

One in eight 5–19-year-olds had a mental disorder in 2017

One in eight (12.8%) children and young people aged between 5 and 19 years, surveyed in England in 2017, had a mental disorder according to a new report (<https://digital.nhs.uk/data-and-information/publications/statistical/mental-health-of-children-and-young-people-in-england/2017/2017>).

Mental Health of Children and Young People in England, 2017, published by NHS Digital, collected information from 9117 children and young people and combined information (depending on their age) from children and young people or their parents and teachers.

Mental disorders were grouped into four broad categories: emotional, behavioural, hyperactivity and other less common disorders. Emotional disorders have become more common in 5–15-year-olds – going from 4.3% in 1999, to 3.9% in 2004 to 5.8% in 2017.

All other types of disorder, have remained similar in prevalence for this age group since 1999.

The report also looked at other aspects of the lives of the children and young people surveyed, including – for the first time – social media, bullying and cyberbullying.

Flu hospitalizations in at-risk groups costs NHS £510 million over 5 years

Analysis of 5 years of Hospital Episodes Statistics data, by a team from Sanofi Pasteur, shows the cost impact of flu hospitalizations alone in people with chronic heart disease, chronic respiratory disease or diabetes was £510 million over a 5-year period (<https://tools.ispor.org/ScientificPresentationsDatabase/Presentation/88441>).

A flu hospitalization significantly increased the average number of inpatient bed days for patients in these high-risk groups, to 47 from 27, raised the likelihood of hospital readmissions and raised the cost of treating these patients by over 50%.

Cancer treatments may affect cognitive function by accelerating biological ageing

Cancer treatments are suspected to accelerate certain ageing processes in the body. A new study has found that indicators of such biological ageing correlate with declines in cognitive function in women who had undergone breast cancer treatment several years earlier (Carroll et al, 2018). The findings point to an ageing-like effect of cancer treatments and further connect this to cognitive decline.

Certain treatments for breast cancer, including radiation and some chemotherapy, work by damaging the DNA of cancer cells, but they can also damage the DNA of normal cells, which can contribute to accelerated biological ageing.

To examine whether indicators of biological ageing are related to cognitive function in breast cancer survivors, Dr Judith E Carroll, Associate Professor of Psychiatry, of the UCLA Cousins Center for Psychoneuroimmunology and the Semel Institute for Neuroscience and Human Behavior, and her colleagues evaluated 94 women who had been treated for breast cancer 3–6 years earlier. Indicators of biological ageing included elevated levels of DNA damage,



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reduced telomerase enzymatic activity, and shorter telomere length in certain blood cells.

Women who had previously been treated for breast cancer who had both higher DNA damage and lower telomerase activity had lower executive function scores. In addition, lower telomerase activity was associated with worse attention and motor speed. Telomere length was not related to any of the neurocognitive domains.

‘These findings are important because they provide further information about what might be happening after cancer treatment that impacts cognitive decline

in some individuals. This information can inform future research and may lead to new interventions to prevent these cognitive declines,’ said Dr Carroll. ‘The work is novel by identifying key factors in biological ageing and connecting them to cognitive function, which initiates new avenues of research.’

Carroll JE, Van Dyk K, Bower JE et al. Cognitive performance in survivors of breast cancer and markers of biological aging. *Cancer*. 2018 26 Nov. <https://doi.org/10.1002/cncr.31777>

Mepolizumab reduces severe attacks and improves control in patients with severe eosinophilic asthma

Results from a long-term open-label safety and efficacy study of Nucala (mepolizumab), a biologic treatment for patients with severe eosinophilic asthma, showed that treatment with mepolizumab had a safety profile similar to previous shorter placebo-controlled studies, when patients received injections of mepolizumab for an average of 3.5 years and a maximum of 4.5 years (Khatiri et al, 2018).

Patients received 100 mg subcutaneous mepolizumab every 4 weeks plus standard of care until a protocol-defined stopping criterion was met. Safety endpoints included frequency of adverse events, serious adverse events and adverse events of special interest. Efficacy endpoints included annualized exacerbation rate, changes from baseline in Asthma Control Questionnaire-5 score and

blood eosinophil counts. Immunogenicity was also assessed.

Patients with severe eosinophilic asthma who were treated with mepolizumab had significant reductions in asthma exacerbations and improvements in the control of their asthma symptoms. The authors concluded that following long-term use in patients with severe eosinophilic asthma, mepolizumab maintains clinical effectiveness and continues to demonstrate a favourable safety profile, with no evidence of inducing neutralizing antibodies.

Khatiri S, Moore W, Gibson PG et al. Assessment of the long-term safety of mepolizumab and durability of clinical response in patients with severe eosinophilic asthma. *J Allergy Clin Immunol*. 2018 Oct 22. pii: S0091-6749(18)31479-9. <https://doi.org/10.1016/j.jaci.2018.09.033>

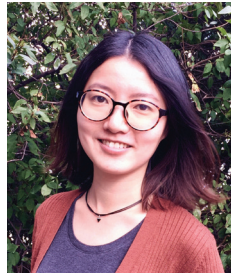
Bullying and violence at work increases the risk of cardiovascular disease

People who are bullied at work or experience violence at work are at higher risk of heart and brain blood vessel problems, including heart attacks and stroke, according to the largest prospective study to investigate the link (Xu et al, 2018).

Although the study is observational and therefore can only show that there is an association between workplace bullying or violence and cardiovascular problems, the researchers say their results are robust and have important implications for employers and national governments.

The researchers looked at data from 79 201 working men and women in Denmark and Sweden, aged 18–65 years, with no history of cardiovascular disease. Participants were asked about bullying and violence in the workplace and how frequently they experienced these. Information on the number of cases of heart and brain blood vessel disease and deaths was obtained from nationwide registries.

Nine per cent of participants reported being bullied at work and 13% reported experiencing violence or threats of violence



Ms Tianwei Xu, PhD Student, Department of Public Health, University of Copenhagen, Denmark

at work in the past year. After adjusting for age, sex, country of birth, marital status and level of education, the researchers found that those who were bullied or experienced violence (or threats of violence) at work had a 59% and 25% higher risk of cardiovascular disease respectively compared to people who were not exposed to bullying or violence. The more bullying or violence that was encountered, the greater the risk

of cardiovascular disease.

Ms Tianwei Xu, a PhD student in the Department of Public Health, University of Copenhagen, Denmark, who led the study, said: 'If there is a causal link between bullying or violence at work and cardiovascular disease, then the removal of workplace bullying would mean we could avoid 5% of all cardiovascular cases, and the eradication of violence at work would avoid more than 3% of all cases.'

Xu T, Magnusson Hanson LL, Lange T et al. Workplace bullying and workplace violence as risk factors for cardiovascular disease: a multi-cohort study. *Eur Heart J*. 2018 Nov 19. <https://doi.org/10.1093/eurheartj/ehy683>

Weight during adolescence may affect risk of developing pancreatic cancer in adulthood

New research has linked adolescent obesity with up to a four-fold increased risk of developing pancreatic cancer later in life (Levi et al, 2018). The results also suggest that overweight and even higher weight within the 'normal' weight range in men may increase the risk of pancreatic cancer in a graded manner.

Pancreatic cancer is the sixth most common cause of cancer-related deaths in the world, and studies have linked adult obesity with an increased risk for its occurrence. To uncover any potential associations with adolescent weight, Dr Zohar Levi of Rabin Medical Center and Tel Aviv University, and his colleagues analysed 1 087 358 Israeli Jewish men and 707 212 Jewish women who underwent a compulsory physical examination between the ages of 16 and 19 years from 1967 to 2002. Pancreatic cancer incidence through

2012 was identified by linkage to the Israeli National Cancer Registry.

Over a median of 23.3 years of follow up, 551 new cases of pancreatic cancer were identified, including 423 cancers among men and 128 cancers among women. Compared with normal weight, obesity was associated with a 3.67-times higher cancer risk among men and a 4.07-times higher risk among women.

Among men, high-normal body mass index and overweight were associated with 49% and 97% higher risks of cancer respectively, compared with low-normal body mass index.

Levi Z, Rottenberg Y, Twig G et al. Adolescent overweight and obesity and the risk for pancreatic cancer among men and women: a nationwide study of 1.79 million Israeli adolescents. *Cancer*. 2018 Nov 12. <https://doi.org/10.1002/cncr.31764>

Workforce challenges are a greater threat to health services than funding

A joint briefing from the Health Foundation, The King's Fund and the Nuffield Trust (<https://www.health.org.uk/sites/default/files/upload/publications/2018/The-health-care-workforce-in-England.pdf>) highlights the scale of workforce challenges facing the health service and the threat this poses to the delivery and quality of care over the next 10 years.

Galcanezumab approved for preventive treatment of migraine in adults

Galcanezumab (Emgality), a once-monthly monoclonal antibody injection, has been approved for preventive treatment of migraine in adults. Galcanezumab blocks the calcitonin gene-related peptide receptor implicated in migraine attacks, and significantly reduces the number of migraine headache days per month.

Nearly half of all mouth cancer cases diagnosed when disease is most advanced

The Oral Health Foundation State of Mouth Cancer UK Report (<https://www.dentalhealth.org/stateofmouthcancer>) reveals that nearly half (45%) of all mouth cancer cases are diagnosed when the cancer is at its most advanced. The incidence of mouth cancer in the UK has grown by 49% in just the last 10 years – there were just under 8500 cases diagnosed last year.

Adding mirtazapine for treatment-resistant depression is not more effective than a single antidepressant

Psychiatrists increasingly combine mirtazapine with an SSRI (selective serotonin-reuptake inhibitor) or SNRI (serotonin-noradrenaline reuptake inhibitor) antidepressant for patients whose depression does not respond to a single antidepressant. A large clinical trial looked at the effectiveness of adding mirtazapine to an SSRI or SNRI in patients who remain depressed after at least 6 weeks of conventional (SSRI or SNRI) antidepressant treatment (<https://doi.org/10.1136/bmj.k4218>).

All 480 patients continued to take their SSRI or SNRI and were randomly assigned to also take either mirtazapine or a placebo. They were followed up at 12, 24 and 52 weeks to see whether their depression had improved. At 12 weeks just under 40% of patients had responded to treatment.

The study found that this combination was no more effective in improving depression than placebo and also found that patients taking mirtazapine in combination with another antidepressant had more adverse effects and were more likely to stop treatment than those in the placebo group.

Residual inflammation risk affects outcomes in patients after percutaneous coronary intervention

Patients who have persistently high levels of inflammation following percutaneous coronary intervention for coronary artery disease are significantly more likely to die from any cause or have a heart attack within 1 year (Kalkman et al, 2018).

Residual inflammatory risk refers to the risk of further heart and blood vessel problems caused by vascular inflammation in patients with known coronary artery disease. High sensitivity C-reactive protein is used as an indicator of the level of risk. Until now it has not been known what proportion of patients treated with percutaneous coronary intervention to widen blocked arteries have persistent high residual inflammatory risk, and what effect it might have on patient outcomes.

Researchers led by Professor Roxana Mehran, from the Mount Sinai Medical Center, New York, USA, looked at data from 7026 patients who had received percutaneous coronary intervention at Mount Sinai Hospital between 2009 and 2016.

Patients were stratified into four groups according to their residual inflammatory risk: high residual inflammatory risk was defined as having levels of high sensitivity C-reactive protein of more than 2 mg/litre of blood.



Professor Roxana Mehran, Professor of Medicine (Cardiology) and Population Health Science and Policy, Icahn School of Medicine at Mount Sinai, Mount Sinai Medical Center, New York, USA

Of the 7026 patients, 2654 (38%) had persistent high residual inflammatory risk, 719 (10%) had increased residual inflammatory risk, 1088 (15%) had attenuated residual inflammatory risk, and 2565 (37%) had persistent low residual inflammatory risk. One year after percutaneous coronary intervention, death from any cause had occurred in 2.6% of persistent high residual inflammatory risk patients, 1% of increased residual inflammatory risk patients,

0.3% of attenuated residual inflammatory risk patients and 0.7% of persistent low residual inflammatory risk patients.

After adjusting for factors that could affect the results, such as age, gender and body mass index, the researchers found that compared to patients with persistent low residual inflammatory risk, those with persistent high residual inflammatory risk were more than three times more likely to die within 1 year from any cause and were 1.6 times as likely to have a heart attack.

Kalkman DN, Aquino M, Claessen BE et al. Residual inflammatory risk and the impact on clinical outcomes in patients after percutaneous coronary interventions. *Eur Heart J*. 2018 Oct 25. <https://doi.org/10.1093/eurheartj/ehy633>

Link between air pollution and intellectual disabilities in children

British children with intellectual disabilities are more likely than their peers to live in areas with high outdoor air pollution, according to a new study (Emerson et al, 2018).

The findings come from a secondary analysis of data extracted from the UK's Millennium Cohort Study, a nationally representative sample of more than 18 000 UK children born in 2000 to 2002.

Averaging across ages, children with intellectual disabilities were 33% more likely to live in areas with high levels of diesel particulate matter, 30% more likely to live in areas with high levels of nitrogen

dioxide, 30% more likely to live in areas with high levels of carbon monoxide, and 17% more likely to live in areas with high levels of sulphur dioxide.

The authors note that intellectual disability is more common among children living in more socioeconomically deprived areas, which tend to have higher levels of air pollution; however, exposure to outdoor air pollution may impede cognitive development, thereby increasing the risk of intellectual disability.

'We know that people with intellectual disabilities in the UK have poorer health and die earlier than they should. This

research adds another piece to the jigsaw of understanding why that is the case and what needs to be done about it,' said lead author Dr Eric Emerson, from the Division of Health Research, Faculty of Health and Medicine, Lancaster University, Lancaster and the Centre for Disability Research and Policy, Faculty of Health Sciences, University of Sydney, Australia.

Emerson E, Robertson J, Hatton C, Baines S. Risk of exposure to air pollution among British children with and without intellectual disabilities. *J Intellect Disabil Res*. 2018 Nov 20. <https://doi.org/10.1111/jir.12561>

'Personalized scheduling' of radiotherapy for patients with breast cancer might reduce toxicity

A new clinical study (Johnson et al, 2018) has revealed the pivotal role that changing the time of day that a patient receives radiotherapy could play in altering radiotherapy toxicity. The findings could be used to optimize the treatment to reduce side effects for some breast cancer patients.

The prediction can be personalized by using the genetics that govern circadian rhythm. The research found that, by identifying differences in two genes that help govern the body's circadian rhythm, it may be possible to predict which patients may benefit from receiving their radiotherapy in the afternoon. This could reduce the side effects in some of the 30 000 breast cancer patients treated with radiotherapy in the UK each year.

In a study of 879 breast cancer patients across two independent cohorts (LeND and REQUITE), the team found that patients with variations of two genes in particular, called PER3 and NOCT, were more at risk of side effects if given radiotherapy in the morning.

Patients with these genetic variants were found to be at a greater risk of long-term side effects, including permanent thickening under the skin and chronic pain, and short-term

effects such as temporary red, peeling skin, if they were treated in the morning compared to the afternoon.

Professor Paul Symonds, a consultant oncologist at Leicester's Hospitals and professor of clinical oncology at the University of Leicester said: 'Our study found that some patients with a particular genetic profile are more at risk of side effects if given radiotherapy in the morning. This happens because the skin of these particular patients divides earlier in the day than others and dividing cells are more easily damaged by X-rays. This could allow an easy way to personalise treatment just by recommending what time of day a patient should be treated.'

Professor Symonds emphasized: 'Around 90% of operable breast cancer patients are treated with radiotherapy so radiotherapy toxicity is a very real and important issue for these patients.'

Johnson K, Chang-Claude J, Critchley AM et al; REQUITE Consortium. Genetic variants predict optimal timing of radiotherapy to reduce side-effects in breast cancer patients. *Clin Oncol (R Coll Radiol)*. 2018 Oct 30. pii: S0936-6555(18)30462-X. <https://doi.org/10.1016/j.clon.2018.10.001>

Breakthrough in treatment of restless legs syndrome

Until now it was thought that restless legs syndrome is caused by genetic, metabolic and CNS mechanisms, but new research has shown that it is not only the CNS but also the nerve cells targeting the muscles themselves that are responsible (Czesnik et al, 2018).

New research indicates that the involuntary leg movements in restless legs syndrome are caused by increased excitability of the nerve cells that supply the muscles in the leg, which results in an increased number of signals being sent between nerve cells. Targeting the way messages are sent between nerve cells to reduce the number of messages to normal levels may help prevent the symptoms of restless legs syndrome occurring. This could be achieved by new drugs that block the ion channels that are essential for the communication between nerve cells.

The research conducted by the University of Göttingen in conjunction with the University

of Sydney and Vanderbilt University involved measuring the nerve excitability of motor nerve cells of patients suffering with restless legs syndrome and healthy subjects.

The next step is to investigate the effect of different medications in patients and the effect on restless legs syndrome.

Dr Dirk Czesnik, corresponding author of the study, commented: 'Patients who suffer from restless legs syndrome complain of painful symptoms in the legs leading to sleep disturbances. The mechanisms for restless legs syndrome are still not completely understood. We have shown that also the nerve cells supplying muscles in the leg are responsible and hereby additional drug treatments may be ahead targeting these nerve cells.'

Czesnik D, Howells J, Bartl M et al. It contributes to increased motoneuron excitability in restless legs syndrome. *J Physiol*. 2018 14 Nov. <https://doi.org/10.1113/JP275341>

Machine learning for real-time prediction of complications in critical care could improve care

The large amount of clinical signals in intensive care units can easily overwhelm health-care personnel and can lead to treatment delays, suboptimal care or clinical errors. A retrospective study applied deep machine learning methods to predict severe complications during critical care in real time after cardiothoracic surgery (Meyer et al, 2018).

Deep learning methods (recurrent neural networks) were used to predict severe complications (mortality, renal failure with a need for renal replacement therapy, and postoperative bleeding leading to operative revision) in post cardiothoracic care in real time. Adult patients who underwent major open heart surgery in a German tertiary care centre formed the main derivation dataset.

The accuracy and timeliness of the forecasts was measured and compared to the predictive quality of established standard-of-care clinical reference tools. Results were externally retrospectively validated with 5898 cases from the published MIMIC-III dataset.

The deep learning models yielded accurate predictions which significantly outperformed the standard clinical reference tools, even immediately after patient admission to the intensive care unit.

The observed improvements in prediction for these clinical outcomes have the potential to improve critical care. These findings are noteworthy in that they exclusively use routinely collected clinical data, without the need for any manual processing. This is encouraging for prospective deployment in critical care settings to direct attention towards patients who are most at risk.

Meyer A, Zverinski D, Pfahringer B et al. Machine learning for real-time prediction of complications in critical care: a retrospective study. *Lancet Respir Med*. 2018. 6(12): 905–914. [https://doi.org/10.1016/S2213-2600\(18\)30300-X](https://doi.org/10.1016/S2213-2600(18)30300-X)