Which tool more accurately predicts chances of IVF success?

Accurately predicting the probability of a live birth after in-vitro fertilization (IVF) treatment is important for both those undergoing the treatment and their clinicians. A comparison study analysed the accuracy of the two most widely-used prediction models (Smith et al, 2015).

Researchers at the universities of Bristol and Glasgow compared how well the Templeton method and IVFpredict – two personalized prediction tools that help couples calculate their chance of a successful birth with IVF treatment – worked in 130 960 IVF cycles.

The team analysed data, held by the UK Human Fertilisation and Embryology Authority, to assess which of the two tools was more accurate at predicting live birth rates.

Although both tools are based on patient and couple measurements and characteristics and history of infertility, the Templeton model was developed using data from couples who received IVF two decades ago. At this time success rates were considerably lower than currently and intra-cytoplasmic sperm injection had not been introduced, which has transformed the use of IVF in couples where male infertility is a key problem.

IVFpredict was developed in 2011 and incorporates treatments such as intra-cytoplasmic sperm injection as well as the characteristics included in the Templeton model.

The findings showed that both models underestimated the chances of a live birth, but this was particularly marked in the Templeton model. The team updated the models to reflect very recent improvements in live birth rates and this improved both models, but IVFpredict still remained the more accurate of the two.

Dr Andrew Smith, one of the study's researchers based in the Medical Research Council Integrative Epidemiology Unit at the University of Bristol, said: 'As clinicians' assessments of success, done without any tool to guide them, are widely varied for the same patients, this study is important. It validates IVFpredict, shows it is more accurate than the other commonly used tool, and can therefore guide clinician assessments of success when they first see patients with infertility. The tool is also available on the internet for patients to use directly themselves.'

Smith ADAC, Tilling K, Lawlor DA, Nelson SM (2015) External validation and calibration of IVFpredict: a national prospective cohort study of 130,960 in vitro fertilisation cycles. *PLoS ONE* **10**(4): e0121357 (doi: 10.1371/journal.pone.0121357)

Dr Andrew Smith, Research Associate, Medical Research Council Integrative Epidemiology Unit, University of Bristol, Bristol

HPV vaccination of boys to prevent oropharyngeal cancer

A new study (Graham et al, 2015) indicates that vaccinating 12-year-old boys against the humanpapilloma virus (HPV) may be cost effective in preventing oropharyngeal squamous cell cancer.

Little is known about the cost effectiveness of male-HPV vaccination, so Dr Donna Graham and colleagues from the Princess Margaret Cancer Centre, University Health Network, Toronto, compared the potential costs and effectiveness of vaccinating adolescent boys in Canada against HPV for preventing HPV-related oropharyngeal cancer.

The investigators applied a statistical model to a population of 192 940 Canadian boys who were 12 years old in 2012, and found that HPV vaccination could save from $8 million to $28 million Canadian dollars over the boys' lifetimes. Factors that could impact the cost savings of HPV vaccination in boys include vaccine cost, vaccine effectiveness, costs of cancer treatment, and survival of patients with HPV-related oropharyngeal cancers.

'HPV-related oropharyngeal cancer has increased significantly in incidence, especially in developed countries,' said Dr Graham. 'It is projected that by 2020, HPV-related oropharyngeal cancer will become the most common HPV-related cancer in the US, surpassing cervical cancer.'

Graham DM, Isaranuwatchai W, Habbous S, de Oliveira C, Liu G, Siu LL, Hoch JS (2015) A cost-effectiveness analysis of human papillomavirus vaccination of boys for the prevention of oropharyngeal cancer. *Cancer* (doi: 10.1002/cncr.29111)

Resources to support fracture liaison service implementation

The National Osteoporosis Society has launched a set of resources to support the implementation of fracture liaison services. These can save the NHS money and save lives by preventing further fractures following a fragility fracture in people over 50 years of age.

Currently only 42% of health-care organizations in the UK offer any fracture liaison service. These proactively case-find patients over 50 years old who have suffered a fragility fracture, and manage and treat those at risk of further fractures.

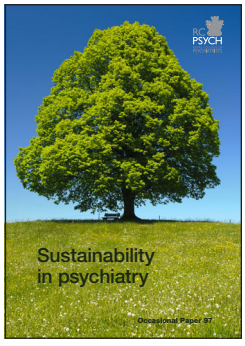
The National Osteoporosis Society wants to ensure a fracture liaison service is accessible to all those over 50 years of age who have suffered a fragility fracture. These resources will ensure that hospitals and health professionals will be in the strongest position to assess and treat patients in a consistent and timely manner.

The resources include:

- Clinical standards for fracture liaison services
- The fracture prevention practitioner online training
- The fracture liaison service implementation toolkit.

They are available from the Society's website at www.nos.org.uk/health-professionals/fracture-liaison-services

College calls for sustainable mental health care



A sustainable approach to health care can provide an answer to some of the current challenges in mental health, according to a new report from the Royal College of Psychiatrists (2015).

Climate change represents an unprecedented threat to human health and survival, and its effect on mental health could be profound. Mental health services will therefore need to be able to respond to potential increases in demand efficiently and responsibly, without adding to the problems that actually underlie climate change.

The NHS is committed to sustainable practices, and there is currently a requirement for all NHS organizations to reduce their carbon footprint by 80% within the next three decades. This will involve a significant degree of change in clinical processes.

A sustainable mental health-care system will need to provide high value care in spite of environmental, economic and social constraints. The aims must be to:

- Prevent mental illness
- Empower patients, staff and carers to manage their mental health
- Eliminate wasteful activity
- Make use of low-carbon alternatives.

By adopting this approach, sustainability within mental health will improve the mental health of the population, reduce disease burden and minimize use of health-care services. By focusing on developing healthy communities and prioritizing preventive strategies, a model of this kind will balance the social, environmental and economic demands within health-care settings.

Lead author, Dr Daniel Maughan, Royal College of Psychiatrists Sustainability Fellow, said: 'A step change in culture and practice is needed, one in which psychiatrists become critical assessors of the resources they use on a daily basis to determine whether they are bringing benefit to the patient and value to the system.

He continued: 'Reducing over-medication, adopting a recovery approach, exploiting the therapeutic value of natural settings and nurturing support networks can all improve patient care while reducing economic and environmental costs.'

Royal College of Psychiatrists (2015) Sustainability in psychiatry. Occasional Paper 97. http://rcpsych.ac.uk/files/pdfversion/OP97.pdf (accessed 28 April 2015)

No preference of antibiotic type to treat community-acquired pneumonia

The choice of empirical antibiotic treatment for patients with clinically suspected community-acquired pneumonia who are admitted to non-intensive care unit hospital wards is complicated by the limited availability of evidence. Researchers from the Netherlands compared strategies of empirical treatment (allowing deviations for medical reasons) with beta-lactam monotherapy, beta-lactam–macrolide combination therapy, or fluoroquinolone monotherapy (Postma et al, 2015).

A cluster-randomized, crossover trial with strategies rotated in 4-month periods, tested the non-inferiority of the beta-lactam strategy to the beta-lactam–macrolide and fluoroquinolone strategies with respect to 90-day mortality, in an intention-to-treat analysis, using a non-inferiority margin of 3 percentage points and a two-sided 90% confidence interval.

A total of 656 patients were included during the beta-lactam strategy periods, 739 during the beta-lactam–macrolide strategy periods, and 888 during the fluoroquinolone strategy periods, with rates of adherence to the strategy of 93.0%, 88.0% and 92.7% respectively. The median age of the patients was 70 years.

The results showed that a strategy of preferred empirical treatment with beta-lactam monotherapy was non-inferior to strategies with a beta-lactam–macrolide combination or fluoroquinolone monotherapy with regard to 90-day mortality.

Postma DF, van Werkhoven CH, van Elden LJR et al for the CAP-START Study Group (2015) Antibiotic treatment strategies for community-acquired pneumonia in adults. *N Engl J Med* **372**: 1312–23 (doi: 10.1056/NEJMoa1406330)

Every doctor a scientist and a scholar

The BMA has published 'Every doctor a scientist and a scholar' which calls for lifelong training and development of research and teaching skills for all doctors. The paper, produced by the BMA's Medical Academic Staff Committee, emphasizes that research and teaching should be viewed as central to the job and professionalism of all doctors, not seen as the preserve of a small group of doctors.

Statement for future research in COPD

The American Thoracic Society and European Respiratory Society have published a statement detailing current evidence on the diagnosis, assessment and management of chronic obstructive pulmonary disease (COPD), identifying gaps in knowledge and making recommendations for future research (doi: 10.1183/09031936.00009015).

Bevacizumab licensed for patients with advanced cervical cancer

The European Commission has authorized bevacizumab (Avastin) in combination with standard chemotherapy to treat women with advanced cervical cancer.

Lung cancer staging and diagnosis with endobronchial ultrasound-guided transbronchial needle aspiration

Diagnosis and staging of lung cancer is an important process that identifies treatment options and guides disease prognosis. The Lung-BOOST trial, a study from six UK centres, assessed endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) as an initial investigation technique for patients with suspected lung cancer (Navani et al, 2015).

Dr Neal Navani, Consultant in Thoracic Medicine, UCLH and MRC Clinical Trials Unit, Department of Thoracic Medicine, UCL Hospital, London

This open-label, multicentre, pragmatic, randomized controlled trial recruited patients who had undergone a computed tomography scan and had suspected stage I to IIIA lung cancer and randomly assigned them to either EBUS-TBNA or conventional diagnosis and staging, for further investigation and staging.

The primary endpoint was the time-to-treatment decision after completion of the diagnostic and staging investigations and analysis was by intention-to-diagnose.

Between 2008 and 2011, 133 patients were randomly allocated to treatment: 66 to EBUS-TBNA and 67 to conventional diagnosis and staging. Two patients from the EBUS-TBNA group underwent endoscopic ultrasound-guided fine needle aspiration.

The median time to treatment decision was shorter with EBUS-TBNA (14 days, 95% confidence interval 14–15) than with conventional diagnosis and staging (29 days, 95% confidence interval 23–35), resulting in a hazard ratio of 1·98 (95% confidence interval 1·39–2·82, $P<0·0001$).

One patient in each group had a pneumothorax from a computed tomography-guided biopsy sample; the patient from the conventional diagnosis and staging group needed intercostal drainage and was admitted to hospital.

Commenting on the findings, Dr Neal Navani, Consultant in Thoracic Medicine at UCL Hospital, London, said: 'Lung cancer remains the bigger cancer killer in the UK and worldwide. The process of coming to an accurate diagnosis and disease stage is very important to determine the best treatment but can often require several investigations over several weeks, and is a time of great anxiety for patients.'

'Endobronchial ultrasound is an important technique for sampling intra-thoracic lymph nodes,' continued Dr Navani, 'The Lung-BOOST trial was the first randomized trial of endobronchial ultrasound in patients with suspected lung cancer and showed that routine use of endobronchial ultrasound halved time to treatment decisions. Intriguingly, the trial also demonstrated that fast and accurate diagnosis with endobronchial ultrasound improved survival from lung cancer.'

The authors concluded that transbronchial needle aspiration guided by endobronchial ultrasound should be considered as the initial investigation for patients with suspected lung cancer.

Navani N, Nankivell M, Lawrence DR et al, on behalf of the Lung-BOOST trial investigators (2015) Lung cancer diagnosis and staging with endobronchial ultrasound-guided transbronchial needle aspiration compared with conventional approaches: an open-label, pragmatic, randomised controlled trial. *Lancet Respir Med* **3**(4): 282–9 (doi: doi.org/10.1016/S2213-2600(15)00029-6)

Early goal-directed therapy does not improve outcomes in patients with septic shock

Early goal-directed therapy is recommended in international guidelines for the resuscitation of patients presenting with early septic shock. However, adoption has been limited, and uncertainty about its effectiveness remains.

A pragmatic randomized trial with an integrated cost-effectiveness analysis was undertaken in 56 hospitals in England (Mouncey et al, 2015). Patients were randomly assigned to receive either early goal-directed therapy (a 6-hour resuscitation protocol) or usual care. The primary clinical outcome was all-cause mortality at 90 days.

A total of 1260 patients were enrolled, with 630 assigned to early goal-directed therapy and 630 to usual care. By 90 days, 184 of 623 patients (29.5%) in the early goal-directed therapy group and 181 of 620 patients (29.2%) in the usual-care group had died (relative risk in the early goal-directed therapy group 1.01, 95% confidence interval 0.85–1.20, $P=0.90$), for an absolute risk reduction in the early goal-directed therapy group of −0.3 percentage points (95% confidence interval −5.4–4.7).

Increased treatment intensity in the early goal-directed therapy group was indicated by increased use of intravenous fluids, vasoactive drugs, and red-cell transfusions and reflected by significantly worse organ-failure scores, more days receiving advanced cardiovascular support, and longer stays in the intensive care unit.

There were no significant differences in any other secondary outcomes, including health-related quality of life, or in rates of serious adverse events. On average, early goal-directed therapy increased costs, and the probability that it was cost effective was below 20%.

In patients with septic shock who were identified early and received intravenous antibiotics and adequate fluid resuscitation, haemodynamic management according to a strict early goal-directed therapy protocol did not lead to an improvement in outcome.

Mouncey PR, Osborn TM, Power GS et al for the ProMISe Trial Investigators (2015) Trial of early, goal-directed resuscitation for septic shock. *N Engl J Med* **372**: 1301–11 (doi: 10.1056/NEJMoa1500896)

Global study finds rabies causes 160 deaths every day

A global study on canine rabies (Hampson et al, 2015) has found that 160 people die every single day from the disease. The report is the first study to consider the impact in terms of deaths and the economic costs of rabies across all countries. Although the disease is preventable, the study says that around 59 000 people die every year of rabies transmitted by dogs.

Dr Katie Hampson, Reader, Institute of Biodiversity Animal Health and Comparative Medicine, University of Glasgow, Glasgow

The multi-author study, by the Global Alliance for Rabies Control's Partners for Rabies Prevention Group, also shows that annual economic losses resulting from the disease are around US$8.6 billion, mostly as a result of premature deaths, but also because of spending on human vaccines, lost income for victims of animal bites and other costs.

Led by Dr Katie Hampson of the University of Glasgow, the study is the first to estimate the impact of canine rabies and the extent of control efforts in every country in the world.

Dr Hampson explained: 'The breadth of data used in this study, from surveillance reports to epidemiological study data to global vaccine sales figures, is far greater than ever analysed before, allowing this more detailed output.'

The study finds that overwhelmingly the greatest risk of canine rabies is in the poorest countries; the death rate (deaths/100 000 people) is highest in countries in sub-Saharan Africa, while India has the highest number of fatalities, with over 20 000 human deaths annually. The proportion of dogs vaccinated is far below that necessary to control the disease across almost all countries of Africa and Asia.

Rabies is close to 100% fatal, but it is also almost 100% preventable, and the best, most cost-effective way of preventing canine rabies is by vaccinating dogs. This needs to be supplemented by improving access to human vaccines.

Hampson K, Coudeville L, Lembo T et al on behalf of the Global Alliance for Rabies Control Partners for Rabies Prevention (2015) Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* **9**(4): e0003709 (doi: 10.1371/journal.pntd.0003709)

Increasing awareness of substance misuse in older adults

Only 6–7% of high-risk people with substance misuse problems over 60 years of age receive the treatment that they require. Although older people are less likely to complain of a substance problem and are more likely to have mild dependence, they are also more likely to be motivated to abstain when compared with younger adults.

A Cross-Faculty Report from the Royal College of Psychiatrists (2015) aims to introduce professionals who have not had the benefit of systematic training in substance misuse, particularly those in old age psychiatry and geriatric medicine, to this developing and challenging field.

The report outlines the key components of age-sensitive treatment: a comprehensive biopsychosocial assessment, the development of treatment plans and appropriate goals, regular monitoring, and the management of comorbid conditions such as pain, cognitive impairment and depression.

It also addresses how the most common comorbid conditions that influence treatment outcome can be better managed by protocols for referral to addiction and geriatric services.

Royal College of Psychiatrists (2015) Substance misuse in older people: an information guide. Older Persons' Substance Misuse Working Group. Cross-Faculty Report OA/AP/01. www.rcpsych.ac.uk/pdf/Substance%20misuse%20in%20Older%20People_an%20information%20guide.pdf (accessed 30 April 2015)

Links between adult height and risk of coronary artery disease

The nature and underlying mechanisms of an inverse association between adult height and the risk of coronary artery disease are unclear.

A genetic approach was used to investigate this, looking at 180 height-associated genetic variants (Nelson et al, 2015).

The association between a change in genetically determined height of 1 standard deviation (6.5 cm) and the risk of coronary artery disease was tested in 65 066 cases and 128 383 controls.

Using individual-level genotype data from 18 249 people, the risk of coronary artery disease associated with the presence of various numbers of height-associated alleles was also examined.

A relative increase of 13.5% (95% confidence interval 5.4–22.1, $P<0.001$) in the risk of coronary artery disease was seen per 1 standard deviation decrease in genetically determined height.

Of the risk factors studied, significant associations were only seen with levels of low-density lipoprotein cholesterol and triglycerides. Several overlapping pathways involving genes associated with both development and atherosclerosis were identified.

There is a primary association between a genetically determined shorter height and an increased risk of coronary artery disease, a link that is partly explained by the association between shorter height and an adverse lipid profile. Shared biological processes that determine achieved height and the development of atherosclerosis may explain some of the association.

Nelson CP, Hamby SE, Saleheen D et al, for the CARDIoGRAM+C4D Consortium (2015) Genetically determined height and coronary artery disease. *N Engl J Med* **372**: 1608–18 (doi: 10.1056/NEJMoa1404881)