education

RESEARCH REVIEWS Fortnightly round up from the leading medical journals

Differences in GLP-1 effectiveness in subpopulations

GLP-1 receptor agonists, now widely used for diabetes, cardiovascular disease, and weight loss, seem to be as effective for these indications regardless of age, race and ethnicity, baseline body mass index, and baseline glycated haemoglobin $A1_c$ ($HbA1_c$). A systematic review and meta-analysis reached this conclusion from data from 48 randomised controlled trials. However, there was a greater average weight loss in women (10.9%, 95% confidence interval 7.0 to 14.8) than men (6.8%, 95% CI 4.6 to 9.0).

JAMA Intern Med doi:10.1001/jamainternmed.2025.8222

A sole treatment for hip arthritis

A trial of different types of shoe suggests there isn't any one size fits all footwear advice for people with hip osteoarthritis. The

study randomised 120 people with pain from hip osteoarthritis to wear either a stable supportive or flexible shoe. They were asked to wear them for at least six hours per day but after six months there was no difference in hip pain between the two groups.

Ann Intern Med doi:10.7326/ANNALS-25-03660

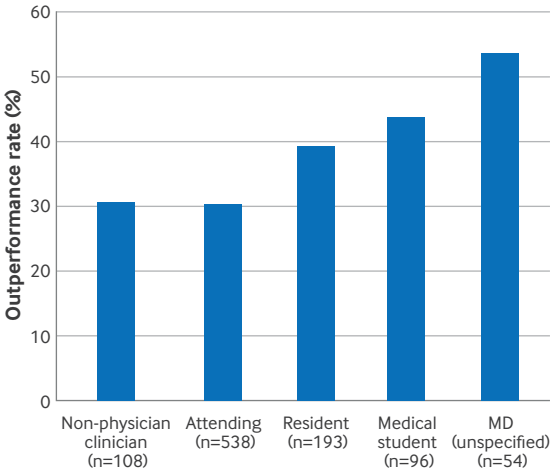
Replacement hips don't die

The NHS website states that "modern hip replacement joints are designed to last for at least 15 years," but a new study suggests that most people can expect them to last for double that time. The systematic review and meta-analysis of nearly two million total hip arthroplasties involving modern bearing surfaces

Chat in the real world

Since ChatGPT was launched in November 2022 there have been an average of three studies per day published investigating them in a clinical context. Much is made of their clinical ability but 3561 out of the 4609 studies found in a review in *Nature Medicine* did not involve any real clinical data—many evaluate large language model (LLM) performance against clinical board exams rather than seeing how they cope with actual patients. When comparing LLMs with humans they tend to do better against medical students and resident doctors than against attending physicians

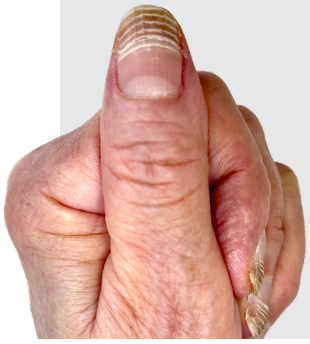
Nat Med doi:10.1038/s41591-026-04229-5



Outperformance rate of large language models against levels of experience

CHEN SF, ALYAKIN A, SEAS A, ET AL. NAT MED DOI:10.1038/S41591-026-04229-5

CLINICAL PICTURE Transverse grooves across nails

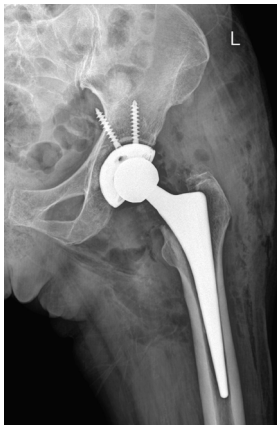


A woman in her 70s presented with an eight month history of transverse nail changes affecting all fingernails and toenails. She had a history of breast cancer treated with mastectomy, followed by six cycles of docetaxel based chemotherapy with concurrent radiotherapy, and she remained in remission. Transverse nail changes were first noted two months after starting chemotherapy. The final cycle was completed four months before presentation.

Physical examination showed six transverse grooves on all nail plates. Fungal cultures and potassium hydroxide tests found no evidence of fungal infection. Nor was there evidence of bacterial infection on microscopic examination of a nail sample.

A diagnosis of Beau's lines was made. Beau's lines present as palpable transverse depressions caused by transient arrest of nail matrix proliferation, affecting the full thickness of the nail plate. In this patient, the six transverse grooves corresponded sequentially to the six chemotherapy cycles.

Changes involving all or multiple nails suggest a systemic cause, such as metabolic disturbance, severe systemic infection, myocardial infarction, or drug reactions, whereas isolated nail involvement usually



found that 93·6% joint replacements "survived" (did not get revised) by 20 years (95% confidence interval 92·3 to 94·7). Extrapolating the data to 30 years the figure fell to only 92·1% (90·1 to 93·7).

Lancet doi:10.1016/S0140-6736(25)02305-0

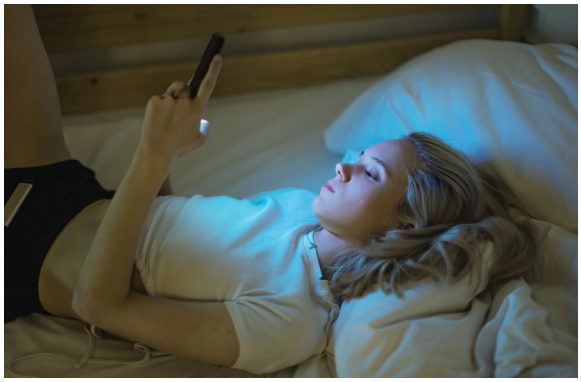
Sleep deprived teenagers on the rise

How much sleep is sufficient for a high school aged child? According to the American Academy of Sleep Medicine less than 7 hours is deemed insufficient—although many teenagers would likely argue for double figures, especially at weekends. A survey of 120 000 students in the US aged between 14 and 18 years found an increase in the proportion who reported insufficient sleep between 2007 and 2023: from 68.9% to 78.3%. Although similar increases were seen across a range of demographic subgroups including sex, school year, and race and ethnicity, there were lower rates of insufficient sleep in those who were more active and spent less time on social media and video games. A linked editorial calls for system wide change to reduce bedtime screen use and make school start times later.

JAMA doi:10.1001/jama.2026.1417

Tom Nolan, clinical editor, *The BMJ*, London; sessional GP, Surrey

Cite this as: *BMJ* 2026;392:s452



indicates localised trauma or infection. Other disorders presenting with transverse nail changes include Mee's lines, which appear as smooth, white transverse bands confined to the superficial layer of the nail plate, Muehrcke's lines, which are non-migratory and arise from vascular changes, and onychomadesis, a severe form of Beau's lines characterised by nail shedding. Beau's lines typically resolve as the nails grow out.

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Patient consent obtained.

Cite this as: *BMJ* 2026;392:e086978

MINERVA Picks from the world of research

Heritability of human life span

Estimates of the genetic contribution to human life span have been surprisingly low, often around 20% or less. A reanalysis of Scandinavian twin cohorts suggests that these figures are distorted by mortality from extrinsic causes, including infection, violence, and unintentional harms (*Science* doi:10.1126/science.adz1187). When such deaths are excluded, heritability of intrinsic life span rises to about 50%, similar to that of other complex traits such as body mass index, blood pressure, or general cognitive ability.

Maternal diabetes and epilepsy in offspring

Maternal diabetes was linked to an increased risk of epilepsy in offspring in a Canadian birth cohort of more than two million children (*Pediatrics* doi:10.1542/peds.2025-071138). After adjustment for socioeconomic and clinical factors, the risk of epilepsy was 30-40% higher among children of mothers with type 1 or type 2 diabetes and about 15% higher among those exposed to gestational diabetes, compared with children of mothers without diabetes. Longer duration of pre-existing diabetes carried a greater risk.

Ketogenic diets for treatment resistant depression

In a small randomised trial of adults with treatment resistant depression, both a ketogenic diet and a control diet were associated with rapid improvements in depressive symptoms (*JAMA Psychiatry* doi:10.1001/jamapsychiatry.2025.4431). At six weeks, depression scores improved more in the group allocated to a ketogenic diet, although the difference was less clear by 12 weeks. Whether the apparent benefit reflects ketosis is another matter. Few patients chose to continue the diet after the trial ended.

Ghrelin

Ghrelin, a hormone with a powerful influence on hunger and appetite, is produced mainly in the stomach and requires acylation by the enzyme GOAT to become biologically active. Genomic analysis of more than 100 reptile species shows that both ghrelin and GOAT have been lost in snakes and chameleons (*Open Biol* doi:10.1098/rsob.250162). It is surely no coincidence that these lineages have a unique ability to endure prolonged periods of fasting.

Regulating ultraprocessed food

Ultraprocessed foods are engineered to heighten reward, drive compulsive consumption, and disrupt appetite regulation. The design and marketing strategies used by manufacturers of these products are not too different from those pioneered by the tobacco industry. The lesson from tobacco control is that strategies to reduce harm should focus less on modifying individual behaviour and more on holding industry accountable (*Milbank Q* doi:10.1111/1468-0009.70066).

Thyroid eye disease and human papillomavirus

Analysis of a large electronic health record database found a higher prevalence of low risk human papillomavirus (HPV) infection among patients with thyroid eye disease than among those with autoimmune hyperthyroidism alone (*JAMA Ophthalmol* doi:10.1001/jamaophthalmol.2025.6244). Patients with eye disease who were HPV positive were also more likely to undergo orbital decompression. Laboratory studies have reported similarities between antigens associated with thyroid eye disease and HPV capsid proteins, raising the possibility that molecular mimicry may contribute to pathogenesis.

Cite this as: *BMJ* 2026;392:s454

GUIDELINES

Chronic heart failure in adults: diagnosis and management—summary of updated NICE guidance

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Further information about the guidance, members of the guideline committee, and the supporting evidence statements are in the full version on bmj.com

CPD READING

0.5 HOURS

The prevalence of heart failure across Europe is estimated to be 1-2% of adults.[1] In the UK, this places a substantial burden on patients and healthcare resources, including hospital admissions, outpatient visits, and ongoing management. According to the 2025 National Heart Failure Audit, index hospital admissions for heart failure increased from 61 401 in 2022/23 to 65 679 in 2023/24.[2]

This article summarises the most recent recommendations from the National Institute for Health and Care Excellence (NICE) guideline on chronic heart failure in adults,[3] updated in September 2025. There have been major advances in therapies since publication of the guideline in 2018, so this update focuses on pharmacological management.

Recommendations for medicines are made at a class level; clinicians should refer to licensing information and consider individual patient circumstances when deciding which individual medicine to prescribe. All medicines in the recommendations are suitable for initiation in primary care.

In line with the definition of heart failure used by the European Society of Cardiology,[1] the update includes recommendations for patients with:

1 Heart failure with reduced ejection fraction (HFrEF); left ventricular ejection fraction (LVEF) of ≤40%
2 Heart failure with mildly reduced ejection fraction (HFmrEF; LVEF of 41-49%) and
3 Heart failure with preserved ejection fraction (HFpEF; LVEF of ≥50%).

WHAT YOU NEED TO KNOW

- Offer four classes of medicine (angiotensin converting enzyme inhibitors, beta blockers, mineralocorticoid receptor antagonists, and sodium-glucose co-transporter-2 inhibitors) for treating heart failure with reduced ejection fraction, and consider these medicines for patients with heart failure with mildly reduced ejection fraction.
- Consider intravenous iron for patients with heart failure with reduced ejection fraction who have a haemoglobin of less than 150 g per litre and iron deficiency.
- Consider sodium-glucose co-transporter-2 inhibitors and mineralocorticoid receptor antagonists for patients with heart failure with preserved ejection fraction.

Recommendations

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost effectiveness. Evidence levels for the recommendations are in the full version of this article on bmj.com.

Newly diagnosed and pre-existing heart failure with reduced ejection fraction (HFrEF)

These updated recommendations advise prescribing a sodium-glucose co-transporter-2 (SGLT-2) inhibitor early, and alongside an angiotensin converting enzyme (ACE) inhibitor, beta blocker, and mineralocorticoid receptor antagonist (MRA), rather than following a sequence for introducing medicines using a "start low, go slow" strategy. This series of recommendations lists treatment combinations for different scenarios, including use of an angiotensin receptor neprilysin inhibitor (ARNI) if symptoms persist, or an angiotensin II receptor blocker (ARB), when there are symptoms of intolerance to ACE inhibitors.

Evidence from randomised controlled trials (RCTs), including DAPA-HF[4] and EMPEROR-Reduced,[5] showed that adding a SGLT-2 inhibitor to existing treatment with an ACE inhibitor/ARB, beta blocker, and MRA reduced mortality and heart failure related hospital admission, without significant increases in adverse events, including hyperkalaemia. Other RCTs reported similar benefits in mortality and in hospital admissions when adding an MRA to existing treatment with an ACE inhibitor or ARB and a beta blocker, although there is an increased risk of hyperkalaemia.

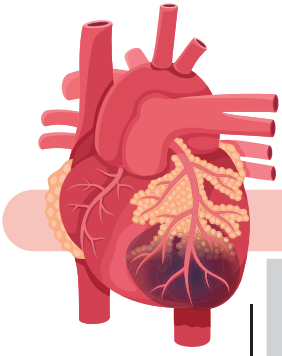
A bespoke cost utility model based on RCTs and real world data was developed that estimated the impact of five treatment strategies on hospital visits, healthcare costs, life expectancy, and quality of life over a patient's lifetime. The combination of MRA, SGLT-2 inhibitor, ACE inhibitor, and beta blocker was the most cost effective. Where this combination of medicines (at maximally tolerated doses) fails to control symptoms of chronic heart failure adequately, consider switching an ACE inhibitor to an ARNI. For patients with intolerable side effects from ACE inhibitors, excluding angioedema, the combination of ARNI, MRA, beta blocker, and SGLT-2 inhibitor was the most clinically and cost effective option. When angioedema is present, ARNIs are contraindicated and an ARB should be considered instead.

thebmj Visual summary

Chronic heart failure medicines

From 2025 update to NICE guidelines

There have been major advances in therapies since the publication of the previous version of the NICE guideline in 2018, including: approval of sodium-glucose co-transporter-2 inhibitors (SGLT-2 inhibitors) for heart failure; recommendations on prescribing medicines early and in combination; and the addition of recommendations on intravenous iron. Recommendations for medicines are made at a class level; clinicians should refer to licensing information and consider individual patient circumstances when deciding which individual medicine to prescribe. All medicines in the recommendations are suitable for initiation in primary care.



People with **newly diagnosed** and **pre-existing** heart failure due to **left ventricular dysfunction** with:

Medicines	**Reduced** ejection fraction ≤40%	**Mildly reduced** ejection fraction 41-49%	**Preserved** ejection fraction ≥50%
	Offer:	Consider:	Consider:
Sodium-glucose co-transporter-2 inhibitors	SGLT-2 inhibitor	SGLT-2 inhibitor	SGLT-2 inhibitor
Mineralocorticoid receptor antagonists	+ MRA	+ MRA	+ MRA
Beta adrenergic receptor antagonists	+ Beta-blocker	+ Beta-blocker	
Angiotensin converting enzyme inhibitors	+ ACE inhibitor	+ ACE inhibitor	

Heart failure symptoms continue on maximum tolerated doses → Consider switching ACE inhibitor to: ARNI

Symptoms of intolerance to ACE inhibitor → Angioedema → Consider switching ACE inhibitor to: ARB

Symptoms of intolerance to ACE inhibitor → Other → Switch ACE inhibitor to: ARNI → Symptoms of intolerance to ARNI → Consider switching ARNI to: ARB

Symptoms of intolerance to ACE inhibitor → Consider switching ACE inhibitor to: ARB

Angiotensin receptor-neprilysin inhibitor: ARNI

Angiotensin II receptor blockers: ARB

Intravenous iron

Assess iron status and check for anaemia

Iron deficiency Transferrin saturation <20% or serum ferritin <100 ng/ml + Haemoglobin <150 g/L

Consider: Iron sucrose | Ferric carboxymaltose | or Ferric derisomaltose

Limited evidence

No recommendations were made for intravenous iron in heart failure with mildly reduced or preserved ejection fraction because trial evidence was limited

- Offer an ACE inhibitor, a beta blocker, a MRA, and a SGLT-2 inhibitor to people with heart failure with reduced ejection fraction.
- For people taking the maximum tolerated dose of each of the four medicines who continue to have symptoms of heart failure, consider switching the ACE inhibitor to an ARNI.
- For people with heart failure with reduced ejection fraction who have symptoms of intolerance to ACE inhibitors (other than angioedema), offer an ARNI, beta blocker, MRA, and SGLT-2 inhibitor.
- For people with angioedema after taking an ACE inhibitor, or who have symptoms of intolerance to ARNIs:
  - Offer a beta blocker, MRA, and SGLT-2 inhibitor and
  - Consider an ARB.

Evidence on the effectiveness of intravenous iron in chronic heart failure was reviewed in the 2018 version of the guideline, but no recommendation was made for its use.

Updated evidence from RCTs, including FAIR-HF,[6] FAIR-HF2,[7] IRONMAN,[8] and CONFIRM-HF[9] was assessed. Overall, for people with HFrEF and iron deficiency, evidence showed that intravenous iron (iron sucrose, ferric carboxymaltose, or ferric derisomaltose) improved exercise tolerance and quality of life. Some trials, including FAIR-HF[6] and CONFIRM-HF,[9] also showed a reduction in total hospital admissions for heart failure, although there was inconsistency in size of effect across all studies.

Based on published economic evidence for ferric carboxymaltose,[10] this form of intravenous iron is thought to be cost effective. However, it is anticipated that other intravenous forms are also cost effective, based on clinical evidence of their effectiveness.[8] As a result, recommendations for considering intravenous iron have been added to the guideline; these specifically relate to management of HFrEF, because trial evidence investigating the impact of intravenous iron in HFmrEF or HFpEF was limited.

- In people with heart failure with reduced ejection fraction, assess iron status and check for anaemia with all of the following blood tests:
  - Transferrin saturation (TSAT)
  - Serum ferritin
  - Haemoglobin.
- Consider iron sucrose, ferric carboxymaltose, or ferric derisomaltose for people with heart failure with reduced ejection fraction and haemoglobin of less than 150 g per litre if they have iron deficiency defined as:
  - TSAT of less than 20% or
  - Serum ferritin of less than 100 nanogram per ml.
- If iron deficiency anaemia is identified, do not assume that it is related to the person's heart failure and think about investigating for alternative causes.

Newly diagnosed and pre-existing heart failure with mildly reduced ejection fraction (HFmrEF)

NICE technology appraisals TA929[11] and TA902[12] already recommend SGLT-2 inhibitors as treatment options for patients with HFmrEF. Updated evidence on the effectiveness of other classes of medicines for this patient group has supported new recommendations.

Additional evidence from RCTs suggests that ACE inhibitors (PEACE trial[13]), beta blockers (meta-analysed using individual patient data[14]), MRAs (FINEARTS-HF[15] and TOPCAT[16] trials), and ARBs (CHARM trial[17]) each reduce admissions to hospital for heart failure and mortality, but with some uncertainty.

Given the low cost of ACE inhibitors, beta blockers, ARBs, and the MRA spironolactone, these treatments are likely to be cost effective because cost savings associated with reduced admissions to hospital are anticipated to outweigh any additional medication costs. This was supported by the bespoke modelling for this guideline applied to the HFmrEF population. The cost effectiveness of the MRA finerenone for treating HFpEF or HFmrEF will be formally assessed by NICE in 2026. Economic modelling found ARNIs not to be cost effective compared with ARBs for this population.

- Consider an ACE inhibitor, a beta blocker, a MRA, and a SGLT-2 inhibitor for treating heart failure with mildly reduced ejection fraction.
- For people who have symptoms of intolerance to ACE inhibitors, consider an ARB, a beta blocker, an MRA, and an SGLT-2 inhibitor.
- For SGLT-2 inhibitors recommended as options in NICE technology appraisal guidance for treating heart failure with mildly reduced ejection fraction, see the guidance on empagliflozin (TA929, 2023)[11] and dapagliflozin (TA902, 2023).[12]

Newly diagnosed and pre-existing heart failure with preserved ejection fraction (HFpEF)

NICE technology appraisals TA929[11] and TA902[12] already recommend SGLT-2 inhibitors as treatment options for patients with HFpEF. Updated evidence on the effectiveness of MRAs for HFpEF has been reviewed as part of this guideline update.

Evidence from RCTs was assessed, including FINEARTS-HF[15] and TOPCAT.[18] Meta-analyses of these trials showed that MRAs reduced admissions to hospital for heart failure in this population. The guideline development group also noted a potential benefit in mortality but with some uncertainty.

Given the low cost of the MRA spironolactone and the anticipated reduction in hospital admissions, MRAs are likely to be cost effective, although the cost effectiveness of the MRA finerenone for treating HFpEF or HFmrEF will be formally assessed by NICE in 2026. The increased risk of hyperkalaemia requires careful monitoring and management.

- Consider an MRA and a SGLT-2 inhibitor for treating heart failure with preserved ejection fraction.
- For SGLT-2 inhibitors recommended as options in NICE technology appraisal guidance for treating heart failure with preserved ejection fraction, see the guidance on empagliflozin (TA929, 2023)[11] and dapagliflozin (TA902, 2023).[12]

Starting and monitoring use of medication

These recommendations were updated to support clinical judgment when introducing four classes of medicine for HFrEF and HFmrEF, and the medicines for HFpEF. The order in which medicines are prescribed should be based on the presenting symptoms, comorbidities, medical history, and preferences of the person, regarding, for example, potential side effects. It is not necessary to optimise the dose of a medicine before introducing another, and the speed at which to introduce all four medicine classes will depend on multiple factors including symptoms, frailty, blood pressure, renal function, electrolyte levels, and appropriate access to monitoring. Some classes of medicine within these recommendations will be required for comorbidities, such as atrial fibrillation or hypertension.

Modest changes in creatinine (up to 50% increase) and potassium (up to 5.5 mmol per litre) concentrations are acceptable and should not require discontinuation or dose reduction of medicines. ARNIs and SGLT-2 inhibitors can both be initiated in primary care to avoid unnecessary delays to treatment. In current practice, ARNIs are usually prescribed by heart failure specialists, whereas SGLT-2 inhibitors are commonly prescribed in primary care for other conditions. Non-specialists in chronic heart failure should seek support from specialists to initiate ARNIs if they are less familiar with this class of medicines.

- Use the person's medical history and findings from their clinical assessment, their frailty status, prognosis, and preferences when deciding:
  - Which specific medicines and medicine combinations to use
  - The order and timing for introducing each medicine
  - The initial dose of each medicine and any subsequent dose increments
  - When and how to optimise the dose of each medicine.
  - See also NICE's guideline on shared decision making.[19]
- Primary care prescribers should consider seeking advice from a heart failure specialist before starting someone on an ARNI.
- Before prescribing an ACE inhibitor, ARNI, ARB, or MRA, measure the person's renal function and electrolyte levels.
- If the person is taking an ACE inhibitor, ARNI, ARB, or MRA, measure their renal function and electrolyte levels:
  - One to two weeks after starting treatment
  - One to two weeks after each dose increment
  - Every three to six months once the maximum tolerated dose has been established
  - Any time renal function may be compromised.
- If the person's serum creatinine level increases by more than 50% or their potassium concentration increases to more than 5.5 mmol per litre, follow local guidelines.
- For potassium binders recommended as options in NICE technology appraisal guidance for treating hyperkalaemia, see the guidance on patiromer (TA623, 2020)[20] and sodium zirconium cyclosilicate (TA599, 2022).[21]

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Co-author RM is a patient and committee member. Committee members involved in this guideline update included lay members who contributed to the formulation of the recommendations summarised here.

GUIDELINES INTO PRACTICE

- When you review a patient with HFrEF or HFmrEF who remains symptomatic, what factors do you consider when deciding which specific medicines and medicine combinations to use?
- Think about a patient newly diagnosed with HFpEF, what classes of medicine do you consider for treatment?

Implementation

Effective and accessible education is needed, particularly within primary care, to improve understanding of heart failure terminology, including the three subtypes (HFrEF, HFmrEF, and HFpEF), the new treatment options for HFmrEF and HFpEF, and the implications of changing the stepwise approach to medication optimisation in HFrEF. This could include tailored webinars, podcasts, and communication through local integrated care board newsletters and national societies effectively to reach each professional group. With respect to the increased expectation of primary care initiation of ARNI treatment, this will need specialist heart failure services to provide support based on local needs. Linked to this support is the requirement to review local formulary guidance to make the necessary changes to ensure a smooth transition to the new recommendations.

The recommendation to offer four medicines (ACE inhibitor, beta blocker, MRA, and SGLT-2 inhibitor) in HFrEF, and to consider these treatments in people with HFmrEF, may increase pressure on resources such as appointments and medicine costs. Similarly, extending the population treated with an MRA and SGLT-2 inhibitor to include HFpEF may also increase pressure on resources, given that HFpEF accounts for over 50% of patients with chronic heart failure. Increases in the number of primary care appointments and treatment costs are anticipated to be offset by the reduction in emergency department attendances and hospital admissions related to heart failure.

Recent evidence suggests there is significant geographical variation in the services and resources available across the UK, with provision of care for patients with HFpEF particularly lacking.[22]

Competing Interests: None declared.

Cite this as: *BMJ* 2026;392:s266

Find the full version with references at http://dx.doi.org/10.1136/bmj. doi: 10.1136/bmj.s266

EDITORIAL

Four pillar treatment of chronic heart failure

New NICE guidance advances care, though key evidence gaps remain

Since the publication of the 2018 National Institute for Health and Care Excellence (NICE) guideline on chronic heart failure, the clinical landscape has been transformed by a series of landmark trials. These developments support the early combined initiation of four drugs: angiotensin converting enzyme (ACE) inhibitors, beta blockers, mineralocorticoid receptor antagonists (MRAs), and sodium glucose transport 2 (SGLT-2) inhibitors for heart failure with reduced ejection fraction, referred to as a four pillar approach.[1] Updated 2025 NICE guidance, summarised by Miles and colleagues (doi:10.1136/bmj.s266), moves away from a sequential strategy—where one drug class is optimised before another is introduced—recognising the additive benefit of early, simultaneous initiation.[2 3] By aiming for rapid up-titration to maximum tolerated doses within two weeks, the guidance seeks to counter the clinical inertia that has historically hindered heart failure outcomes.[4-7]

However, the success of these early interventions in heart failure is dependent on the recognition of heart failure in primary care. A pivotal component of the management remains the measurement of N-terminal-Pro B-type natriuretic peptide (NT-Pro BNP), alongside clinical findings and electrocardiogram results.[1] Defined thresholds provide a "rule out" safety net, but clinicians must remain wary of "false negative" results.

The risk of missed cases of heart failure in primary care is further compounded by the higher recommended rule out threshold for NT-Pro BNP in the NICE guidelines.[9] The threshold (NT-Pro BNP <400 pg/mL) is substantially higher than thresholds seen in recent European and American guidelines of <125 pg/mL.[10 11] However, lowering the diagnostic threshold also presents a challenging trade-off: although it would reduce the risk of missed cases, the resulting surge in testing and referral volume could overwhelm existing health service capacity.

Adherence to guideline directed medical therapy can add an estimated 8.3 years of life for a patient aged 55

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Once a referral has been triggered by a raised NT-Pro BNP level, the echocardiogram remains the key investigation, because it determines the left ventricular ejection fraction that guides subsequent therapy.[1] The 2025 NICE guidance aligns with other international guidelines,[10 11] by stratifying heart failure into three types: heart failure with reduced ejection fraction (ejection fraction ≤40); heart failure with mildly reduced ejection fraction (41-49); and heart failure with preserved ejection fraction (≥50%).

Notably absent from the NICE guidance, however, is the category of heart failure with improved ejection fraction. This omission is unfortunate, because we expect that, with four pillar therapy and potential improvements in left ventricular ejection fraction, this guidance would be welcomed by clinicians who might be unsure of the correct approach to management should the ejection fraction improve considerably.

Evidence base of treatment pillars

Although the shift towards early initiation is welcome, specific drug preferences within the guideline remain points of contention. For patients who remain symptomatic despite taking maximum tolerated doses of these four classes of drugs, the guideline recommends replacing an ACE inhibitor with an angiotensin receptor neprilysin (ARN) inhibitor. However, the continued preference for ACE inhibitors over ARN inhibitors is out of step with American, Australian, and New Zealand recommendations.[11 13] The superior efficacy of ARN inhibitors over ACE inhibitors is well established.[14] Secondly, angiotensin 2 receptor blockers (ARBs) remain underutilised, despite evidence suggesting lower rates of cough and angioedema, compared with ACE inhibitors.[11 15] With one in five patients experiencing an ACE inhibitor induced cough,[16] prioritising ARBs from the outset—rather than as an alternative—warrants greater consideration where ARN inhibitors are not accessible.

Overall, the new guideline changes are welcome, reflecting the benefits of life extending therapies. Adherence to guideline directed medical therapy can add an estimated 8.3 years of life for a patient aged 55 with heart failure with reduced ejection fraction—a dividend that justifies the perseverance required from primary care teams and patients.[21] However, we cannot ignore the implementation gap. Rapid titration and frequent monitoring will inevitably strain primary care resources and might increase the burden on patients.[22 23] For these guidelines to truly change outcomes, they must be met with the necessary clinical support to turn the drug potential into a clinical reality.

Cite this as: *BMJ* 2026;392:s450

Find the full version with references at http://dx.doi.org/10.1136/bmj.s450

STATE OF THE ART REVIEW

Management of obsessive-compulsive disorder in adults

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This is a summary of Management of obsessive-compulsive disorder in adults. The full version can be read here: https://www.bmj.com/content/392/bmj-2024-083443

CPD READING
0.5 HOURS

Obsessive-compulsive disorder (OCD) is a chronic, often debilitating psychiatric condition characterised by intrusive thoughts and behavioural or mental rituals. Although exposure and response prevention (ERP) remains the first line treatment, many individuals do not experience full remission, highlighting the need for innovation.

OCD often interferes with occupational, academic, family, and social functioning, as well as daily living activities.[2] Its chronicity, associated distress, and impact mean that it is classified among the most disabling psychiatric conditions.[3-5]

Obsessions and compulsions present with a wide range of themes, often organised around germs and contamination, responsibility for harm and mistakes, the need for symmetry and exactness, and taboo thoughts related to sex, immorality, and violence.[6 7] Their cause is similarly heterogeneous and not yet fully understood, likely stemming from an interplay of psychological, sociocultural, and biological factors.[8] Despite the lack of clear causal models, empirically supported treatments exist in the form of cognitive behavioural therapy (CBT), particularly exposure and response prevention (ERP), and pharmacotherapy with selective serotonin reuptake inhibitors (SSRIs).

WHAT YOU NEED TO KNOW

- Obsessive-compulsive disorder (OCD) is a complex psychiatric condition that is characterised by obsessions—persistent intrusive thoughts and images that provoke anxiety and other aversive internal states—and compulsions—repetitive behaviours or mental acts performed to alleviate obsessional distress.
- Exposure and response prevention (ERP) is first line treatment; however, response rates and treatment accessibility remain imperfect.
- Recent advances, including process based therapies such as acceptance and commitment therapy (ACT) and inference based cognitive behavioural therapy (I-CBT), technology assisted formats, and novel biological interventions have potential to expand the reach, acceptability, and personalisation of care.
- Growing attention to cultural and identity related factors reflects a necessary emphasis on inclusive and equitable treatment.

Epidemiology

OCD has a one year prevalence of 1.2% and a lifetime prevalence of 2.3% in the adult population (~1 in 40 adults).[9] It may affect women slightly more often than men, and the age of onset, although earlier for men, is around 19 years on average. Even in the most advanced healthcare systems, individuals may experience OCD for 10 years or more before it is recognised, and in many countries no access to proper evaluation exists. Factors contributing to the under-recognition of OCD include the failure of clients to disclose sometimes embarrassing symptoms, failure of professionals to screen for OCD during routine examinations, and difficulties with differential diagnoses.[10]

Established treatments for OCD

Psychological approaches and treatments

The most established short and long term intervention for OCD is ERP, which is a form of CBT.[16] Use of ERP derives from several empirically supported conceptual models of OCD that share an emphasis on the role of cognitive processes and behavioural learning principles in the maintenance of obsessions and compulsions.[17] As illustrated in figure 1, these models view unwanted senseless intrusive negative thoughts, images, and doubts as universal experiences.

Treatment process

This model clarifies targets for reducing OCD symptoms: misappraisals of intrusive thoughts must be corrected, and avoidance and compulsions must be decreased. The aim is to foster a new perspective towards obsessional thoughts and stimuli as safe and manageable, and not demanding avoidance or compulsions. Treatment protocols call for 12-20 therapy sessions, the first of which involves psychoeducation about OCD and a rationale for ERP. Exposure involves gradually approaching situations and thoughts that evoke obsessive fear. For example, a patient who fears sickness from the floor would be coached to practise touching the floor and imagine the possibility of becoming ill. The patient repeatedly approaches the feared situation (such as becoming ill) without compulsive rituals: for example, while refraining from washing compulsions. After each

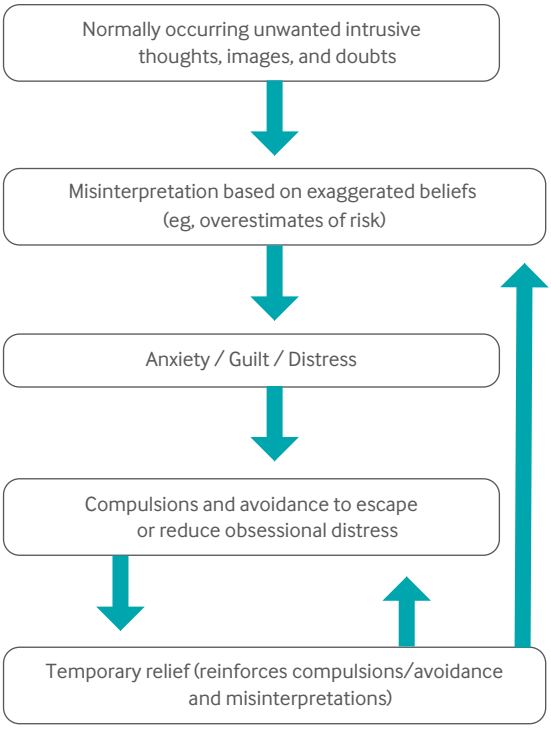

Fig 1 | The general cognitive behavioural model of obsessive-compulsive disorder forms the basis of exposure and response prevention

ERP practice, the patient observes that the predicted feared consequences are less likely than expected and the distress evoked during the exercise is temporary and manageable.

Evidence

Since the early 1990s, many randomised controlled trials (RCTs) have evaluated the efficacy of CBT involving ERP for adults with OCD, typically using the Yale-Brown obsessive compulsive scale (Y-BOCS), a clinician rated scale of 10 items with total scores ranging from 0 (no symptoms) to 40 (extremely severe) (fig 2).[23] These studies consistently show that patients who complete ERP generally achieve clinically significant improvement (that is, >35% Y-BOCS reduction) that is maintained for several months with average Y-BOCS reductions from 50% to 70%.[24 25]

Although ERP is effective for most people with OCD, about 20% do not respond. Moreover, a meta-analysis of 21 RCTs reported a weighted mean ERP dropout (attrition) rate of about 14.7% for adults who began treatment, with overall attrition (including refusals) estimated to be 18.7%.[29] Research has identified factors associated with poorer outcomes, although studies show small effects and not all findings have been replicated. These factors include greater severity of OCD, poor insight into the senselessness of OCD symptoms (and more strongly held dysfunctional beliefs), general cognitive rigidity, comorbidity (that is, with depression, obsessive-compulsive personality disorder, and autism spectrum disorder), a history of poor treatment outcomes, family over-involvement in rituals, and poorer overall quality of life.[25 30-32]

Biological approaches and treatments

The biological approach to OCD views the disorder as a neuropsychiatric disease and incorporates neurochemical and structural models that attempt to explain the development and persistence of symptoms. The serotonin hypothesis suggests that OCD involves abnormalities in the serotonergic system, which is involved in mood regulation, impulse control, and cognitive flexibility, all of which are associated with OCD. Importantly, however, in vivo studies provide no consistent evidence of such abnormalities in OCD[38]; the model is supported primarily by the effectiveness of SSRIs.[39] Yet treatment response is not a sufficient basis for theories of causation, as SSRIs might exact their effects via different mechanisms (for example, placebo effects[40]). Moreover, the serotonin hypothesis is inherently circular, having been initially formulated from the observation that drugs targeting serotonergic pathways alleviate symptoms of OCD.[41]

Structural and functional models of OCD posit dysfunction in specific brain circuits, particularly the orbitofrontal-subcortical pathways, which are involved in decision making, behavioural regulation, and error detection.[42] The orbitofrontal cortex is associated with evaluation of risk, which is often exaggerated in OCD. The orbitofrontal cortex also communicates with the caudate nucleus, which helps to regulate behavioural responses. The thalamus, which relays information between cortical and subcortical areas, may also be hyperactive in its resting state, reinforcing compulsive behaviours to relieve distress. Neuroimaging studies have found differences in structure and activity levels in the orbitofrontal cortex, caudate nucleus, and thalamus among people with OCD relative to healthy individuals.[43] However, because they rely exclusively on correlational data, whether the observed differences in studies represent causal factors or merely epiphenomena of OCD is not clear. Consistent with this limitation, no reliable biological or genetic tests are available that can diagnose OCD or distinguish it from other psychiatric conditions.

Evidence

Reviews of the literature indicate that SSRIs are generally associated with a 30-40% reduction in OCD symptoms, and approximately half of patients fail to respond to initial trials.[39]

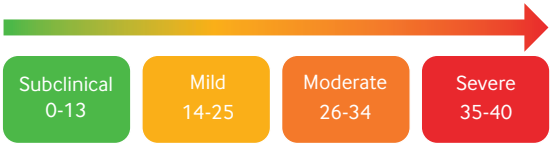

Fig 2 | The Y-BOCS is a clinical interview that is widely used to assess the breadth and severity of symptoms of obsessive-compulsive disorder in clinical and research settings. It contains three sections. The first section provides definitions of obsessions and compulsions. The second section includes a symptom checklist of >50 different types of obsessions (eg, thoughts of germs) and compulsions (eg, excessive hand washing). The third section is a 10 item severity scale that assesses the time, interference, distress, resistance to, and control over obsessions (items 1-5) and compulsions (items 6-10). Total scores range from 0 to 40; the figure shows empirically derived clinical cut-offs.

Evidence suggests that clomipramine, a tricyclic antidepressant with serotonergic effects, is slightly more efficacious than SSRIs.[45 46] The apparent edge of clomipramine over SSRIs may reflect its older trial era as much as its pharmacology. Many RCTs of clomipramine pre-dated pre-registration, enrolled more medication naive samples, and were easier to "unmask" owing to noticeable side effects—factors that inflate drug-placebo separation. Some advantage, however, may be because of its exceptional potency as a serotonin transport blocker and the fact that its primary metabolite, desmethyl-clomipramine, adds norepinephrine reuptake inhibition, giving it broader monoaminergic effects. Regardless, SSRIs are favoured for their more modest side effect profiles.[47]

Meta-analyses indicate that higher doses of SSRIs are more effective than low or medium doses, in terms of both symptom reductions and responder rate.

Patients who do not respond sufficiently to SSRI treatment can benefit from augmentation with glutamatergic agents or specific antipsychotics (for further details, see bmj.com).

Combined treatment

Several RCTs have also examined the efficacy of combining ERP and pharmacotherapy relative to monotherapy with either ERP or drugs for OCD. A meta-analysis of 12 studies (698 patients, including six RCTs that included children, but did not report separate effects by age group) found that combining ERP with drugs (primarily SSRIs) conferred only a 0.08 (95% CI −1.13 to 0.96) point Y-BOCS advantage over ERP alone (or with a placebo) at post-treatment, which was not a significant difference.[53] On the other hand, across nine studies (415 patients), ERP combined with drugs was significantly more effective than drugs alone, including SSRIs, clomipramine, and risperidone (mean Y-BOCS difference 6.60, 95% CI 8.35 to 4.84). This suggests that patients using a combination of drugs and ERP have similar outcomes to those using ERP alone but better outcomes than patients using medication alone.

Innovations in psychological treatments

Application of inhibitory learning to ERP

Traditionally, the success of ERP has been attributed to extinction via habituation—the natural decline in distress with repeated exposure.[54] However, research on learning and memory has recently broadened this framework, and feared stimuli are now understood to retain their original threat related meaning while also acquiring an inhibitory (that is, safety) meaning. The therapeutic goal, then, is strengthening inhibitory associations so that they override the fearful ones.

In practice, optimising inhibitory learning involves disconfirming negative expectancies and promoting generalisation of safety learning across contexts. To achieve disconfirmation of expectancy, exposure is designed to maximise the discrepancy between feared outcomes and actual outcomes—for instance, increasing intensity, frequency, or duration of exposure beyond what the patient perceives as "safe." To promote generalisation, exposures are conducted in different contexts, such as varying the treatment setting (office versus home). This tackles the context specific nature of learning, increasing the likelihood that safety associations will transfer to real world situations.

About 20% of patients do not respond to exposure and response prevention

Integration of acceptance and commitment therapy

Acceptance and commitment therapy (ACT) offers a framework for treating OCD that shifts the focus from symptom reduction to psychological flexibility—engaging in valued activities despite the presence of obsessional thoughts and anxiety, without the use of compulsive rituals.[59] Rather than trying to lessen obsessions and anxiety, ACT helps patients to relate differently to these experiences, seeing them as transient mental events rather than threats that must be neutralised.

In practice, the goal is to foster willingness to experience obsessional distress and guide behaviour towards personally meaningful values. Experiential exercises and metaphors are used to support this work. For example, patients clarify their values in different domains (for example, relationships, work/school) and explore how OCD interferes with living in line with such principles.

Recent studies show promising results, especially when ACT is combined with ERP. A meta-analysis of eight RCTs (366 patents) reported a large effect size (Cohen's d=1.19, 95% CI 1.87 to 0.51) favouring ACT over control conditions for OCD.[59] RCTs comparing ACT and ERP suggest comparable outcomes, with one study (n=58) reporting no significant differences on the Y-BOCS either at post-treatment or at six months' follow-up.[26] Improvement in Y-BOCS scores was 54.4% (post-treatment) and 51.9% (follow-up) for the ACT plus ERP group and 55.0% (post-treatment) and 56.9% (follow-up) for the ERP group. Psychological flexibility consistently emerges as a moderator of symptom improvement with ACT.[60 61] Overall, although more high quality research is needed, ACT seems to be effective for OCD, especially when tailored to individual presentations and combined with ERP.

Inference based cognitive behavioural therapy

Inference based cognitive behavioural therapy (I-CBT) conceptualises obsessions as the result of reasoning errors rather than intrusive thoughts themselves.[62] Rather than targeting exaggerated perceptions of threat, I-CBT targets a process called inferential confusion, in which individuals blur imagined or hypothetical possibilities with real life probabilities. Patients are helped to recognise how and when they begin to doubt reality, examine the basis of their obsessional doubts, and learn to better trust their sensory experiences.

I-CBT has received growing research and clinical consideration over the past decade. One RCT with 111 patients compared I-CBT with traditional cognitive therapy and mindfulness based stress reduction (MBSR).[63] All three treatments produced large reductions

in severity of OCD at post-test, with Y-BOCS score reductions of 11.45 points for I-CBT, 11.72 for cognitive therapy, and 10.20 for MBSR; however, I-CBT was not more effective than the other treatments. Nevertheless, 61.1% of patients treated with I-CBT achieved at least a 35% reduction in Y-BOCS scores and improvement was maintained up to six months, suggesting durability of treatment gains.

The evidence base for I-CBT is considerably smaller than that for ERP, but existing studies support its efficacy and suggest that it may be particularly suited for clients with poor insight or difficulties tolerating ERP.[62] Research on I-CBT has largely been generated by the developers of the treatment, however. Additional independent research is needed to more firmly establish its effectiveness and clarify the profiles of individuals who might benefit most from this approach.

Telehealth based (virtual) ERP

Virtual platforms can provide continuous, effective care when in-person sessions are not practical.[66] As shown in table 1 (bmj.com), however, each format has advantages and drawbacks that need to be considered.[67]

An RCT with 14 patients with OCD found that the outcomes of group ERP delivered virtually (Y-BOCS reduction 9.06 points) or in person (Y-BOCS reduction 8.52 points) were not significantly different.[68] Accordingly, we recommend an approach that enables flexibility and personalised care based on the patient's needs. Box 1 (bmj.com) includes important factors to consider when deciding on in-person, virtual, or hybrid treatment.

Digital and technology assisted interventions

Internet based ERP (IB-ERP) programmes, such as OCD-NET and NOCD, typically deliver structured modules incorporating psychoeducation, exposure exercises, and homework assignments through online platforms, with varying degrees of therapist support. Across 10 studies (of mixed quality), a meta-analysis found that therapist guided IB-ERP was associated with a mean Y-BOCS reduction of 8.2 points from pre-treatment to post-treatment; unguided IB-ERP was associated with a mean 5.1 point reduction.[70] This underscores the importance of the involvement of a clinician to maximise adherence and help with any necessary troubleshooting.

Smartphone applications that provide tools for self-monitoring OCD symptoms and psychoeducation[71] may be integrated with therapist led treatment but can also function as standalone self-help adjuncts. An RCT in 192 individuals without a diagnosis but reporting OCD symptoms showed that one such tool—the self-guided OCD module in the Intellect app (without therapist guidance)—only minimally outperformed a control condition (an app focused on developing cooperation and teamwork skills) on a self-report measure of OCD symptoms after eight days of use (partial eta-squared (η_p^2)=0.031) and at four week follow-up (η_p^2=0.021).

Barriers to use include data privacy questions, inconsistent regulation, and variable digital literacy among patients and providers. Moreover, they may not be suitable for individuals with severe symptoms, complex comorbidities, or limited insight who need support face to face. Hybrid approaches beginning with clinician led ERP and transitioning to digital maintenance or booster modules may offer the optimal balance between scalability and therapeutic alliance. Table 2 (bmj.com) provides a concise overview of recent developments in psychological treatments for OCD.

Innovations in biological approaches

Glutamate modulating agents

Although targeting serotonergic pathways has long dominated OCD pharmacology, growing interest in glutamatergic dysfunction stems from high rates of incomplete response to SSRIs. Although glutamate is the brain's primary excitatory neurotransmitter and plays a role in learning and neural plasticity, findings linking it to OCD are mixed, largely preliminary, and correlational. No glutamate modulating agents have received approval for OCD from the US Food and Drug Administration. Ketamine, a rapid acting glutamate modulator (via N-methyl-D-aspartate (NMDA) receptor antagonism) has also attracted attention for its potential effects on OCD (see *Emerging treatments*, bmj.com). Several compounds have shown promise in small trials, but inconsistent results, methodological variability, and limited replication temper enthusiasm.[73] As such, the glutamate modulating agents remain potentially interesting, but experimental.[74]

Memantine, an NMDA receptor antagonist traditionally used in Alzheimer's disease, has been examined as an augmenting agent in treatment resistant OCD. Its mechanism involves down regulation of NMDA receptor mediated excitotoxicity and enhancement of neuroplasticity. In an eight week RCT with 42 patients with OCD comparing fluvoxamine plus memantine with fluvoxamine plus placebo, all patients in the memantine arm met criteria for partial response (≥25% reduction in Y-BOCS) by week 8, compared with 32% in the placebo group. Remission (Y-BOCS ≤16) was achieved in 89% of memantine treated patients compared with 32% of the placebo group.[75] A meta-analysis of four double blind, placebo controlled studies of memantine augmentation showed that patients receiving the agent were 3.61 times more likely to be classified as responders (≥35% Y-BOCS reduction) than those on placebo.[76]

Riluzole, which is approved for amyotrophic lateral sclerosis, is another glutamate antagonist that acts by reducing presynaptic glutamate release and enhancing glutamate re-uptake. Open label trials initially indicated efficacy for OCD.[77] However, in a subsequent RCT, 38 patients who had not responded to at least one previous SSRI were randomly assigned to receive either riluzole or placebo alongside their ongoing medication. After 12 weeks, the mean reduction in Y-BOCS scores was 15% for riluzole and 11% for placebo, which was not statistically different.[78]

N-acetylcysteine, which modulates the cystine-glutamate antiporter, has also been studied as an

Targeting serotonergic pathways has long dominated OCD pharmacology

adjunct to SSRIs in OCD. A meta-analysis of six augmentation RCTs (195 patients), however, showed maximum improvements of <3 points on the Y-BOCS with the addition of N-acetylcysteine, which is well below the 25% reduction typically considered a partial response.

Neuromodulation techniques

Transcranial magnetic stimulation

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive procedure that uses powerful magnetic pulses to stimulate neuronal activity (excitatory or inhibitory) in the brain. The most common rTMS target sites are the supplementary motor area, dorsolateral prefrontal cortex, and orbitofrontal cortex.[79] A review of 12 meta-analyses based only on RCTs comparing rTMS with sham control for OCD (282-791 patients) found small to medium effect sizes (adjusted for heterogeneity) of Hedges' g=0.29-0.49 in favour of rTMS.[80] Sources of heterogeneity include rTMS methods (such as precision location of target brain areas), frequency, number of pulses per treatment session, number of sessions, and comorbidities. Although rTMS is considered safe, more research is needed to determine the best procedures, targets, and predictors of outcome.

Transcranial direct current stimulation is a similar procedure involving a lower, constant electrical current to modulate neuronal excitability more subtly and broadly than rTMS. A recent meta-analysis of six RCTs (147 patients) found no advantage over sham control (mean between group difference in Y-BOCS scores −1.13, 95% CI −5.35 to 3.10).[81]

Deep brain stimulation

Deep brain stimulation (DBS) is an invasive neurosurgical procedure wherein an electrical device is implanted in a particular region of the brain to send electrical pulses via a pacemaker. In contrast with ablative neurosurgery, DBS allows clinicians to modify the electrical pulse's voltage to optimise the patient's response. The most common targets are the ventral capsule/ventral striatum and the nucleus accumbens, but other targets include the nucleus of stria terminalis, the anterior limb of the internal capsule, and the subthalamic nucleus.[82] Studies on DBS are limited by small sample sizes, and most are uncontrolled, unmasked open trials.

Integration with ERP

A recent RCT (with 61 patients), however, examined the impact of rTMS (targeting two separate sites) and sham control delivered immediately before ERP sessions.[83] Overall, treatment was effective, with Y-BOCS reductions ranging from 35.8% to 40.3% across groups. However, no significant difference was seen between the rTMS+ERP group and the sham rTMS+ERP group. Table 3 (bmj.com) provides a concise overview of recent developments in biologically based treatments for OCD.

Cultural and identity based considerations

Cultural influences on OCD and its treatment

As obsessions concern themes of personal salience, their content varies considerably across cultures. This underscores the need to adapt treatment to the cultural context of each individual, promoting both clinical effectiveness and cultural sensitivity in therapeutic care. Culturally informed intervention emphasises the need to recognise and adapt to the cultural, racial, religious, and gendered experiences of patients.[95 96]

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Members of the International OCD Foundation who have lived experience with OCD, as individuals with the disorder and as people with family members with OCD, reviewed a draft of this manuscript and made suggestions and edits on the content and presentation. The primary suggestions concerned avoiding lengthy discussions of individual study methodology and instead focusing on the relevant results and conclusions. We agreed with this feedback and incorporated it into the final drafts.

Identity related OCD symptoms

OCD symptoms frequently focus on the fear of (or the fear of becoming) an identity that is marginalised in society, and these obsessions may intersect with societal biases, stereotypes, and stigmas.[95 97] For example, patients with obsessive doubts about their own sexual orientation (such as a fear of being gay) do not typically have negative attitudes towards LGBTQ+ identities. Rather, they fear uncertainty, judgment, and condemnation. As a result, the treatment of such symptoms requires careful attention to the unique challenges posed by obsessions tied to aspects of personal identity, such as race, gender, sexual orientation, or cultural background. In such cases, ERP should involve exposures that focus on the anxiety linked to unwanted thoughts and doubts about their sexual orientation (for example), while ensuring that the treatment does not inadvertently reinforce the mistaken idea that being gay is inherently immoral (that is, "justice based" ERP).[95]

Guidelines

Treatment guidelines for OCD in adults, including older recommendations from the American Psychiatric Association and standards from the UK's National Institute for Health and Care Excellence,[111 112] as well as more recent guidelines from the Indian Psychiatric Society and International OCD Foundation (IOCDF),[113 114] have been consistent in endorsing a stepped care model that prioritises evidence based interventions tailored to symptom severity and individual needs. ERP is reliably recognised as the first line psychological treatment owing to its strong empirical support. SSRIs are first line drugs, often prescribed at higher doses and for longer durations than in depression. The combination of ERP and SSRIs is frequently recommended for moderate to severe OCD.

When first line approaches are insufficient, guidelines recommend clomipramine or antipsychotic augmentation (for example, risperidone or aripiprazole). Adjunctive therapies, including ACT and I-CBT, are supported as second line options. Recent updates also recognise the growing role of telehealth.[114] For treatment refractory cases, neuromodulation techniques such as rTMS may be considered.[114] The IOCDF guidelines caution against unproved treatments such as over-the-counter supplements and emphasise culturally sensitive care, especially in underserved and under-represented populations.

Competing interests: See bmj.com.

Cite this as: *BMJ* 2026;392:e083443

Find the full version with references at doi: 10.1136/bmj-2024-083443

EDITORIAL

Innovation in treating obsessive-compulsive disorder will not solve the care gap

Inadequate trials hinder translation into effective treatments

Obsessive-compulsive disorder (OCD) remains one of psychiatry's most disabling conditions, affecting about 1-2% of the population.[1] People with OCD have an 82% increase in all cause mortality compared with unaffected matched people from the general population,[2] with suicide being a major contributor.[3] The disorder is also associated with academic underachievement and labour market marginalisation, even after adjustment for psychiatric comorbidity,[4 5] as well as reduced quality of life.[6 7] The review by Abramowitz and colleagues (doi:10.1136/bmj-2024-083443)[8] summarises the current treatment evidence for OCD, identifying cognitive behavioural therapy (CBT) with exposure and response prevention (ERP) and serotonin reuptake inhibitors (SRIs) as first-line treatments. People with OCD face a dual challenge: many never get these treatments—particularly CBT—because of structural, financial, and geographical barriers[9] and, among those who do, only about a third have a robust response (defined as 50% or higher symptom improvement from baseline).[10] Most will experience persistent symptoms, and few proved alternatives are available when first-line treatments fail. Despite advances in understanding the disorder, the overall management approach for the average patient has changed remarkably little over the past two decades.

Lack of treatment response affects 25–50% of patients

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Delivering treatments more effectively

One of the most important pillars of OCD management is CBT. However, access to CBT remains limited, largely because of a shortage of trained professionals and geographical barriers.[11] Telemedicine and internet based treatments are emerging as promising ways to expand access, with the potential to deliver care more cost effectively than traditional face-to-face treatment.[12] A Swedish non-inferiority randomised clinical trial of 120 adults with OCD compared therapist guided internet-based CBT, unguided internet-based CBT, and individual face-to-face CBT over 14 weeks. The study could not conclusively show that the internet-based interventions were as effective as face-to-face therapy. However, therapist guided internet-based CBT was more cost effective, with lower societal costs per treated participant—roughly $6000 less per patient than face-to-face therapy.[13]

Implementing such approaches within a stepped care model of healthcare—where treatment progresses from the least to the most intensive evidence based intervention according to clinical need and response—may allow more efficient use of existing resources.[14]

Persisting evidence gaps

Even among patients who have access to CBT or SRIs, treatment non-response remains a major issue, affecting 25-50% of patients, with many experiencing substantial residual symptoms.[19] As highlighted by Abramowitz and colleagues,[8] innovative treatments are needed for patients who do not respond to first line interventions. However, it remains unclear if new psychological approaches—such as cognitive therapies, inhibitory learning ERP, or acceptance and commitment therapy—offer meaningful advantages over established CBT with ERP. Adequately powered head-to-head comparisons and non-inferiority trials are largely lacking.

Pharmacological augmentation strategies—including antipsychotics, glutamatergic agents, and neuromodulation—are discussed repeatedly across guidelines and reviews,[20-23] but evidence for many of these approaches is limited by small samples, short follow-up periods, and inconsistent replication.

Finally, progress in OCD treatment is constrained by a lack of research funding, which has been exacerbated by the pharmaceutical industry's reduced investment in psychiatric conditions.[31] Over the past two decades, several large drug companies have closed or substantially downsized their neuroscience research divisions after costly late stage trial failures, perceiving psychiatric drug development as financially unviable because of the heterogeneity of mental disorders, difficulty demonstrating efficacy in unstratified populations, and strong placebo effects.[31 32] Current funding levels remain incommensurate with the societal and economic burden of complex mental health conditions, such as OCD.[31] Within these constraints, focusing on improving access to existing evidence-based treatments, and generating higher quality evidence for promising experimental treatments should be key priorities.

Cite this as: *BMJ* 2026;392:s472

Find the full version with references at http://dx.doi.org/10.1136/bmj.s472

WHAT YOUR PATIENT IS THINKING

Living with an increased risk of cancer

CPD READING
0.5 HOURS

Elspeth Davies describes how living with an elevated risk of cancer damaged her relationship with her body, and how she sought to repair it

At the age 17 I received a diagnosis of melanoma in situ, described as the earliest stage of skin cancer in which malignant cells are confined to the top layer of skin. Following two surgeries, my treatment was said to be "curative," with all malignant cells deemed to have been removed. But a tension persisted between this supposed cure and my ongoing status as "at risk" of both recurrence of the original cancer and new primary melanomas.

After being discharged from specialist care, I was asked to check my body regularly. A health professional once explained I could "never relax," emphasising the importance of lifelong vigilance. GPs became newly eager to refer me for further investigations on the basis of even very minor abnormalities, such as slightly unusual moles, stating that this was necessary because of my medical history. In the 10 years since the diagnosis, this vigilance has resulted in five urgent suspected cancer referrals to secondary care services and a series of further examinations, scans, and biopsies, none of which have resulted in additional malignant diagnoses.

Reassurance via investigations

I was constantly reminded that I could feel well while also harbouring a deadly cancer. Early detection efforts instructed me that my body was potentially dangerous. My health became knowable through technological and medical interventions—doctors' examinations, biopsies, mole mapping cameras, and AI monitoring apps—rather than through how I actually felt. This fuelled a reliance on medical investigations: seemingly only they could reassure me of my safety. And yet sometimes they created more questions than they answered, leading to further tests and ongoing monitoring. Urgent investigations helped me live with the worry in the short term, but ultimately increased the feeling of unease and distrust in my body. Such well intentioned attempts to facilitate early cancer detection left me feeling like a ticking time bomb.

PRIYA SUNDRAM

After being discharged from specialist care, I was asked to check my body regularly.

I strove to be a compliant patient, reporting concerns to my doctors in a timely fashion. But this vigilance eventually resulted in a diagnosis of "health anxiety," or "hypochondria." I felt stuck between a rock and a hard place: worry too little and I was reckless and vulnerable to metastatic disease, but worry too much and I was irrational, even mad.

Re-establishing bodily safety

I realised that I needed to find ways of restoring a feeling of being "at home" in my body. For me, solutions included yoga and singing, and I know others have found dance, drawing, somatic experiencing, or mindfulness to be helpful. My activities helped me to reconnect mind and body, reminding me that our bodies not only hold the potential for developing disease but also experiencing joy, creativity, and connection.

Health professionals were not wrong to be concerned about my cancer risk or to offer follow-up investigations. But I wish they had supported me to find ways to live with an elevated risk that went beyond further medical tests and examinations. This does not mean dismissing my worry, it means responding to the root cause of it. As the NHS shifts increasingly towards early detection and risk management, we need to support patients to live with the sometimes difficult consequences of early detection and cancer risk. This means not just helping us to reduce risk of future disease but also to live well in the present.

Patient author

Cite this as: *BMJ* 2026;392:s359

WHAT YOU NEED TO KNOW

- Being at elevated risk of disease can fundamentally disrupt a person's sense of trust in their body
- Helping people live with risk is not only about offering further monitoring and investigations
- Some people find that embodied practices (for example, yoga) help them to create a sense of safety in their bodies

EDUCATION INTO PRACTICE

- How could you best support someone who is living at increased risk of cancer?
- What information or guidance could you share with someone who is trying to trust their body again?