Early exposure to pollution affects long-term health

There is increasing evidence that exposure to air pollution in early life has detrimental long-term health consequences (https://doi.org/10.1136/bmjopen-2017-018231).

A geographical study conducted in local government districts in England and Wales found direct geographical correlations between coal consumption in the 1950s and deaths caused by respiratory and cardiovascular disease, as well as certain cancers, in England and Wales over the subsequent six decades.

The data have implications for the long-term health of the populations of countries that still depend on large amounts of coal for their domestic markets.

Incidence and cost of medication harm in older adults following hospital discharge

Polypharmacy is increasingly common in older adults, placing them at risk of medication-related harm. Patients are particularly vulnerable to problems with their medications in the period following hospital discharge because of medication changes, and poor information transfer between hospital and primary care. A study investigated the incidence, severity, preventability and cost of medication-related harm in older adults in England post-discharge (https://doi.org/10.1111/bcp.13613).

The observational multicentre prospective cohort study recruited 1280 older adults (median age 82 years) from five teaching hospitals in southern England. Of these, 413 (37%) experienced medication-related harm; 336 (81%) cases were serious, and 214 (52%) potentially preventable. Four cases were fatal. The most common medication-related harm events were gastrointestinal and neurological.

Post-discharge medication-related harm in older adults is estimated to cost the NHS £396 million a year, of which £243 million is potentially preventable.

Body composition study reveals link between specific fat distributions and metabolic diseases

A collaborative study has investigated the value of imaging-based multivariable body composition profiling by describing its association with coronary heart disease, type 2 diabetes, and metabolic health on individual and population levels (Linge et al, 2018).

The first 6021 participants scanned by UK Biobank were included. Body composition profiles were calculated, including abdominal subcutaneous adipose tissue, visceral adipose tissue, thigh muscle volume, liver fat, and muscle fat infiltration, determined using magnetic resonance imaging. Associations between body composition profiles and metabolic status were investigated using matching procedures and multivariable statistical modelling.

Dr Olof Dahlqvist Leinhard, Senior Lecturer, Department of Medical and Health Sciences (IMH), Linköping University, Linköping, Sweden

Matched control analysis showed that higher levels of visceral adipose tissue and muscle fat infiltration were associated with coronary heart disease and type 2 diabetes ($P<0.001$). Higher levels of liver fat were associated with type 2 diabetes ($P<0.001$) and lower levels of liver fat with coronary heart disease.

Multivariable modeling showed that lower levels of visceral adipose tissue and muscle fat infiltration were associated with metabolic health ($P<0.001$), and the level of liver fat was non-significant. Associations remained significant adjusting for sex, age, body mass index, alcohol, smoking and physical activity.

Body composition profiling enabled an intuitive visualization of body composition and showed the complexity of associations between fat distribution and metabolic status, stressing the importance of a multivariable approach. Different diseases were linked to different body composition profiles, which could not be described by a single fat compartment alone.

Dr Olof Dahlqvist Leinhard, senior author of the study, commented: 'By using a multivariable approach and an intuitive visualization of body composition, we have been able to identify a wide range of body composition profiles that could provide the link to increased risk of metabolic diseases.'

Linge J, Borga M, West J et al. Body composition profiling in the UK Biobank Imaging Study. Obesity 2018; https://doi.org/10.1002/oby.22210

Heart muscle cells die during acute HIV infection

The impact of excess viral RNA on myocardial function and morphology in the setting of acute HIV infection remains unknown.

Schuster et al (2018) found increased levels of N-terminal prohormone of brain natriuretic peptide (a surrogate of myocardial function) in 49 patients with acute HIV infection (approximately 1–2 weeks after transmission). This decreased with viral suppression and normalization of systemic inflammation (79 pg/ml *vs* 28 pg/ml; $P<0.001$). A comparable change was seen with levels of troponin T (4.9 ng/litre *vs* 1.5 ng/litre; $P<0.001$). In approximately one in four patients, heart muscle cells died in the acute phase as a result of the massive increase in HIV viral load and the simultaneous immune activation that occurs.

The authors concluded that significant functional and morphological myocardial impairment occurs during acute HIV infection, fuelled by inflammatory activation and extensive viral replication, resulting in a reversible subclinical inflammatory cardiomyopathy.

Schuster C, Mayer FJ, Wohlfahrt C et al. Acute HIV infection results in subclinical inflammatory cardiomyopathy. J Infect Dis. 2018. https://doi.org/10.1093/infdis/jiy183

Pain relief from percutaneous vertebroplasty for vertebral compression fractures no better than sham

A randomized, double-blind, sham-controlled clinical trial was performed in four community hospitals in the Netherlands to assess whether percutaneous vertebroplasty provides more pain relief than a sham procedure in 180 patients with acute osteoporotic compression fractures of the vertebral body (Firanescu et al, 2018).

Participants were randomized to either vertebroplasty (n=91) or a sham procedure (n=89). They received local subcutaneous lidocaine (lignocaine) and bupivacaine at each pedicle. The vertebroplasty group also received cementation, which was simulated in the sham procedure group.

The main outcome measure was mean reduction in visual analogue scale (VAS) scores at 1 day, 1 week, and 1, 3, 6, and 12 months. Secondary outcome measures were the differences between groups for changes in the quality of life for osteoporosis and Roland–Morris disability questionnaire scores during 12 months' follow up.

The mean reduction in VAS score was statistically significant in the vertebroplasty and sham procedure groups at all follow-up points after the procedure compared with baseline. These changes in VAS scores did not differ statistically significantly between the groups during 12 months' follow-up. The results for secondary outcomes were not statistically significant. Percutaneous vertebroplasty did not result in statistically significantly greater pain relief than a sham procedure during 12 months' follow up among patients with acute osteoporotic vertebral compression fractures.

First author Dr Christina Firanescu, interventional radiologist in ETZ Hospital, Tilburg, The Netherlands, said: 'Although percutaneous vertebroplasty did not result in statistically significantly greater pain relief than a sham procedure we do hope that these results will be carefully scrutinized leading to thoughtful interpretation and conclusions. After 1 year more patients showed secondary fractures and persistent pain in the sham group. A future therapeutic pain strategy could be a combined regimen of periosteal infiltration during natural healing. Additional cement seems indicated only in a selected subgroup of patients with insufficient pain relief after this early phase.'

Firanescu CE, de Vries J, Lodder P et al. Vertebroplasty versus sham procedure for painful acute osteoporotic vertebral compression fractures (VERTOS IV): randomised sham controlled clinical trial. BMJ. 2018 May 9;361:k1551. https://doi.org/10.1136/bmj.k1551

Does armodafinil improve driving task performance and weight loss in patients with sleep apnoea?

A placebo-controlled, double-blind, randomized trial of armodafinil *vs* placebo daily for 6 months was undertaken in 113 adult patients with obstructive sleep apnoea who had rejected standard treatment and suffered daytime sleepiness (Chapman et al, 2018). These patients were also randomized to one of two diets for 6 months with follow-up at 1 year.

Researchers from the Woolcock Institute for Medical Research, University of Sydney, Sydney, Australia, hypothesized that wakefulness-promoter armodafinil would improve driving task performance over placebo in patients undergoing weight loss. The primary outcome was change in steering deviation in the final 30 minutes of a 90-minute afternoon driving task at 6 months.

Armodafinil improved driving task performance over placebo at 3 months, but not at 6 months. Patients on armodafinil lost 2.4 kg more fat than those on placebo at 6 months. Other secondary outcomes (Epworth Sleepiness Scale, Functional Outcomes of Sleep Questionnaire) were not significantly improved.

The authors concluded that armodafinil did not improve driving task performance at 6 months. Armodafinil might be a useful adjunct to weight loss in patients with obstructive sleep apnoea who reject conventional treatments but this needs to be directly tested in a specific, properly powered clinical trial.

Chapman JL, Cayanan EA, Hoyos CM et al. Does armodafinil improve driving task performance and weight loss in sleep apnea? A randomized trial. Am J Respir Crit Care Med. 2018 May 18. https://doi.org/10.1164/rccm.201712-2439OC

New treatment option for patients with acute myeloid leukaemia

Gemtuzumab ozogamicin (Mylotarg) in combination with daunorubicin and cytarabine has been approved by the European Commission for the treatment of patients aged 15 years and above with previously untreated, de novo, CD33-positive acute myeloid leukaemia.

One in three people who die in hospital could spend their final days at home

As many as one in three people who die in hospital could spend their final days at home or in more appropriate care settings, but only if the government is prepared to increase investment in community-based health and social care, according to a new report *End of Life Care in England* from the Institute for Public Policy Research think-tank (https://www.ippr.org/research/publications/end-of-life-care-in-england).

Emollient bath additives no benefit in treating childhood eczema

A UK-wide study has found that using emollient additives in the bath does not add any benefit over standard management. A total of 482 children from 96 general practices were randomly allocated to either use bath additives or not for a whole year. The study found no meaningful difference in eczema severity between the groups (https://doi.org/10.1136/bmj.k1332).

28th ECCMID Madrid, Spain, 21–24 April

West Nile virus has re-emerged and is spreading in Greece

After a 2-year gap, West Nile virus has re-emerged in southern Greece and is now affecting new regions. This is the conclusion of a study of 45 laboratory-diagnosed cases identified between July and September 2017. Twenty-six cases (57.8%) were classified as West Nile virus neuroinvasive disease, while the other 19 (42.2%) were West Nile virus fever (Maria Mavroul et al, 2018).

According to presenting author Professor Athanassios Tsakris, Athens, Greece: 'The re-emergence of West Nile virus after a 2-year hiatus of reported human cases and its subsequent geographical expansion into newly affected areas demonstrates that Greece provides the appropriate ecological and climatic conditions for West Nile virus circulation. The virus has become established in Greece and disease transmission may continue in the future.'

West Nile virus is transmitted to humans via infected mosquito bites. The transmission period is typically between mid-summer and early autumn when mosquitos are most active.

Maria Mavroul M, Vrioni G, Tsakris A et al. 2018. Reemergence of West Nile Virus infections in humans in Southern Greece, July to September 2017. Abstract P0550

Positive outcomes for imipenem–relebactam in pivotal phase 3 study

The investigational beta-lactamase inhibitor relebactam in combination with imipenem results in a favourable overall response in imipenem-non-susceptible bacterial infections compared with imipenem + colistin, according to the RESTORE-IMI 1 study (Motsch et al, 2018).

Lead investigator Professor Johann Motsch, Professor of Anaesthesia and Head of Clinical Research, University of Heidelberg, Heidelberg, Germany, commented: 'Relebactam is a very efficacious treatment that restores the activity of imipenem against carbapenem-resistant Gram-negative infections. The combination is well tolerated, with a more favourable safety profile than colistin-based therapy.'

Professor Johann Motsch, Professor of Anaesthesia and Head of Clinical Research, University of Heidelberg, Heidelberg, Germany

RESTORE-IMI 1 was a randomized, comparator-controlled trial that included patients with hospital-acquired or ventilator-associated bacterial pneumonia, complicated intra-abdominal infection or complicated urinary tract infection caused by imipenem-non-susceptible pathogens. A total of 47 patients were randomized and treated, 31 of whom met microbiological intention to treat criteria.

On the primary endpoint, favourable overall response in the microbiological intention to treat population was comparable for imipenem–relebactam and colistin + imipenem (74% *vs* 70%). Clinical response at day 28 was higher with imipenem–relebactam (71.4% *vs* 40.0% with colistin + imipenem) and 28-day all-cause mortality was lower (9.5% *vs* 30.0%).

Drug-related adverse events occurred in 16% of imipenem–relebactam patients and 31% of colistin + imipenem patients, while treatment-emergent nephrotoxicity occurred in 10% and 56% of patients respectively (P=0.001). Three patients discontinued the study drug (all receiving colistin + imipenem) because of adverse events. Serious treatment-emergent adverse events occurred in 10% of imipenem–relebactam and 31% of colistin + imipenem patients.

Motsch J, de Oliveira C, Stus V et al. 2018. RESTORE-IMI 1: a multicentre, randomised, double-blind, comparator-controlled trial comparing the efficacy and safety of imipenem/relebactam versus colistin plus imipenem in patients with imipenem-non-susceptible bacterial infections. Abstract O0427

Youngest children are at highest risk of dying during measles outbreaks

A study from the European Centre for Disease Prevention and Control (Robesyn et al, 2018) concluded that children under 2 years of age are at a higher risk of dying than older patients, and that the majority of measles cases occur in unvaccinated people.

'Measles is not an innocent disease. In children aged under 1 year, the current vaccine may offer insufficient long-lasting immunity. In Europe, measles vaccination is offered from 12 months of age, meaning that the youngest children depend on passively transferred measles antibodies and herd immunity for protection,' said presenting author Dr Emmanuel Robesyn, European Centre for Disease Prevention and Control, Stockholm.

From 2013 to 2017, 37 365 measles cases were reported to the European Centre for Disease Prevention and Control: 10% were aged under 1 year, 9% aged 1 year, and 81% above 1 year. Italy, Romania, Germany, the Netherlands and the UK each reported more than 5% of cases. These countries also had the most cases that were unconnected with imported measles.

Most (81%) measles cases occurred in unvaccinated patients. One in 1000 patients died, 33% were hospitalized and 11% had pneumonia. The odds of dying was six (2.8–12) times higher for children aged 1 year compared with children aged 2 years or older. For children aged less than 1 year, the risk of dying was seven (3.5–13.5) times greater.

Robesyn E, Nakitanda OA, Sdona E et al. 2018. How does the outcome of measles cases under one year of age differ from that of older cases, EU/EEA 2013-2017. Abstract O0060

Sue Lyon

Effect of reporting surgeons' outcomes in colorectal cancer surgery

A national cohort study has looked at the effect of surgeon-specific outcome reporting in colorectal cancer surgery on risk-averse clinical practice, 'gaming' of clinical data and 90-day postoperative mortality (Vallance et al, 2018).

The main outcome measure was the proportion of patients with colorectal cancer who had an elective major resection, predicted and observed 90-day mortality.

The proportion of patients with colorectal cancer undergoing major resection did not change after the introduction of surgeon-specific public outcome reporting. The proportion of these resections categorized as elective or scheduled did not change. The predicted 90-day mortality remained the same, but the observed 90-day mortality fell.

This study did not find evidence that the introduction of public reporting of surgeon specific 90-day postoperative mortality in elective colorectal cancer surgery has led to risk averse clinical practice behaviour or 'gaming' of data. However, its introduction coincided with a significant reduction in 90-day mortality.

Professor Jan van der Meulen, Professor of Clinical Epidemiology, Department of Health Services Research and Policy, Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London, said: 'The improvement in surgical outcomes that we saw immediately after the public reporting of outcomes began demonstrates that surgeons have an important role in galvanising the entire team involved in managing patients before, and after this major surgical procedure.'

Professor Jan van der Meulen, Professor of Clinical Epidemiology, Department of Health Services Research and Policy, Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London

Vallance AE, Fearnhead NS, Kuryba A et al. Effect of public reporting of surgeons' outcomes on patient selection, "gaming," and mortality in colorectal cancer surgery in England: population based cohort study. BMJ. 2018;361:k1581. https://doi.org/10.1136/bmj.k1581

Risk score developed to help frail older people receive better support in hospital

A 'risk score' has been devised which will be used to help frail older people have better support in hospital (Gilbert et al, 2018).

Using the concept of frailty (which captures vulnerability), researchers from the Nuffield Trust and the Universities of Leicester, Newcastle, Southampton and the London School of Economics have created a tool to help identify older people who are more vulnerable.

A three-step approach was used to develop and validate the Hospital Frailty Risk Score from International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) diagnostic codes. A cluster analysis was performed to identify a group of older people (≥75 years) admitted to hospital who had high resource use and diagnoses associated with frailty. A Hospital Frailty Risk Score was then created based on ICD-10 codes that characterized this group. The score was tested in separate cohorts to see how well it predicted adverse outcomes and whether it identified similar groups as other frailty tools.

Professor Simon Conroy, Department of Health Sciences, University of Leicester, Leicester, and geriatrician at University Hospitals of Leicester, said: 'The Hospital Frailty Risk Score was able to identify older people at significantly increased risk of harms, longer stays in hospital and readmission following discharge from hospital.

He added: 'It is hoped that by identifying and focussing upon this high risk group that hospitals will be able to provide more holistic care to vulnerable older people to improve their outcomes.'

Gilbert T, Neuburger J, Kraindler J et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet. 2018;391(10132):1775–1782. https://doi.org/10.1016/S0140-6736(18)30668-8

Is rivaroxaban suitable for preventing venous thromboembolism in patients with cancer?

Long-term daily subcutaneous low molecular weight heparin has been standard treatment for patients with cancer to reduce the risk of developing venous thromboembolism. Young et al (2018) assessed if rivaroxaban, an oral factor Xa inhibitor, would offer an alternative treatment for venous thromboembolism in this group.

This multicentre, randomized, open-label, pilot trial recruited patients with active cancer who had symptomatic or incidental pulmonary embolism, or symptomatic lower extremity proximal deep vein thrombosis. Patients were allocated to dalteparin (200 IU/kg daily during month 1, then 150 IU/kg daily for months 2–6) or rivaroxaban (15 mg twice daily for 3 weeks, then 20 mg once daily for a total of 6 months).

The primary outcome was venous thromboembolism recurrence over 6 months. Safety was assessed by major bleeding and clinically relevant non-major bleeding.

A total of 203 patients was randomly assigned to each group, 58% of whom had metastases. Twenty-six patients experienced recurrent venous thromboembolism (dalteparin, $n = 18$; rivaroxaban, $n = 8$). The 6-month cumulative venous thromboembolism recurrence rate was 11% with dalteparin and 4% with rivaroxaban. The 6-month cumulative rate of major bleeding was 4% for dalteparin and 6% for rivaroxaban. Corresponding rates of clinically relevant non-major bleeding were 4% and 13% respectively.

Rivaroxaban was associated with relatively low venous thromboembolism recurrence but higher clinically relevant non-major bleeding than dalteparin.

Young AM, Marshall A, Thirlwall J et al. Comparison of an oral factor Xa inhibitor with low molecular weight heparin in patients with cancer with venous thromboembolism: results of a randomized trial (SELECT-D). J Clin Oncol. 2018 May 10:JCO2018788034. https://doi.org/10.1200/JCO.2018.78.8034