New hope for lipid profile chat

Looking for something new to spice up those cholesterol consultations? Lipoprotein(a) might be just what you’re looking for. It’s thought to be a marker of cardiovascular disease and therefore a candidate for new preventive treatments. A phase 2, dose-finding trial examined the effect of olpasiran (which reduces lipoprotein(a) synthesis in the liver) on lipoprotein(a) levels.

This small study, which recruited 281 people with established atherosclerotic cardiovascular disease and high lipoprotein(a) levels, did indeed find a dose dependent reduction in lipoprotein(a) levels in those who received olpasiran. But it’s early days: will this reduction translate into clinically meaningful endpoints? Until then, it’s back to the familiar “good and bad cholesterol” and “let’s take a look at your overall risk” chat.

*Cite this as:* BMJ 2022;379:o2804

What goes up must come down

Using 11 variables commonly available in patient records, such as body mass index and blood pressure, researchers were able to create a prediction score that would identify people at greater risk of having an ascending aortic aneurysm. Their model had a number needed to screen somewhere between 1.8 and 22.8, depending on which cohort it was tested against and the sensitivity threshold.

But how many of those diagnosed would actually benefit? A cut-off of 4 cm was chosen as the lower bound of moderate ascending aortic dilatation because it had been used in other studies. However, surgery isn’t indicated unless aneurysms are much bigger (>5.5 cm according to European Society of Cardiology guidelines, with some exceptions such as Marfan syndrome and rapid growth), and there is no effective medical treatment to slow progression—or, as the authors put it, “evidence for effectiveness [of medical treatment] in nonsyndromic aneurysm remains understudied.”

*Cite this as:* JAMA 2022;328:19701

Covid vaccine match of the day

The New England Journal of Medicine gets into the football World Cup spirit with some research from Qatar. Like the World Cup, this cohort study examining the effects of covid vaccination in children involved a lot of matches: matching unvaccinated and vaccinated children and waiting to see which of the matched pair scores the own goal of getting covid. It found that vaccination was associated with modest, rapidly waning protection from the omicron variant in 5-11 year olds, with only 2.1% of the vaccinated children in this age group getting covid in the 110 day follow-up period, compared with 2.4% of unvaccinated controls.

There was a larger reduction in covid rates in adolescents, who received a higher 30 μg dose of the BNT162b2 vaccine—but the benefits of vaccination in a pre-omicron cohort were much greater, estimated at 95%, compared with 30% in the omicron era.

*Cite this as:* N Engl J Med doi: 10.1056/NEJMoa2210058

Monoclonal antibodies for malaria prevention

Could monoclonal antibodies be effective in preventing malaria? Results from a phase 2 study of CIS43LS, a monoclonal antibody against the sporozoites of *Plasmodium falciparum*, show some promise, but there may still be a long way to go. Laboratory diagnosed *P falciparum* infection was used to determine efficacy among the 330 people enrolled onto the study in Mali—episodes of clinical malaria were not recorded.

The higher of the two doses studied had an efficacy of 88% at six months compared with placebo. Further studies will tell us how this translates into prevention of clinical malaria, but the need for a 30 minute intravenous infusion may limit its potential to be rolled out for widespread use.

*Cite this as:* N Engl J Med doi: 10.1056/NEJMoa2206966

Ankle replacement or arthrodesis?

It must be strange being a participant of the TARVA trial, where the decision to have either a total ankle replacement or arthrodesis was made by a sophisticated computer version of the toss of a coin. It’s no wonder that, of the 933 people with end stage ankle osteoarthritis who were eligible for the study across 17 sites in the UK, only 303 agreed to take part.

A year after surgery, both groups of patients showed a considerable improvement in the primary endpoint for the study—a Manchester-Oxford Foot Questionnaire walking/standing domain score—but there was no significant difference in these scores between the two groups.

*Cite this as:* Ann Intern Med doi:10.7326/M22-2058
Towards net zero healthcare

Rachel Stancliffe, Aarti Bansal, Georgina Sowman, Frances Mortimer

The climate footprint of healthcare worldwide is equivalent to 4.4% of global net carbon emissions

LIMITATIONS TO EVIDENCE ON SUSTAINABLE HEALTHCARE

- A dearth of standards for measurement and reporting means that studies mostly use different boundaries and are of variable quality
- The contextual element of the evidence makes comparison between different interventions difficult. Because the result of interest is multi-faceted (at its simplest, patient outcome per resource input), it is more difficult to measure than most clinical research, which focuses on outcomes alone. Sustainable healthcare research bears more resemblance to health economics research, but with the inclusion of environmental metrics alongside financial cost
- When studying an intervention or procedure, as well as assessing the material object itself (a drug or tool), assessment of its production and implementation—in terms of materials, people, energy use, water use, and staff and patient time—is also needed, which adds complexity

What is the problem?

The direct impacts of the climate emergency, such as heatwaves, wildfires, and flooding, affect human health through increased air pollution and by changing the distributions of vector borne, diarrhoeal, and other infections. Indirectly, climate instability (including fast rising temperatures and changing rainfall patterns) causes failed harvests, shortages of food and water, malnutrition, and increased conflict over scarce resources.

What is net zero?

Net zero is an internationally agreed goal for avoiding worsening global heating in the second half of the 21st century. As a concept, net zero aims to balance the quantities of greenhouse gases (also referred to as carbon emissions because they mostly comprise carbon dioxide) released into and removed from the atmosphere, that is, to achieve carbon neutrality or net zero.

What is the evidence?

Evidence showing that climate change affects health was summarised over a decade ago. Now, we need research that prioritises solutions. Many studies for measuring and achieving sustainability in healthcare are still at the stage of defining frameworks and presenting data based on economic input-output methodology, but more specific evidence is also available. Examples include studies of how one intervention differs from another in terms of carbon emissions, patient outcomes, and other factors, including several life cycle analyses and systematic reviews.
Principles of sustainable clinical practice with description of how it is relevant to the above fictional case, and other clinical examples

<table>
<thead>
<tr>
<th>Principle</th>
<th>Relevance to the fictional case example</th>
<th>Other clinical examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention</td>
<td>Reduced air pollution exposure and increased physical activity in high quality green spaces</td>
<td>Early identification of patients with declining kidney function can reduce the number of people going on to require carbon intensive dialysis</td>
</tr>
<tr>
<td>Patient empowerment</td>
<td>Person centered discussion to discover what matters to patients helps to develop self-management approaches to long term conditions</td>
<td>Patients with good inhaler technique need fewer inhalers and achieve better asthma control</td>
</tr>
<tr>
<td>Lean care systems</td>
<td>Reducing the need for medical appointments and medicines saves healthcare resources; patients may instead draw on wider support systems (e.g., through a social prescriber, use of local green spaces, and social groups)</td>
<td>Adherence to prescribing guidelines for flupentixol decanoate depot antipsychotic by reducing the frequency of doses from 2 weekly to 6 weekly saves travel, equipment, money, and time</td>
</tr>
<tr>
<td>Low carbon alternatives</td>
<td>Medicines are one of the most carbon intensive elements of the health system. When clinically appropriate, ensure evidence based non-medication alternatives are available for shared decision making with patients, such as green social prescribing or brief advice on physical activity</td>
<td>The carbon footprint of one hour of general anaesthetic using inhaled desflurane is equivalent to driving 190 miles, compared with only four miles using inhaled sevoflurane</td>
</tr>
</tbody>
</table>

What can clinicians do?

Healthcare practitioners can participate in innovation, adoption, and embedding of low carbon practices. By openly framing the climate emergency as a health crisis, they can inspire sustainable practice in colleagues, the public, and leaders.

Apply sustainable clinical practice principles to daily clinical practice (table)

Healthcare professionals can use The Centre for Sustainable Healthcare (CSH)'s Principles of Sustainable Clinical Practice to improve patient outcomes while minimising the environmental, social, and financial costs:

- **Prevention**—e.g., early identification of patients with declining kidney function can reduce the number of people going on to require carbon intensive dialysis.
- **Patient empowerment and self-care**—e.g., patients with good inhaler technique need fewer inhalers and achieve better asthma control.
- **Lean care systems**—e.g., adherence to prescribing guidelines for flupentixol decanoate depot by reducing the frequency of doses from two to six weekly saves travel, equipment, money, and time.
- **Low carbon alternatives**—e.g., the carbon footprint of one hour of general anaesthetic is equivalent to driving 190 miles (300 km) using inhaled desflurane compared with only 4 miles (6.5 km) using inhaled sevoflurane.

Despite the research limitations outlined above, a growing evidence base supports the following widely applicable actions:

- Choose reusable instruments instead of single-use varieties.
- Use thorough handwashing instead of gloves for infection control when exposure to blood or other body fluids is not anticipated, in line with NHS guidelines.
- When clinically appropriate and preferred by patients, arrange remote consultations for follow-up.

Agree standard metrics for measuring impacts over time

Clinicians can collaborate with those involved in carbon measurement to suggest and develop standard metrics that routinely measure environmental and social impacts (such as carbon footprint or waste produced per unit of care), and use these to make balanced decisions about progression towards net zero care.

Link sustainability to quality improvement

Actively address sustainability as part of healthcare quality improvement (QI) activities. CSH has developed a sustainable QI approach (see example, fig 2) that allows assessment of sustainable value on potential service changes.

Maximise the theoretical sustainable value of a service or care pathway

In partnership with management colleagues, when improving or redesigning systems (e.g., concerning energy or water use, lower emission transport, home visiting strategies, procurement of low carbon treatments or technologies), weigh up the outcomes for patients and populations against the environmental, social, and financial costs.

Use decarbonisation actions to help address health inequality

As outlined in the 2020 Marmot Review, prioritising preventive health, encouraging the growth of food locally, and encouraging access to green space can all contribute to reducing inequalities. The principles are applicable globally.

Case continued

When asked what matters most to her, the patient says that she is currently inactive, with several barriers to everyday exercise—she drives to school and work and finds few opportunities or incentives to be active at work. With her permission, the GP discusses the benefits of physical activity and healthy eating. The patient decides that three times a week she will get up 20 minutes earlier than usual, park away from the children’s school, and walk that distance through a park with her children.

The patient is pleased that she will spend less time in a car in traffic, and that she and her children will be exposed to less air pollution, spend active time together in a green space, and benefit from being active at work. She is introduced to a local walking group and runs in the park on Saturdays.

The patient is referred to the practice’s social prescriber, who further supports her, and shares information and maps of safe local walking routes through nature.

The table (middle column) shows how the principles of sustainable clinical practice care have been applied to this case.

Figure 1 shows the wider population level benefits that may follow from this intervention.
In partnership with management colleagues, when improving or redesigning systems weigh up the outcomes for patients and populations against the environmental, social, and financial costs.
Supporting healthcare workers with work related stress

Lara Shemtob,1,2 Larissa Good,3 Mark Ferris,4 Kaveh Asanati,1,2 Azeem Majeed1,2

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A registrar notices that a foundation year two doctor on her team has become withdrawn. He is cynical and hostile in conversation but seems to need more support in basic tasks, frequently asking her to double check his prescribing. Work has been chaotic for everyone, and she is beginning to find his slow pace frustrating.

Two months later, he presents to his GP with sleep disturbance, dreading work, and feeling constantly on edge. He has been this way for weeks but felt afraid to ask for help. He thinks he needs time off work but is worried about letting his team down. He felt exhausted after four months of rota gaps when he couldn’t get enough time off. Demands seem insatiable with a constantly bleeping pager, strained relationships with seniors, and a feeling that he has no control over his workload.

Mental illness accounts for about 25% of days lost as sickness absence by the NHS workforce

We can all support colleagues with work related mental illness—whether as a colleague, manager, or simply as their GP. Observational studies globally suggest that around 30-50% of the healthcare workforce have experienced work related stress or burnout in the past three years. Mental illness accounts for about 25% of days lost as sickness absence by the NHS workforce; over 40% of staff reported feeling unwell as a result of work related stress in the 2020 NHS staff survey. Workforce stress exacerbates challenges with staff retention and performance, affecting teams, services, and entire health systems.

This article outlines the role that GPs and other support services, employers, and colleagues can play in supporting a healthcare worker with work related stress. Collaboration across these roles is essential in successfully addressing work related stress.

WHAT YOU NEED TO KNOW

- Work related stress is an important problem in the NHS workforce. Addressing the underlying cause, which may relate to factors such as workplace demand, relationships, and support, is necessary for sustained recovery and full engagement with work
- Healthcare workers may experience guilt or shame due to stigma, preventing them from seeking help if they experience work related mental illness
- Time off work and workplace changes to control the triggers may be necessary to allow recovery and sustainable return to work
- Healthcare workers experiencing work related stress can seek support from colleagues, their own GP, occupational health, and specialised services for healthcare workers such as local mental health and wellbeing hubs and NHS Practitioner Health

HOW PATIENTS WERE INVOLVED IN THIS ARTICLE

One of our author team has overcome a period of work related stress during clinical training and highlighted the invaluable role of peer and manager recognition and support and the system-wide consequences of work related stress.

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Box 1 | Signs and symptoms of work related ill health

Work related stress
- Stressed or aggrieved about work
- Reduced motivation or confidence
- Withdrawn, tearful, sensitive, agitated, or aggressive

Burnout
- Physical and mental exhaustion
- Cynicism towards work
- Reduced perception of accomplishments at work

Post-traumatic stress disorder
- Flashbacks
- Avoidance
- Hyperarousal

Moral injury
- Guilt, shame, anger
- Self criticism, feelings of worthlessness
Identifying causes

Identifying a clear diagnosis is not essential in the first instance, either for a GP in a consultation or a manager or colleague providing support. What is more important is listening, providing validation, considering and managing risk, signposting to further support, and ensuring the healthcare worker has follow-up. Healthcare workers may experience a spectrum of work related ill health including stress, moral injury, burnout, and specific mental illnesses such as post-traumatic stress disorder (PTSD), anxiety, or depression. These all overlap, but inquiring about the nature and duration of symptoms, the effect on functioning, and specific workplace triggers helps to differentiate between them. Box 1 lists some of the symptoms and signs that we commonly see in different forms of work related ill health.

Burnout results from unmanaged chronic workplace stress. Workers with public-facing roles undertake emotional labour, regulating their feelings to meet the emotional requirements of their job, a risk factor for burnout. Healthcare workers are exposed to traumatic situations at work, including caring for very unwell patients with inadequate resources. In addition to burnout, this can trigger PTSD.

Moral distress occurs after violation of an individual’s moral code and, when long term effects on mental state and functioning ensue, is termed moral injury. For healthcare workers, this can be due to resource constraints limiting their ability to deliver the quality of care they expect to provide. In a 2021 survey by the British Medical Association (BMA), 51% of just under 2000 doctors said moral injury resonated with their experiences at work. The most commonly reported contributing reasons were staff shortages and mental fatigue.

Box 2 | Factors in assessing occupational contribution to stress in healthcare workers

- **What are their working hours and shift pattern?**
- **Do they work overtime?**
- **What is the breakdown of component tasks in their working day (such as ward round, clinic, on calls)?**
- **How does each aspect of their role map to stress and their health and function?**
- **Is there any requirement to work above their clinical competency?**
- **Do their mental state improve away from work?**
- **Do they feel supported by colleagues and seniors?**
- **Has mental ill health or stress been an issue in the wider team?**

Is the mental ill health work related?

If work is implicated as a cause of stress or burnout, explore which aspects of work are responsible. Box 2 lists some of these factors, which will differ depending on job roles. Non-work factors, such as financial pressure or stressors in family life are also important to explore.

Box 3 | HSE management standards

- **Demands**—Is workload realistic compared with the resources and time to do it?
- **Control**—Does the individual have autonomy in how they work?
- **Support**—Are the organisation/managers/peers supportive to the individual worker?
- **Relationships**—Is conflict, inappropriate behaviour, or confrontation common?
- **Role**—Are employees and the organisation clear about what each role involves?
- **Change**—Is organisational change managed and communicated well?

Considering time off work and the fit note

When occupational factors are implicated in the cause of ill health, time off is unlikely to be a long solution, but it can be an important part of recovery. Healthcare workers can face barriers to taking time off, including pressure from managers, colleagues, and themselves, putting patients’ needs before their own. Around half of NHS staff report presenteeism, attending work despite not being well enough to perform their duties. Raising the issue of time off work is important; many healthcare workers presenting to their GP with work related stress may be reluctant to bring it up or feel a sense of guilt or failure. Stigma is a well documented barrier to those living with mental illness seeking help.

A decision to recommend sickness absence should be based on whether the healthcare worker’s mental health may affect patient care or colleagues and whether time away from work may facilitate recovery. Many symptoms of work related ill health, including impaired concentration and fatigue, can interfere with professional standards of conduct and safety. Willingness to seek help, demonstrating insight, cooperation, and communication may be all that is required from a healthcare worker living through a period of ill health.

Adjustments to hours and duties can help keep individuals working through a period of ill health. The longer somebody is off work through ill health, the less likely they are to return. Short review periods for reassessment of functioning, plus frequent but not excessive contact with managers, may help avoid long term sickness absence.

The UK Health and Safety Executive (HSE) has published management standards which provide a framework of factors that contribute to work-related stress (box 3). Sharing these with healthcare workers as risk factors that they can map to their workplace can clarify occupational triggers and facilitate a discussion on addressing them, progressing towards recovery and return to work.

Longstanding workplace stressors are often not acknowledged between a healthcare worker and their manager until functioning deteriorates to the extent that time off is necessary. Fit notes contain a free-text box, which can be used by GPs to communicate with managers about occupational causes and advise early referral to occupational health, where more resources are available to assess work related illness.
Seeking treatment

As well as dealing with workplace triggers, a healthcare worker with work related mental illness may need to seek treatment such as talking therapy and medication, depending on factors such as presentation, availability of services, and personal preference (box 4). The latest NHS people plan prioritised “looking after our people,” leading to more initiatives to improve staff health and wellbeing and provide support for staff with mental ill health. Some of these services can be accessed through work or self referral rather than via general practitioners. Local staff mental health and wellbeing hubs provide a clinical assessment service and referral to other local services, and to NHS Practitioner Health for healthcare workers with needs that cannot be met locally.

Supporting colleagues and self care

Maintaining good relationships with colleagues, even if they become less communicative, can help to identify when they are struggling and support them in seeking help. This may help to address issues earlier and avoid longer term sickness. Often if one individual is experiencing work related stress, the whole team will be exposed to similar triggers, making supporting colleagues even more challenging as we try to manage our own stress, worry about the impact of sickness absence on the team workload, and try to find the time and headspace needed to provide support. Where there are systemic factors leading to high levels of stress within the team, consider which tools and strategies may help to bring about system change (box 5).

Managers may need support in dealing with work related stress in their team and need to have a sound understanding of occupational stress and be empowered to find solutions. If sickness absence is not covered appropriately, it is likely to increase work related stress in the rest of the team. Addressing stress and its risk factors as a long term strategy will help staff retention and productivity, and ultimately have financial as well as human benefits.7

As well as knowing how to support each other, we need the tools to recognise work related ill health in ourselves. Understanding our own triggers, stress responses, and the degree and duration of stress that are difficult to manage and interfere with function can help us to know when to seek help.

Competing interests: None declared.

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Find the full version with references at doi: 10.1136/bmj-2022-070779

The role of occupational health

Occupational health interfaces between employers and employees on issues that affect work and health, usually accessed via referral from a line manager or self referral. The aim is to assess the factors limiting return to work and collaborate to overcome them. For a healthcare worker with work related mental illness, occupational health can advise adjustments to a working schedule that protect against triggers, such as coming off an on-call rota, pausing night shifts, or moving into a supernumerary position.

Where there are high levels of work related mental illness within teams, occupational health can work with managers to assess risk and make wider changes. Occupational health has the resources to work with the healthcare worker to achieve this, and has an understanding of the workplace context, sickness absence policies, and ability to liaise with managers—all beyond the scope of a general practitioner’s role.

### Box 4 | Resources for further support available to healthcare workers in the UK

- NHS England staff mental health and wellbeing hubs
  - 40 sites across England, accessed through self referral or referral from colleagues
  - Rapid clinical assessment for health and social care staff
  - After assessment, they can refer on to local services for further support
- NHS Practitioner Health
  - Doctors and senior staff can self refer
  - Other healthcare workers in England referred by local hubs
  - Assessment and treatment of mental illness and addiction, specialising in the needs of healthcare workers, particularly when confidentiality is a barrier to accessing help
  - Regulated professionals working in health and social care in Scotland have access to the Workforce Specialist Service delivered by NHS Practitioner Health
- Canopi
  - Free confidential service for NHS and social care staff in Wales with access to different levels of support including talking therapies accessible via self referral
  - Employee assistance programmes
  - Available at many hospital trusts through self or manager referral
  - Counselling and mental health support as well as legal and financial advice
- Helplines available to healthcare staff working across the UK
  - Samaritans confidential staff support line: 0800 069 6222
  - FRONTLINE text support service: 85 258
  - Hospice UK bereavement support line relating to loss experienced through work: 0300 303 4434
  - BMA counselling and peer support for doctors, medical students, and their partners and dependents (not conditional on BMA membership): 0330 123 1245
  - Additional NHS helplines for staff working in Scotland
- Intensive Care Society wellbeing resources
- Short summary pages on self care and wellbeing

### Box 5 | Challenging workplace culture that contributes to work related stress

System factors such as demand that outweighs resource, inadequate support, and strained relationships within a team are known to contribute to work related stress. Challenging these is difficult but can help bring about change.

- Acknowledge workplace factors implicated in stress
- Challenge behaviours that cause stress in others
- Challenge systems and cultures that contribute to stress
- Make use of processes such as exception reporting, incident reporting, “guardians of safe working,” and “freedom to speak up guardians”
The study

This review included data from nine high quality studies. In all, they included 4864 people who had been treated for depression at general practices in the UK. Treatment was with medicines, talking therapies, and/or structured exercise. Participants were 42 years old on average, and more than half (67%) were women.

Each individual’s recovery was assessed three to four months after treatment started. The researchers considered four socioeconomic factors: employment status, housing, financial wellbeing, and education. They adjusted results for other factors that might influence recovery (depression severity and duration, anxiety, age, sex, and marital status).

What did this study do?

This review included data from nine high quality studies. In all, they included 4864 people who had been treated for depression at general practices in the UK. Treatment was with medicines, talking therapies, and/or structured exercise. Participants were 42 years old on average, and more than half (67%) were women.

Each individual’s recovery was assessed three to four months after treatment started. The researchers considered four socioeconomic factors: employment status, housing, financial wellbeing, and education. They adjusted results for other factors that might influence recovery (depression severity and duration, anxiety, age, sex, and marital status).

What did it find?

The study found that, three to four months after treatment started:

- People who were unemployed had worse treatment outcomes than people in employment (depression symptom scores were 28% higher)
- People living with family or friends, in hostels, or homeless had worse treatment outcomes than home owners (depression symptom scores were 18% higher)
- People who were experiencing financial difficulties and had no qualification beyond school appeared to have a poorer recovery, but the link was less strong when other factors were taken into account
- Employment and secure housing had an ongoing effect. The researchers saw similar patterns six to eight months, and nine to 12 months after treatment started.

Why is this important?

The authors believe this is the first review to consider the link between socioeconomic factors and recovery from depression across different types of treatment.

The findings can help tailor treatment for depression. In the initial assessment, GPs and other clinicians could ask people with depression about their employment status and housing. GPs might consider increasing the number of appointments offered, or the intensity or duration of treatment.

What’s next?

Future research is needed to explore what types of support would best help people at risk of poor recovery. Studies could investigate the optimal order in which to offer help. It may be that medicines or therapy are more effective for people with unfavourable social circumstances once they have received help with employment or housing, for example. In addition, this group of people might routinely need more intensive treatment strategies, and more regular reviews to adjust their treatment plan according to their progress. They may need a longer follow-up period.

This research did not include people with bipolar depression, other psychotic or personality disorders, neurological conditions, or children under age 16. In addition, some communities were not well represented, for example, people who are homeless or from marginalised backgrounds. Further research in all of these groups is needed.

Competing interests The BMJ has judged that there are no disqualifying financial ties to commercial companies.

Further details of other interests, disclaimers, and permissions can be found on bmj.com

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NIHR ALERTS

Unemployment and insecure housing are linked to less successful treatment for depression

Socioeconomic indicators of treatment prognosis for adults with depression: a systematic review and individual patient data meta-analysis

Buckman JEJ, Saunders R, Stott J, et al

JAMA Psychiatry 2022;79:5

Why was this study needed?

Between 2 and 4 million adults in the UK have depression. Many treatments are effective, but one in two people do not recover with the first treatment they receive. This can prompt them to disengage from services and increase the chance of poor long term outcomes.

The more severe and long term the depression is, the harder it is to treat. Anxiety, marital status, social support, and other factors also have an impact on people’s recovery.

What was this study about?

Individuals whose social circumstances (income, housing, or education, for example) are less favourable are more likely to develop mental health problems such as depression. However, before this study, it was not known how these circumstances affect people’s response to treatment.

The researchers wanted to learn more about the impact of these socioeconomic factors on people’s recovery from depression. Understanding this link could help health and care professionals tailor the support and treatment they offer.

Why is this important?

Understanding the impact of socioeconomic factors on depression treatment outcomes is important. It can help health and care professionals design more effective treatments and support strategies.

What’s next?

Future research is needed to explore what types of support would best help people at risk of poor recovery. Studies could investigate the optimal order in which to offer help. It may be that medicines or therapy are more effective for people with unfavourable social circumstances once they have received help with employment or housing, for example. In addition, this group of people might routinely need more intensive treatment strategies, and more regular reviews to adjust their treatment plan according to their progress. They may need a longer follow-up period.

This research did not include people with bipolar depression, other psychotic or personality disorders, neurological conditions, or children under age 16. In addition, some communities were not well represented, for example, people who are homeless or from marginalised backgrounds. Further research in all of these groups is needed.
A woman in her 30s presented to the obstetric emergency department with fatigue and light headedness in her third pregnancy at 35 weeks’ gestation. Previous pregnancies resulted in an uneventful vaginal delivery and spontaneous pregnancy loss in the first trimester. There was no history of breathlessness, palpitations, fever, weight loss, chronic condition, or substance use disorder, or family history of blood disorders or malignancy. She had been prescribed oral iron and folate (cobalamin) supplementation according to local antenatal guidelines but took these irregularly.

She had a vegetarian diet. The patient had severe pallor, pedal oedema, and a body mass index of 19. Her pulse rate was 110 beats/min, blood pressure 118/70 mm Hg, respiratory rate 14 breaths/min, and oxygen saturation 98% on room air. Cardiorespiratory and neurological examinations were normal. There was no hepatosplenomegaly on palpation. On obstetric examination, there were no signs of fetal distress. The table shows the results of relevant blood tests.

### Relevant blood test results

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/L)</td>
<td>29</td>
<td>117-155</td>
</tr>
<tr>
<td>Platelet count (×10^9/L)</td>
<td>11</td>
<td>150-450</td>
</tr>
<tr>
<td>Reticulocyte count (%)</td>
<td>1</td>
<td>0.2-2.0</td>
</tr>
<tr>
<td>Corrected reticulocyte count (%)</td>
<td>0.08</td>
<td>0.5-2.5</td>
</tr>
<tr>
<td>Total leucocyte count (×10^9/L)</td>
<td>2.43</td>
<td>4-11</td>
</tr>
</tbody>
</table>

Peripheral smear: Normocytic, normochromic erythrocytes with Cabot rings and basophilic stippling, moderate anisopoikilocytosis, leucopenia with hypersegmented neutrophils and reduced platelets, evidence of Howell-Jolly bodies on erythrocyte membrane, and no atypical cells or parasites noted.

Ferritin (μg/L) 194.6 (12-150)

Iron (μmol/L) 63.9 (11-32)

Transferrin saturation (%) 97 (20-50)

Vitamin B₁₂ (pmol/L) 51.6 (140-701)

Haemoglobin (g/L) 29 (117-155)

### Test Result

1. What is the most likely diagnosis?

Megaloblastic anaemia (secondary to vitamin B₁₂ deficiency and causing macrocytosis) was confirmed in bone marrow biopsy. Elevated total iron binding capacity (TIBC) and decreased serum iron indicated iron deficiency. Hypersegmented neutrophils, basophilic stippling, and reduced platelets are suggestive of vitamin B₁₂ deficiency. Evidence of Howell-Jolly bodies on erythrocyte membrane, and no atypical cells or parasites noted.

2. What is the most likely aetiology?

Nutritional deficiency of vitamin B₁₂ due to inadequate dietary and supplemental intake. In higher resource settings, malabsorption (intrinsic factor deficiency). In resource limited settings, it results primarily from inadequate dietary intake, especially in patients who consume plant based diets. The daily requirement of B₁₂ is 1-3 μg/day, with higher demands during pregnancy.

3. What are other potential aetiologies of pancytopenia?

Infectious (HIV, tuberculosis, hepatitis B, hepatitis C, glandular fever/Epstein-Barr virus, typhoid, cytomegalovirus, malaria); autoimmune (systemic lupus erythematosus, sarcoidosis); alcohol use disorder; atrophic gastritis; metformin; and bone marrow disorder (aplastic anaemia, myelodysplastic syndrome, hypoplastic acute myeloid leukaemia, acute lymphoblastic leukaemia, cytotoxic drug intake, and, albeit it rare, hairy cell leukaemia).

### Relevant Blood Test Results

- Ferritin: 194.6 μg/L
- Iron: 63.9 μmol/L
- Transferrin saturation: 97%
- Vitamin B₁₂: 51.6 pmol/L
- Haemoglobin: 29 g/L

### Patient Outcome

The patient was admitted to the intensive care unit with severe anaemia. No fetal abnormalities were detected. Ultrasonography showed normal fetal development (estimated fetal weight 2600 g), adequate amniotic fluid, and normal Doppler indices.

The patient had severe pallor, pedal oedema, and a body mass index of 19. Her pulse rate was 110 beats/min, blood pressure 118/70 mm Hg, respiratory rate 14 breaths/min, and oxygen saturation 98% on room air. Cardiorespiratory and neurological examinations were normal. There was no hepatosplenomegaly on palpation. On obstetric examination, there were no signs of fetal distress. The table shows the results of relevant blood tests. The results of tests for HIV and hepatitis B and C were negative. Abdominal ultrasonography showed mild splenomegaly. Ultrasonography showed normal fetal development (estimated fetal weight 2600 g), adequate amniotic fluid, and normal Doppler indices.

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Neurogenic pulmonary oedema

This is a computed tomography scan of the lungs of a previously fit and well person in their 60s. The patient presented with a one day history of breathlessness, cough, and dizziness. Bilateral crepitations were audible on auscultation, and nuchal rigidity was present. Inflammatory markers were within normal limits, including white blood cell count and neutrophil count: 11.35 (range 4-10×10⁹/L) and 10.14×10⁹/L (range 2-7×10⁹/L), respectively. Bilateral shadowing suggestive of pulmonary oedema was detected on computed tomography of the chest. No cardiomegaly or pleural effusion was present. A computed tomography scan of the brain showed a subarachnoid haemorrhage from rupture of a left middle cerebral artery aneurysm.

Neurogenic pulmonary oedema was diagnosed, which can be due to a range of intracranial factors, such as traumatic brain injury, cerebrovascular events, or brain tumours. The pulmonary oedema resolved within five days after embolisation of the cerebral aneurysm. Neurogenic pulmonary oedema is managed by treating the underlying cause.

If you would like to write a Minerva picture case, please see our author guidelines at bit.ly/29HCBAL and submit online at bit.ly/29yyGSx

Reducing dietary fodmaps

A diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (fodmaps) is better than treatment with musculotropic spasmyotics in people with irritable bowel syndrome, according to a randomised trial in primary care. At eight weeks, around seven of 10 of those allocated to a smartphone fodmap lowering diet app reported symptomatic improvement. This compares with six of 10 of those receiving spasmyotics (Gut doi:10.1136/gutjnl-2021-325821).

Genetics and physical activity

Among two twin cohorts from Finland, 17 monozygotic twin pairs were identified who were discordant for their levels of leisure time physical activity. On average, the more active twin took three times more physical exercise than the less active twin. More active twins had lower body fat, larger lumen diameters in lower limb arteries, greater bone mineral density, and higher concentrations of high density lipoprotein particles than their less active sibling. Proof, if any were needed, that exercise is good regardless of genetics (Scand J Med Sci Sports doi:10.1111/sms.14205).

Thymectomy for myasthenia gravis

A retrospective study of people with myasthenia gravis compared 139 patients treated surgically by thymectomy with age and sex matched controls managed medically. Remission rates were higher in those treated with thymectomy (58% versus 25%). The best outcomes occurred in those who had a thymectomy early in the course of the disease but, even among people having a late thymectomy, remission rates were higher than in the controls (J Neurol Neurosurg Psychiatry doi:10.1136/jnnp-2022-329834).

Mosquito magnets

Go outside on a summer evening with a group of friends and it soon becomes obvious that people vary in how attractive mosquitoes find them. Chemical analysis of compounds collected from skin revealed that people who are mosquito magnets produce larger amounts of several carboxylic acids, including pentadecanoic, heptadecanoic, and nonadecanoic acids, than those who are rarely bitten (Cell doi:10.1016/j.cell.2022.09.034).

Kawasaki disease

Kawasaki disease is an acute febrile illness of young children characterised by inflammation in medium sized arteries. The cause is unknown but the idea that an unidentified infectious agent is involved gets support from an epidemiological study from Japan. The incidence of Kawasaki disease decreased by more than 30% across the country in 2020 when measures such as mask wearing and social distancing were in place (JAMA Pediatr doi:10.1001/jamapediatrics.2022.3756).

People who are mosquito magnets produce more of several carboxylic acids than those rarely bitten

Last will and testament of the human race

The title of a short piece of science fiction in Nature isn’t quite right. It’s less of a last will and testament and more of a confession of error. The failure to recognise the existence of sentient species that weren’t oxygen breathing and carbon based was one serious mistake. The imaginary author wants to make amends by funding a charitable foundation dedicated to supporting newly detected life forms and guiding them through that difficult first 100 million years (www.nature.com/articles/d41586-022-03428-7).

Artificial light at night

A huge cross sectional survey in China, including 100 000 participants from 162 sites across the country, finds an association between levels of artificial light at night (estimated from satellite data) and the prevalence of type 2 diabetes. The investigators suggest that artificial light is a novel risk factor for diabetes, affecting glucose homeostasis by disrupting circadian rhythms. However, both type 2 diabetes and high levels of light at night are features of urbanisation, so many other factors could underly the association (Diabetologia doi:10.1007/s00125-022-05819-x).