revealed that 93% of breast conservation patients and 81% of mastectomy patients agreed with the statement 'If future patients knew the real truth about radiation therapy, they would be less scared about treatment.'

Shaverdian N, Wang X, Hegde JV, Aledia C, Weidhaas JB, Steinberg ML, McCloskey SA (2018) The patient's perspective on breast radiotherapy: Initial fears and expectations versus reality. *Cancer* https://doi.org/10.1002/cncr.31159