education

RESEARCH REVIEWS Fortnightly round up from the leading medical journals

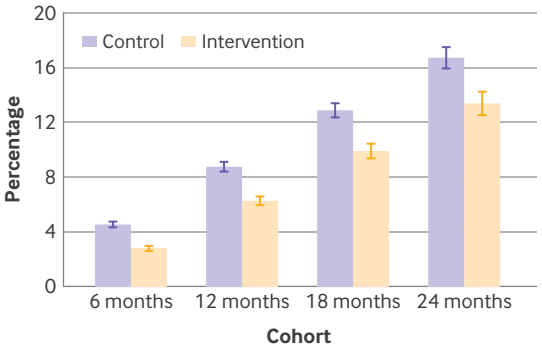
(What's the story) night sweats?

In July the Medicines and Healthcare products Regulatory Agency was the first regulator in the world to approve elinzanetant for the treatment of moderate to severe vasomotor symptoms associated with the menopause. Approval was based on evidence from the OASIS 1 and 2 trials. Now that the OASIS 3 trial has been published, what's the story? At 12 weeks women in the elinzanetant arm had, on average, a reduction in moderate to severe hot flashes from 6.7 to 1.3 per day, whereas those in the placebo arm saw a reduction from 6.8 to 3.3 per day—a difference between the groups of −1.6 (95% CI −2.0 to −1.1). Adverse events were more frequent in those taking elinzanetant, most commonly somnolence, fatigue, and headache. Elinzanatent seems to add a much needed non-hormonal option for vasomotor symptoms—or at least a definitely maybe.

JAMA Intern Med doi:10.1001/jamainternmed.2025.4421

Aspirin and clopidogrel in photo finish

Aspirin and clopidogrel have been competing in a marathon race for the prize of first choice antiplatelet for coronary artery disease. Although aspirin has been leading since the start, is clopidogrel about to overtake it on the finish line? A new systematic review and meta-analysis published in the *Lancet* analysed individual participant data from 28 982 people across seven trials. It finds that clopidogrel monotherapy is superior to aspirin monotherapy for prevention of major adverse cardiovascular or cerebrovascular events with no increase in the risk of bleeding. In a photo finish, cardiovascular death, myocardial infarction, or



Multiple long term condition incidence in NHS diabetes prevention programme completers *v* control (matched non-attenders). Data presented as proportions with 95% confidence intervals

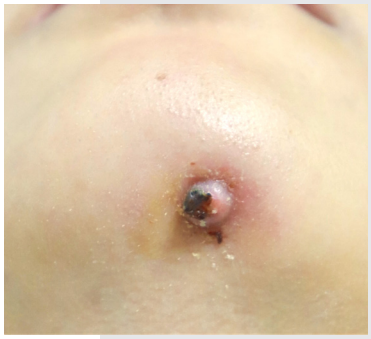
BARRON E, CHAPPELL P, HATFIELD I, ET AL. NAT MED 2025 HTTPS://DOI.ORG/10.1038/S41591-025-03922-1

Preventing diabetes and multimorbidity

Although a borderline HbA1c result has been used as the main criterion for referral to the NHS diabetes prevention programme, the risk of developing diabetes (and its complications) can vary wildly from person to person depending on other risk factors. I've seen patients with low risk and few (if any) modifiable risk factors who feel worried, helpless, or simply bemused when they get the news—often by text message—that they have "prediabetes" and are asked to go on a behaviour change course. A new cohort study finds that completing the course is associated with a lower chance of developing multiple long term conditions and diabetes compared with matched controls who didn't enrol (figure). Given the observational study design, however, it's likely that there are important differences between the two groups that account for some—if not all—of the findings.

Nat Med doi:10.1038/s41591-025-03922-1

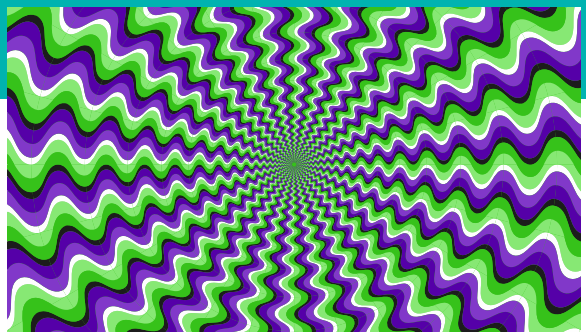
CLINICAL PICTURE



A nodule on the chin

This woman in her late teens presented to the dermatology department with a one month history of a pea sized nodule on her chin. The lesion was characterised by superficial ulceration, surrounding skin depression (figure), and no associated pain or itching. She reported no history of trauma or medical history, and took no regular medication. Clinically, pyogenic granuloma was suspected, and surgical excision was performed. Histopathology showed pseudoepitheliomatous hyperplasia and prominent granulation tissue. Results of stains for bacteria and fungi were negative. On the basis of the histopathology results, dental imaging was advised to rule out odontogenic cutaneous fistula (OCF). The patient had experienced no dental symptoms so she declined further imaging.

One month later, a similar nodule recurred at the same site. Subsequent imaging showed apical periodontitis of left mandibular central incisor. Intra-oral examination identified non-vitality of the tooth, with negative response to cold sensation testing. The diagnosis of OCF was confirmed. OCF describes a



stroke occurred at a rate of 2.61 per 100 patient years for clopidogrel and 2.99 per 100 patient years for aspirin (hazard ratio 0.86, 95% confidence interval 0.77 to 0.96).

Lancet doi:10.1016/S0140-6736(25)01562-4

Antihistamines to prevent covid-19?

Was effective prevention for covid-19 right under our nose all along? A phase 2 randomised control trial recruited healthy volunteers and allocated them to take the antihistamine nasal spray azelastine or a placebo three times a day for two months. Participants had twice weekly nasal rapid antigen testing for covid-19, and positive results were confirmed by polymerase chain reaction. Incidence of covid-19 was 2.2% in the azelastine group and 6.7% in the placebo group (odds ratio 0.31, 95% CI 0.11 to 0.87). There remain various caveats from this small single centre study, and larger, more robust studies are needed to see if the findings are valid and reproducible.

JAMA Intern Med doi:10.1001/jamainternmed.2025.4283

Under no illusions about LSD for anxiety

Expect to hear more about psychedelics as treatment for mental illness in the next few years, with phase 3 trials currently underway. A phase 2b study of MM120—commonly known as LSD—given as a single dose, sought to determine dose-response relationships for reducing symptoms of generalised anxiety disorder and adverse events. At higher doses of 100µg and 200µg side effects of illusion, pseudo-hallucination, and visual hallucination occurred in 92.5% and 100%, respectively—these were also the only doses in which a statistically significant reduction in symptoms after four weeks was found.

JAMA doi:10.1001/jama.2025.13481

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

Cite this as: *BMJ* 2025;390:r1932

pathological connection between the skin and oral cavity arising from chronic periodontal infection. It should be considered in the differential diagnosis of persistent or recurring facial skin lesions even in the absence of dental symptoms. After root canal treatment, this patient's skin nodule resolved, with residual scarring at 10 month follow-up.

Bin Peng; Songmei Geng (gengsongmei73@163.com), Xi'an Jiaotong University Second Affiliated Hospital, China.

Patient consent obtained.

Cite this as: *BMJ* 2025;390:e084382

MINERVA From the wider world of research

Alcohol and diabetes

Rather surprisingly, the incidence of type 2 diabetes among participants in three large longitudinal studies in North America was substantially lower in those who drank alcohol often than in non-drinkers or infrequent drinkers (*Diabetes Care* doi:10.2337/dc24-1902). The smallest risk of diabetes was observed in people who drank small or moderate amounts of alcohol on more than 5 days a week. The underlying mechanisms are a mystery, and the investigators are at pains not to suggest initiating alcohol consumption as a means of prevention.

Antibiotics during pregnancy

A database study from South Korea compared more than a million children exposed to antibiotics during pregnancy or early infancy with a similar number who were not exposed (*Plos Med* https://doi.org/10.1371/journal.pmed.1004677). As far as the later occurrence of autoimmune diseases was concerned, the findings were resoundingly negative. Over 7 years follow-up, no evidence emerged of an increased risk in type 1 diabetes, juvenile idiopathic arthritis, inflammatory bowel disease, systemic lupus erythematosus, or Hashimoto's thyroiditis.

Viral infections awaken metastatic cancer cells

In a laboratory mouse model, exposure to two respiratory viruses, influenza and a mouse-adapted SARS-CoV-2 virus, activated dormant cancer cells in the lungs and promoted an interleukin-6 dependent proliferation of metastatic lesions (*Nature* doi:10.1038/s41586-025-09332-0). This may be relevant to human cancers. Analyses of cancer survivors from the UK Biobank and Flatiron Health databases found that SARS-CoV-2 infection was associated with higher cancer related mortality and a higher incidence of lung metastases than in uninfected cancer survivors.

Body mass index and surgical outcomes in older adults

Although higher BMI is associated with a range of chronic conditions, including cardiovascular disease and type 2 diabetes, a postoperative series of 400 older adults undergoing major elective surgery reports that mortality was lowest in people categorised as overweight (BMI 25 to 30) (*JAMA Netw Open* doi:10.1001/jamanetworkopen.2025.28875). Only one out of 128 overweight patients died in the 30 days after the operation compared with 25 out of 133 patients whose BMI was in the normal range (20 to 25). Traditional advice that overweight people should try to lose weight before surgery may need rethinking.

Ultra-processed foods

Dozens of studies have linked ultra-processed foods with health problems that range from auto-immunity to obesity. But, as a news feature in *Nature* (https://www.nature.com/articles/d41586-025-02754-w) points out, food processes such as fermentation, salting, pickling, smoking, and canning have long histories, and the term "ultra-processed" is unhelpfully broad. What's more, any risks from ultra-processed foods may relate more to the sugar and fat content and energy density of the food than to the processing itself. And we shouldn't forget that some ultra-processed foods—fortified cereals are a good example—are an effective way to provide essential nutrients.

Cite this as: *BMJ* 2025;390:r1936

CLINICAL UPDATE

Diagnosis and management of multidrug resistant tuberculosis

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CPD READING

0.5 HOURS

A 45 year old man with diabetes mellitus self presents to the TB clinic with productive cough for the past month. The sputum was yellow in colour, copious, and was streaked with blood twice. In that time, he has also had continuous fevers around 38°C, not associated with rigors, and he has lost around 5 kg of weight in the past two months. He reports undergoing treatment for drug sensitive TB three years ago, although he did not take his treatment regularly and did not complete the 6 month course. He lives with his wife and two children, none of whom have had any major respiratory illnesses or have been diagnosed with TB. He works in a garment factory for daily wages, does not drink alcohol, and is a former smoker, having smoked 10 cigarettes per day for 20 years, and quitting three years ago. A cartridge based nucleic acid amplification test of his sputum detected *Mycobacterium tuberculosis* with rifampicin resistance. A sputum smear for acid fast bacilli showed 3+, and X ray imaging of the chest showed extensive parenchymal infiltrates in bilateral lung fields with cavitations.

WHAT YOU NEED TO KNOW

- Universal drug susceptibility testing is key for early diagnosis of drug resistant tuberculosis (TB) and should be offered to all people with bacteriologically confirmed TB; rapid molecular diagnostic tests used as an initial diagnostic investigation can simultaneously detect *Mycobacterium tuberculosis* and drug susceptibility early
- Treatment of people with multidrug resistant TB or rifampicin resistant TB with shorter oral regimens based on bedaquiline results in improved treatment success with better tolerability
- Conduct monthly clinical and laboratory assessments (including sputum smear and culture) for people who are being treated for multidrug resistant TB or rifampicin resistant TB to monitor the treatment response and promptly detect and address adverse events
- Refer people for evaluation and initiation of TB preventive treatment if they have been in contact with people with multidrug resistant TB

Globally, of the 10.8 million people estimated to have tuberculosis (TB) in 2023, 400 000 (3.2%) are estimated to have developed multidrug resistant TB or rifampicin resistant TB.[1] Multidrug resistant TB is associated with worse treatment outcomes, allows further TB transmission, and promotes antimicrobial drug resistance.[1] Since 2010, substantial progress in managing drug resistant TB has been made through increased access to newer molecular World Health Organization (WHO) recommended rapid diagnostic tests.[2] Evolution of various shorter oral regimens consisting of fewer pills, resulting in lesser toxicity, and giving rise to better treatment outcomes has revolutionised treatment of multidrug resistant TB, with treatment success improving from 50% in 2012 to 63% in 2020.[2] However, case detection remains a major challenge: only an estimated 44% of people thought to have multidrug resistant TB or rifampicin resistant TB globally were correctly diagnosed and treated in 2023.[1] Early diagnosis and treatment of drug resistant TB with effective regimens are essential for successful treatment. Monitoring the treatment response, assessing for side effects of anti-TB drugs, and providing person centred care are also vital. Here we describe the latest evidence and guidelines underpinning diagnostic evaluations, treatment, care, and support for adults with pulmonary multidrug resistant TB.

What is multidrug resistant TB?

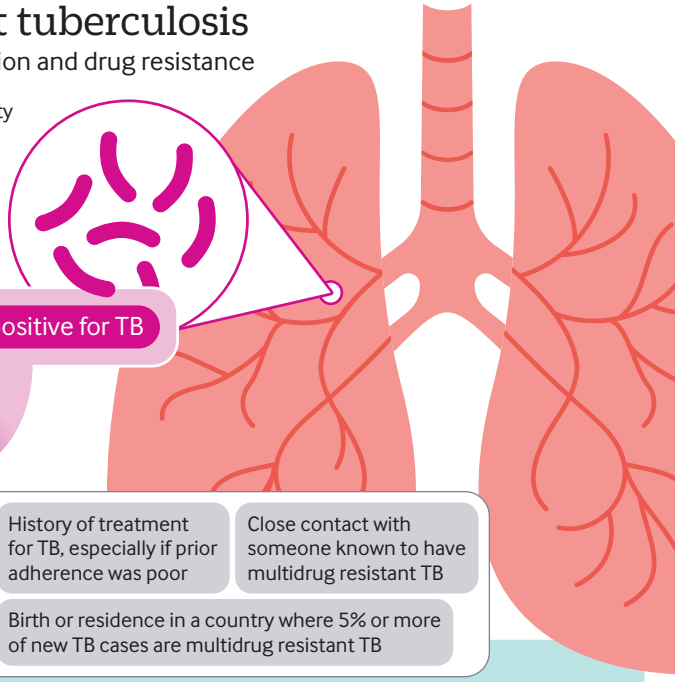
Multidrug resistant TB refers to *Mycobacterium tuberculosis* strains that are resistant to both isoniazid and rifampicin (box 1).[6] In contrast, rifampicin resistant tuberculosis refers to *Mycobacterium tuberculosis* strains that are resistant to rifampicin, with or without resistance to other anti-TB drugs.[6] Strains of TB that are sensitive to rifampicin are managed with rifampicin based treatment regimens. Factors that could promote the development of anti-TB drug resistance in mycobacterial strains include treatment interruptions, substandard drugs, interrupted drug supply, and incorrectly prescribed dosage or duration. Malabsorption leading to suboptimal concentrations or poor drug penetration at target tissue sites despite good adherence can also lead to resistance.[7 8] Individual risk factors for developing multidrug resistant TB relate to the specific strain, the individual patient factors, and the surrounding environment (box 2).

thebmj Visual summary

Drug resistant tuberculosis

Testing for *M.tb* detection and drug resistance

Diagnosis of multidrug resistant tuberculosis (TB) depends on drug susceptibility testing to identify anti-TB drug resistance. Rapid molecular diagnostic tests used as an initial diagnostic investigation can simultaneously detect *Mycobacterium tuberculosis (M.tb)* and drug susceptibility early. This visual summary presents the features of some commonly used tests that can be used to detect a range of types of resistance.



Assessment

TB signs and symptoms or Screened positive for TB

Respiratory samples
- Sputum, expectorated, or induced
- Bronchoalveolar lavage, if required
- Tracheal aspirate

Risk factors
- History of treatment for TB, especially if prior adherence was poor
- Close contact with someone known to have multidrug resistant TB
- ⚠ Birth or residence in a country where 5% or more of new TB cases are multidrug resistant TB

Initial tests for TB detection and anti-TB drug resistance

WHO recommends testing all people with TB for rifampicin resistance; drug susceptibility testing is also indicated for people with poor response to treatment. NICE recommends anyone with suspected TB also undergo rifampin resistance testing if one or more risk factors for multidrug resistant TB are present

Test	Turnaround time (hours)	Detects resistance to: Rifampicin	Isoniazid	Fluoroquinolone	Ethionamide	Amikacin	Pyrazinamide	Second line injectables	Ethambutol	Bedaquiline	Streptomycin	Clofazimine	Linezolid
Xpert MTB/RIF and MTB/RIF Ultra	2	✓											
Truenat MTB Plus with MTB-RIF Dx	2	✓											
Loopamp MTBC detection kit (TB LAMP)	2	Detects *Mycobacterium tuberculosis* only											
FluoroType MTB and MTBDR	2.5	✓	✓										
BD MAX MDR-TB	4	✓	✓										
Cobas MTB and MTB-RIF/INH	4	✓	✓										
Abbott RealTime MTB and MTB RIF/INH	13	✓	✓										

Follow on tests for detecting additional resistance to anti-TB drugs

Xpert MTB/XDR	1.5		✓	✓	✓	✓							
GenoType MTBDRplus v1 and v2	5	✓	✓										
Genoscholar PZA-TB	5						✓						
GenoType MTBDRsl assay	5			✓				✓					
Deeplex Myc-TB or AmPORE-TB	72-120	✓	✓	✓			✓		✓				
TBseq	72-120		✓	✓		✓	✓		✓	✓	✓	✓	✓

Phenotypic drug susceptibility tests identify drug resistance to new and repurposed anti-TB drugs at treatment initiation and detect the emergence of additional drug resistance during treatment, but have a longer turn around time.

Clinical presentation

People with pulmonary multidrug resistant TB typically present with symptoms similar to those of drug sensitive TB. Common signs and symptoms include cough, fever, loss of appetite, weight loss, breathlessness, haemoptysis, chest pain, and night sweats (table 1). Longer duration of cough does not increase sensitivity for diagnosis of TB. Systematic reviews underpinning WHO TB screening guidelines found that cough of 2 weeks or more has a sensitivity for TB diagnosis of 0.42 and a specificity of 0.94. The presence of any cough has a slightly greater estimated diagnostic sensitivity of 0.51 with a specificity of 0.88. The presence of any of cough, haemoptysis, fever, night sweats, or weight loss had an overall sensitivity of 0.71 for detection of TB, but a reduced specificity of 0.74.[24 25] However, a substantial proportion of people with bacteriologically confirmed TB have no cough at all or are asymptomatic. A meta-analysis of nationally representative surveys conducted between 2007 and 2020 in 12 countries with high incidence of TB found that 39.8% of participants with bacteriologically confirmed TB had reported no cough of any duration (but this figure could be higher), whereas 40.9% reported cough for 2 weeks or more.[26]

People who present with presumed TB or those already on treatment for drug sensitive TB with persistent or worsening respiratory symptoms, fever, poor weight gain, appearance of new (or deterioration of pre-existing) lesions on chest x ray imaging, and/or persistently positive sputum smears or cultures warrant evaluation for drug resistant TB.

Table 1 | Common signs, symptoms, and exposures in pulmonary drug resistant TB

Signs and symptoms	Estimated prevalence (%)
Cough	10-74[16-19]
Fever	15-78[16-19]
Weight loss	23-63[16-19]
Loss of appetite	32-52[17-19]
Breathlessness	18-64[16-18]
Haemoptysis	10-46[16-18]
Chest pain	7-29[16-18]
Contact with people known to have drug resistant TB	2-38[17 20 21]
BMI <18.5	27-84[18 21 22]
History of treatment for TB	42-80[16 20 22 23]

Box 1 | Classification of drug resistant tuberculosis

According to WHO, there are five categories of drug resistant TB[3]

- Rifampicin resistant TB: TB bacteria resistant to rifampicin, which could be susceptible or resistant to isoniazid, or resistant to other first line or second line anti-TB drugs
- Rifampicin susceptible, isoniazid resistant TB: TB bacteria resistant to isoniazid but susceptible to rifampicin
- Multidrug resistant TB: TB bacteria resistant to isoniazid and rifampicin
- Preextensively drug resistant TB: TB bacteria resistant to rifampicin (might also be resistant to isoniazid) and at least one fluoroquinolone drug (levofloxacin or moxifloxacin)
- Extensively drug resistant TB: TB bacteria resistant to rifampicin (might also be resistant to isoniazid), at least one fluoroquinolone drug (levofloxacin or moxifloxacin), and resistant to linezolid or bedaquiline (or both).

Resistance can either be primary or secondary.[4 5] Primary drug resistance occurs when someone is infected with a drug resistant *Mycobacterium tuberculosis* strain. Secondary drug resistance occurs when a TB strain acquires resistance conferring mutations to anti-TB drugs while a person is on drug treatment.

Box 2 | Risk factors for developing multidrug resistant TB[9-13]

Agent factors

- Infection with Beijing strain of *Mycobacterium tuberculosis*, a globally significant lineage of the bacteria, which is known to be associated with anti-TB drug resistance[14 15]

Patient factors

- Male sex
- Comorbidities (eg, HIV, concurrent chronic lung disease, diabetes)
- Lifestyle factors (eg, smoking, alcohol consumption)
- History of TB
- Prior TB treatment interruptions
- Previous TB treatment failure
- Failure to respond to first line anti-TB drugs in the current treatment course

Environmental factors

- Living in crowded settings
- Close contact with people with pulmonary drug resistant TB
- Residing in areas with high prevalence of drug resistant TB
- Use of poor quality anti-TB drugs

How should I assess for multidrug resistant TB?

Collect a detailed history from people with symptoms suggestive of TB, including respiratory and constitutional symptoms, comorbidities including HIV infection and diabetes, history of TB diagnosis and treatment, TB contact history, high risk occupations, housing conditions, travel history including previous or current residence in areas where TB is endemic, as well as lifestyle factors such as smoking and alcohol consumption. Complete a detailed, comprehensive physical examination including assessment of nutritional status, involvement of extrapulmonary sites and signs such as icterus or pedal oedema, which could relate to organ dysfunction and lead to drug related toxicities.

Early diagnosis of pulmonary multidrug resistant TB depends on the rapid and accurate detection of *Mycobacterium tuberculosis* in respiratory samples (eg, expectorated or induced sputum, tracheal aspirate, or bronchoalveolar lavage, if required) from people with signs or symptoms of TB or from asymptomatic people who screened positive in community based TB screening or contact tracing programmes based on chest x ray imaging, C reactive protein in people living with HIV, or by molecular WHO recommended rapid diagnostic tests.[27] Diagnosis of multidrug resistant TB also depends on drug susceptibility testing to identify anti-TB drug resistance. Nucleic acid amplification tests that simultaneously detect *Mycobacterium tuberculosis* and rifampicin resistance in respiratory samples are the initial diagnostic tests of choice for all people undergoing evaluation for pulmonary TB (table 2, see bmj.com),[27 31] largely replacing sputum smear microscopy.

Of note, chest x ray imaging is not the initial diagnostic test of choice for pulmonary TB, but most clinical guidelines for evaluating respiratory symptoms and possible pulmonary TB recommend it to rule out alternative diagnoses and to estimate the extent of lung involvement.

WHO recommends universal drug susceptibility testing, which aims to test all people with bacteriologically confirmed TB for rifampicin resistance if this was not done concurrently with *Mycobacterium tuberculosis* detection.

In people with confirmed rifampicin resistant TB, tests for additional resistance to anti-TB drugs including isoniazid and fluoroquinolones are indicated. Low complexity automated nucleic acid amplification tests, line probe assays, and targeted next generation sequencing assays could be used (table 2, see bmj.com).[27] For people with bacteriologically confirmed TB who did not have simultaneous drug susceptibility testing for rifampicin and isoniazid, line probe assays and other dedicated drug susceptibility tests could be used as follow-on tests to detect resistance to anti-TB drugs.[27] For people with confirmed multidrug resistant TB or rifampicin resistant TB, second line probe assays could be considered to detect resistance to fluoroquinolones and second line drugs administered by injection.[27] Next generation sequencing assays can detect additional mutations to several anti-TB drugs with a reduced turnaround time and acceptable costs.[34 35]

How is multidrug resistant TB treated?

WHO updated its drug resistant TB treatment guidelines in 2022 to recommend a 6 month oral BPaLM or BPaL regimen for people with either multidrug resistant TB or rifampicin resistant TB (box 3, see bmj.com).[1 46] As of April 2025, WHO also recommends a 6 month oral regimen containing bedaquiline, delamanid, linezolid, levofloxacin, and clofazimine (BDLLfxC) that can be given to pregnant or lactating women and others (box 3, see bmj.com).[37] Additional treatment regimens include a 9-11 month oral, a modified 9 month oral and a longer 18-20 month regimen (preferably administered orally or by injection) for multidrug resistant TB or rifampicin resistant TB treatment.[37]

Baseline laboratory investigations can aid in selecting the most appropriate treatment regimen and are useful reference points for monitoring the side effects of anti-TB drugs. Baseline laboratory tests typically include liver function tests, serum electrolytes, a complete blood count, HIV antigen/antibody if HIV status is unknown (also check the CD4 cell count in people living with HIV), hepatitis B surface antigen, hepatitis C antibodies, and a pregnancy test for women of reproductive age (if indicated). Depending on the specific treatment regimen, baseline testing might also include thyroid stimulating hormone, uric acid, and electrocardiography.[47] People undergoing testing and treatment for multidrug resistant TB might also benefit from psychosocial assessments to enhance provision of person-centred care and support interventions during treatment.[48 49]

There are nuances to treatment for people in unique or vulnerable populations. All multidrug resistant TB treatment regimens can potentially be used safely in people living with HIV after thoroughly considering drug-drug interactions.[50] Refer people living with HIV who have been diagnosed with multidrug resistant TB or rifampicin resistant TB to specialist care, where available, to consider adjustments to antiretroviral therapy while undergoing treatment for multidrug resistant TB. Refer pregnant or breastfeeding women to obstetric and/or TB specialists for initiation of multidrug resistant TB treatment and its management during pregnancy and for appropriate treatment while breastfeeding.

Baseline laboratory investigations can aid in selecting the most appropriate treatment regimen

Some people with multidrug resistant TB will need longer treatment regimens, up to 18-20 months (or 15-17 months after conversion of positive sputum culture to a negative culture result),[2] depending on an individual's response to therapy. Indications for longer treatment regimens for multidrug resistant TB or rifampicin resistant TB are listed in box 4, and WHO provides detailed guidance on extended treatment options.[37]

How should I monitor treatment response and adverse events from drugs in people with multidrug resistant TB?

Closely monitor all individuals undergoing treatment for multidrug resistant TB or rifampicin resistant TB to assess the treatment response and detect adverse events from anti-TB drugs. Monthly clinical examination, sputum smear, and culture are recommended for monitoring the response to treatment in all people on treatment regardless of the regimen they are on or their baseline smear or culture result.[47]

Some guidelines, including the American Thoracic Society, recommend more frequent monitoring until sputum smear conversion, biweekly until culture conversion, and then monthly until treatment completion.[51] Molecular WHO recommended rapid diagnostic tests are not recommended for treatment response monitoring and do not replace sputum smear microscopy and culture for this purpose because they could detect dead *Mycobacterium tuberculosis* as well.[52] Sputum culture is more sensitive than microscopy for monitoring the bacteriological status during treatment

Box 4 | Indications for a longer multidrug resistant TB or rifampicin resistant TB treatment regimen[37]

- Extensive drug resistance (box 1)
- Severe forms of extrapulmonary TB (eg, tuberculous meningitis, disseminated TB, pericardial TB, osteoarticular TB)
- Extensive pulmonary TB disease
- Exposure to any of the drugs in a shorter regimen for more than 1 month
- Resistance to drugs in the shorter regimens
- Intolerance to the drugs in a shorter regimen
- Treatment failure or lack of bacteriological conversion or clinical response after taking a 6 or 9 month regimen
- Pregnancy, lactation, or younger age for which a shorter regimen is contraindicated
- BMI <17
- Altered liver function tests suggestive of hepatic inflammation or injury (liver enzymes more than three times the upper normal limit)
- Severe anaemia (haemoglobin <80 g/L) or thrombocytopenia (platelet count $<150\times10^9$/L)
- Severe peripheral neuropathy (grade 3 or 4)

(77.9% *v* 68.9%).[53] Limitations of *Mycobacterium tuberculosis* culture include the need for well equipped laboratory facilities and longer turnaround time for results. Sputum microscopy can be performed rapidly with minimal laboratory facilities, but viability of the mycobacteria cannot be confirmed. An individual's ability to produce a good quality sputum sample can also influence smear and culture results.[54]

Chest x ray imaging is indicated at baseline, after the second month of treatment, at the end of treatment, as well as 6 and 12 months post treatment (or when otherwise clinically indicated) to confirm resolution and/or detect the appearance of new or worsening lesions.[47] Respiratory symptoms might persist even after sputum conversion, but improvement is common within 2 months of treatment with an appropriate treatment regimen.[12] Weight gain of more than 5% during the first 3 months of treatment is consistent with a good response.[55 56]

Failure of bacteriological sputum culture conversion (ie, persistent culture positivity) at or after 4 months of treatment or sputum culture reversion (negative to positive culture) during treatment or follow-up warrants drug susceptibility testing by genotypic (Xpert MTB/XDR) or line probe assay as well as phenotypic testing (table 2, see bmj.com).[47] Malnutrition (BMI < 18) and culture conversion more than 2 months after treatment initiation are risk factors for unfavourable treatment outcomes, including treatment failure, relapse, and death.[57] Restoration of adequate nutritional status is essential,[58] and hospital stays might be required for people with severe anaemia and malnutrition (haemoglobin <70 g/L, BMI <16 with pedal oedema, mid upper arm circumference <16 cm) to address nutritional status.[48]

Care and support for people undergoing treatment for multidrug resistant TB

Fear of testing positive for TB, stigma, apprehensions related to the cost of treatment, frequent clinic visits, and drug toxicities are important deterrents for undergoing diagnostic tests for TB and for completing TB treatment.[64] Health centre accessibility, pill burden, duration of treatment, and misconceptions can also affect adherence to treatment.[65] Provide person centred multidrug resistant TB care that is based on individuals' needs and choices to support individuals and families to overcome unique social, economic, cultural, legal, and psychological barriers they might be facing.[47] Education about TB and adherence to treatment, alongside psychosocial support, improve treatment adherence and outcomes.[66] For example, in a pilot of counselling to improve drug resistant TB treatment among 331 people with drug resistant TB in Papua New Guinea, education by counsellors including peers and counselling sessions about TB, TB medications, and adherence to treatment reduced loss to follow-up during treatment from 18% (baseline) to 4% (with interventions).[67] Other measures that could support individuals to complete multidrug resistant TB treatment include material support, such as food, financial assistance or travel support; social connectedness via support groups and other kinds of companionship; tailored treatment support in which health workers or trained lay supporters help an individual to take TB medications; and various digital tools such as SMS medication reminders, event monitoring devices, or video-observed treatment.[47] It might not be possible or appropriate to provide care in the community or at home for people with extensive disease, serious comorbidities and/or with treatment adherence difficulties.

EDUCATION INTO PRACTICE

- Think about the last time you talked to patients about treatment adherence, pill burden, and adverse events from drugs for a given treatment course. What are the most common barriers to treatment adherence?
- What initial assessments are appropriate for people with respiratory symptoms concerning for TB?
- How often do you offer advice about treatment adherence to people being treated for TB?
- How would you discuss the possible adverse events from drugs with people diagnosed with multidrug resistant TB at the time of treatment initiation and during follow-up?

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

The author Paran Sarimita Winarni is a drug resistant TB survivor and TB activist. Her experiences and suggestions about the importance of person centred care, nutrition in TB management, training, and involvement of community volunteers in treatment supervision and monitoring of adverse events helped to strengthen the care and support section of this manuscript.

SOURCES AND SELECTION CRITERIA

We conducted a review of the literature to gather the latest evidence, guidelines, and recommendations for the diagnosis and management of multidrug resistant TB. We performed two searches—a more generalised search regarding drug resistant TB, followed by a more focussed search using key words such as "drug resistant tuberculosis", "multidrug resistant tuberculosis", "rifampicin resistant tuberculosis", "risk factors", "diagnosis", "diagnostic tests", "treatment", "care and support", "toxicity", "safety", and "treatment outcome". A combination of these words was used to search for articles in PubMed, Google Scholar, and Cochrane databases. We chose articles that were related to multidrug resistant TB. We also identified appropriate articles from the reference lists of the chosen articles.

How can multidrug resistant TB be prevented?

Transmission of drug resistant TB—like drug sensitive TB—is widely reported and is closely linked to social determinants of health such as overcrowded housing, income insecurity, gender, and absence of social protection that make certain populations more vulnerable to TB risk factors (including HIV infection, tobacco and alcohol use, and undernutrition), TB exposure, and previous TB treatment failure.[1 68] Rapid diagnosis and timely initiation of effective TB treatment, appropriate ventilation, use of N-95 masks, and good hand hygiene (especially in hospital settings, contact screening, and preventive treatment in exposed contacts) prevents the transmission of drug resistant TB.[69]

Refer close contacts of individuals with multidrug resistant TB or rifampicin resistant TB in whom TB disease is not detected to specialist services for consideration of TB preventive treatment.[47]

Competing interests: None declared.

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OPINION Jirair Ratevosian and Jeffrey L Sturchio

How can we stop GLP-1 receptor agonists becoming another story of global health inequity?

The arrival of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) such as semaglutide and tirzepatide marks an important moment in the treatment of obesity and diabetes. Clinical trials show that these agents can deliver substantial and sustained weight loss, improve glycaemic control, and reduce cardiovascular risk.

Yet their current annual cost—often exceeding $8000 per patient in high income markets—places them far out of reach for most people in low and middle income countries. Without urgent planning and coordinated global action, GLP-1 RAs risk becoming the latest emblem of the innovation access gap that divides people in rich and poor countries.

Non-communicable diseases (NCDs) such as diabetes, cardiovascular disease, and certain cancers are already the leading causes of death worldwide. Overweight and obesity is another chronic condition of increasing global prevalence that interacts with the NCD epidemic. According to the World Health Organization (WHO), 2.5 billion adults—nearly one in three—are overweight, including 890 million with obesity. The global economic impact will exceed $4tn by 2035, with the sharpest increases projected in Asia and Africa.

This month, WHO updated its essential medicines list to include GLP-1 RAs for the first time, underscoring their importance for diabetes and obesity care globally. But will GLP-1 RAs be made equitably accessible to all or remain confined to wealthy nations?

A similar challenge confronted the global health community 25 years ago. Then antiretroviral therapy (ART) for HIV cost more than $10 000 annually and was largely inaccessible outside wealthy countries. Coordinated global action drove prices down 99%, bringing ART to over 31 million people and averting 21 million deaths, enabling the most extensive treatment scale-up in modern public health. The HIV experience offers key lessons for how we can bridge the innovation access gap with GLP-1 RAs.

Making obesity a priority

If governments, civil society, and the private sector are going to enable access to GLP-1 RAs as a major tool in tackling the global obesity epidemic, then this will require political will to catalyse dedicated financial investment at national and international levels, and governments setting priorities for obesity prevention and treatment in national budgets.

RICHARD LEVINE/ALAMY

Just as HIV was a disease, not a moral or lifestyle choice, so too is obesity

HIV treatment scale-up relied on global procurement and effective supply chain systems. Voluntary licensing agreements with pharmaceutical companies; pooled procurement through donor mechanisms like the US President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund; and regulatory innovation all helped to widen access to ART. A similar approach for GLP-1 RAs could combine transparent licensing arrangements, pooled financing, and coordinated market shaping between countries to expand global access.

The private sector advanced ART access through innovations in supply chain logistics, diagnostics, and laboratory networks. It also used creative distribution channels to deliver public goods, partnered with civil society organisations and national health systems to train frontline health workers, and introduced new technologies to support enhanced HIV prevention, treatment, and care programmes at the community level.

For GLP-1 RAs, public-private partnerships could leverage telemedicine platforms for prescribing and follow-up, and engage insurers and pharmacy chains to integrate access into benefits packages.

The response of affected populations to the HIV/AIDS epidemic was decisive to raise public awareness of the problem, reduce stigma, mobilise resources, and advocate for sound public policy and investments. The global obesity crisis will require the same: civil society organisations and the populations they represent must hold governments accountable, generate political will, and ensure that prevention and treatment strategies are prioritised.

Barriers to prevention

Stigma and discrimination proved dangerous in the HIV/AIDS epidemic by creating barriers to prevention, care, and treatment, particularly for people in the most marginalised populations. Just as HIV infection was a disease, not a moral or lifestyle choice, so too is obesity a chronic condition that is driven in part by the unaffordability and unavailability of healthy diets, as well as obesogenic environments and psychosocial and genetic factors.

People living with this condition should be afforded equitable access to the resources needed to assist them, and renewed efforts should be made to improve obesity prevention. Tackling the global obesity crisis will take more than medical solutions—it requires confronting the structural and commercial forces that prevent people eating healthy diets, and investing in civil society and community organisations that can challenge stigma and amplify lived experience.

HIV was once a matter of life and death for millions of people. The world rose to meet that challenge, with governments, activists, and the private sector working together to drive down drug prices; scale up prevention, treatment, and care; and make HIV infection a chronic condition for those with access to ART—proving that collective action can rewrite the trajectory of a global epidemic.

Obesity now presents a parallel crisis. Just as the HIV movement showed that global solidarity and smart policy can overcome barriers, the obesity challenge is an opportunity to show that we have learnt from the past.

Jirair Ratevosian, Hock fellow, Duke Global Health Institute

Jeffrey L Sturchio, chair, Friends of the Global Fight Against AIDS, Tuberculosis and Malaria

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PRACTICE POINTER

New treatments for migraine: CGRP monoclonal antibodies, gepants, and ditans

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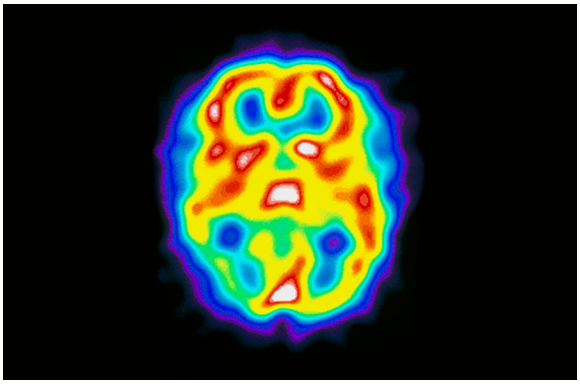
CPD READING
0.5 HOURS

A 44 year old woman with longstanding migraine presents for follow-up. She has an average of 12 headache days each month, and about half of these are severe enough to affect her ability to work. Trials of amitriptyline and propranolol for prevention, and three triptans and two non-steroidal anti-inflammatories for acute treatment, have not been effective. She has heard that there are new migraine treatments available and wonders if any of them would be right for her. She notes that she sometimes has trouble remembering to take medications every day.

Migraine is a chronic neurological disease characterised by recurrent attacks of headache pain, sensory sensitivity, and other accompanying symptoms.[1] Roughly 1 in 7 adults, 1 billion people worldwide, experience migraine each year, and twice as many women as men are affected. Migraine is the second leading contributor to years of life affected by disability.[2-4] Lack of access to care and underdiagnosis of migraine are the primary barriers to optimal migraine treatment. Most patients with migraine worldwide therefore do not have access to prescription treatments.[5] The treatment landscape for migraine has undergone rapid change as new classes of both acute and preventive treatments have been brought to market since 2018.[6 7] Access to these treatments varies among countries and healthcare settings. In many settings, including the UK, use of calcitonin gene-related peptide (CGRP)-targeted treatments is limited by access to specialist care and a requirement for multiple prior treatment failures.

WHAT YOU NEED TO KNOW

- Calcitonin gene-related peptide (CGRP)-targeted preventive treatments for migraine are better tolerated than older options, with similar effectiveness. These treatments should be considered in patients who do not tolerate or respond to at least one trial of an older preventive, or who have contraindications to using them.
- Gepants (CGRP receptor antagonists) and ditans (serotonin receptor antagonists) are options for treatment of acute migraines in patients who do not respond to triptans or in whom triptans are contraindicated. Gepants are likely slightly less effective than triptans but have fewer side effects. Ditans do not cause vasoconstriction and, like gepants, may be used in patients with cardiovascular contraindications to triptan use.
- Debate about whether newer treatments should be first or second line is ongoing. The higher cost of new treatments and unclear evidence for cost-effectiveness in most situations is a limitation.



Coloured single photon emission computed tomography (SPECT) scan of the brain of a patient during a migraine attack

Approach to pharmacological treatment of migraine

Comprehensive migraine treatment includes behavioural interventions and lifestyle management, integrative therapies, and pharmacological treatments. Pharmacological management of migraine is separated into acute and preventive interventions.

Acute treatment

Acute treatments are used at the time of a migraine attack to relieve pain and accompanying symptoms. Because migraine causes moderate to severe pain, nearly all people with migraine require acute treatment at least sometimes.[6] Goals of acute treatment are freedom from pain two hours after treatment, resolution of bothersome accompanying symptoms such as nausea, few side effects, and limited need for repeat treatment.[6]

Non-specific analgesics such as paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) may be tried for less severe attacks. Triptans are first line among migraine-specific treatments. A network meta-analysis from 2024 compared drug interventions for acute treatment of migraine and included 137 randomised controlled trials with 89 445 participants: it found that freedom from pain at two hours was more likely with use of triptans (odds ratios compared with placebo 1.73 to 5.19) than with NSAIDs (odds ratios 1.83-3.05), gepants (odds ratios 1.96-1.99), or lasmiditan (odds ratio 2.32).[8] Migraine-specific treatments (see box 1) may be combined with non-specific treatments, and use of several triptan and NSAID combinations are supported by positive clinical trial data.[9] Treatment of nausea, which often accompanies attacks, should be considered routinely. The antiemetics metoclopramide, promethazine, and prochlorperazine may be effective for reducing migraine pain as well as nausea.[9]

Preventive treatment

Preventive treatment is indicated for a subset of patients with more severe, frequent, or disabling disease. A US based study including a representative sample of 162 576 people found that 38.8% met criteria for considering or offering preventive treatment.[10] Expert consensus and treatment guidelines from multiple countries suggest that preventive treatment may be offered to patients who experience at least four to six moderate to severe headache or migraine days per month, or who have significant disability related to migraine attacks.[6-12] Goals of preventive treatments include reduced headache frequency and severity, reduced disability, improved response to acute treatment, and few side effects. Effective preventive treatment may reduce the likelihood of worsening migraine burden over time. Box 2 lists preventive treatments with strong evidence for effectiveness. The tricyclic antidepressant amitriptyline and the serotonin noradrenaline (norepinephrine) reuptake inhibitor (SNRI) venlafaxine have lower quality evidence for benefit but are commonly prescribed. The choice of which first line preventive treatment to start should be individualised and consider comorbidities and potential side effects.

Although older migraine medications are helpful for many patients, they have limitations that prevent successful treatment for some patients. The most common barriers for use of older medications are side effect burden, lack of or partial efficacy, contraindications due to medical comorbidities, and medication interactions.[13] The most common contraindication to triptan use is cardiovascular disease.[14] Due to the potential for vasoconstriction, triptans are contraindicated in the setting of known cardiovascular disease, multiple cardiovascular risk factors, or poorly controlled hypertension. Newer migraine treatments aim to ameliorate these limitations.

What new medications are available for acute treatment of migraine?

Gepants and ditans, two new classes of migraine-specific acute treatment, were introduced in 2019 and 2020.

Gepants are small molecule calcitonin gene related peptide (CGRP) receptor antagonists. CGRP is a neuropeptide involved in pain transmission and neurogenic inflammation, and it has a central role in the pathophysiology of migraine attacks.[15] The orally dissolving tablet rimegepant has been approved by both the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) for acute treatment, while oral ubrogepant and zavegepant nasal spray have been approved by the FDA only. Gepants were well tolerated in clinical trials. Use should be avoided in pregnancy due to lack of safety data. Gepants and lasmiditan have not shown any signal of cardiac adverse events and are therefore considered safe in patients with cardiovascular risk factors.[16]

Box 1 | Migraine-specific acute treatments

- Triptans (agonists for serotonin (5-HT) 1B and 1D receptors): almotriptan, eletriptan, frovatriptan, naratriptan, sumatriptan, rizatriptan, zolmitriptan
- Ergot derivatives: dihydroergotamine
- Gepants (CGRP receptor antagonists): rimegepant, ubrogepant, zavegepant
- Ditans (5-HT1F receptor agonist): lasmiditan

Box 2 | Preventive treatments for migraine

Migraine-specific

- CGRP monoclonal antibodies: eptinezumab, erenumab, fremenezumab, galcanezumab
- Gepants (CGRP receptor antagonists): atogepant, rimegepant

Not migraine-specific

- Antidepressants: amitriptyline,* venlafaxine
- Antiseizure medications: topiramate,* divalproex sodium
- Beta blockers: metoprolol,* propranolol,* timolol
- Angiotensin receptor blockers: candesartan*
- Onabotulinum toxin A (for chronic migraine only)

*Recommended as first line treatments by most guidelines

Fewer than 5% of participants in clinical trials of CGRP mAbs discontinued treatment due to adverse events

Ditans are 5-HT1F receptor agonists. The 5-HT1F receptor produces anti-nociception without the vasoconstriction induced by the 5-HT1B and 1D receptors targeted by triptans. Lasmiditan is the only currently available medication in the ditan class and has been approved by both the FDA and EMA but has not been recommended by the National Institute for Health and Care Excellence (NICE). Lasmiditan has a higher incidence of side effects, including dizziness, fatigue, and sedation.[17] Patients should be counselled to avoid any activity requiring alertness, including driving, for at least eight hours after taking the drug. Although we have no data from direct comparisons between these newer treatments and triptans or other traditional acute medications, the network meta-analysis described above suggests that gepants and lasmiditan are likely to be somewhat less effective than triptans.[8]

When should new acute migraine treatments be considered?

Guidelines from the International Headache Society state that gepants and lasmiditan may be considered in patients for whom three trials of triptan monotherapy or triptans in combination with NSAIDs are ineffective, partially effective, or not tolerated, or in individuals with contraindications to triptans.[9] Similarly, a consensus statement from the American Headache Society and NICE guidance both recommend that newer acute treatments for migraine be considered for patients with contraindications to or intolerance of triptans, or who have had an inadequate response to two or more oral triptans.[6 18] In patients with contraindications to triptans, we recommend a trial of gepants due to the lower risk of side effects, with lasmiditan a third line agent.

Preliminary data suggest that gepants may not cause medication overuse headache, a concern with frequent use of triptans or combination analgesics.[19] Two gepants, rimegepant and atogepant, are used for migraine prevention as well as acute treatment. Gepants may therefore be an acute treatment of choice for patients with medication overuse headache.

What new medications are available for preventive treatment of migraine?

Four monoclonal antibodies (mAbs) to CGRP or its receptor have been developed for use as migraine preventive treatments (box 2). Two gepants are also used preventively[20]: rimegepant is used for prevention when taken at a 75 mg dose every other day; atogepant, which has been studied for preventive treatment only, is dosed once daily. All four CGRP monoclonal antibodies and both gepants used for migraine prevention have been approved by both the FDA and EMA and are recommended by NICE for migraine prevention. Clinical trials and real world studies have found that CGRP-targeted treatments are effective in both episodic migraine (<15 days per month) and chronic migraine (>15 days per month). Follow-up studies have shown continued benefit after several years, effectiveness in patients who have not responded to at least two other preventive treatments, and effectiveness in those with medication overuse headache.[21-23] A single randomised controlled trial of 777 participants that compared topiramate with erenumab favoured the CGRP mAb for both efficacy and tolerability (>50% reduction in monthly migraine days 55.4% in erenumab group *v* 31.2% with topiramate, odds ratio 2.76 (95% CI 2.06 to 3.71)).[24] No other direct comparisons of older versus newer treatments have been conducted.

All CGRP-targeted preventive treatments were well tolerated in clinical trials.[26] Fewer than 5% of participants in clinical trials of CGRP mAbs discontinued treatment due to adverse events. Injection site reactions and hypersensitivity reactions, including anaphylaxis and angioedema, are the primary concerns related to injected CGRP mAbs. Nausea, fatigue, and constipation are the primary side effects of preventive gepant use.[20] Post-marketing surveillance of CGRP mAbs in clinical practice has revealed additional adverse events: the FDA labelling for CGRP mAbs was recently updated to reflect the risk of new hypertension or worsening of existing hypertension, and development or worsening of Raynaud's phenomenon. Real world evidence has also identified the risk of constipation with serious complications related to erenumab use.

The safety of CGRP mAbs has not been studied in pregnancy or lactation, and they should be avoided in women who are pregnant or at risk of pregnancy, and during lactation. Due to their long half-life, CGRP mAbs should be stopped 4-5 months before conception.

CGRP mAbs are metabolised by the reticular endothelial system and may be given to patients with hepatic or renal disease without dose adjustment. They do not have drug-drug interactions and are therefore a good choice in patients with polypharmacy.

When should new preventive migraine treatments be considered?

Recent guidelines from the American College of Physicians and the Canadian Headache Society suggest trying a CGRP-targeted treatment after an unsuccessful trial of one or more older preventive medications.[12 27] NICE and the Australian Pharmaceutical Benefits Scheme recommend use of available CGRP-targeted treatments after three unsuccessful preventive treatment trials.[11] In contrast, recommendations from the American Headache Society, European Headache Federation, and the British Association for the Study of Headache, among others, recommend considering CGRP-targeted therapies as a first line option.[28-30] Guidelines that support first line use of CGRP-targeted treatments typically cite their specificity for migraine as well as better quality evidence for efficacy and safety compared with the evidence for older treatments, while recommendations for trying other treatments first are more likely to cite cost as a major determining factor.[28]

While insurance coverage and patient access varies among payers and countries, CGRP-targeted treatments are typically more expensive than older migraine preventives.

Based on available evidence and guideline recommendations, our recommendation is to consider a CGRP-targeted treatment in patients who have tried and failed at least one older migraine preventive treatment. CGRP mAbs may be considered first line in patients who have contraindications to use of older drugs or in whom polypharmacy is a concern. Patients should be encouraged to keep a detailed headache diary to establish headache frequency, disability, and treatment response.

Treatment efficacy, defined as a 30-50% reduction in headache frequency (depending on initial migraine frequency) or a clinically meaningful improvement in a validated migraine-specific patient-reported outcome measure (that is, MIDAS, HIT-6) should be evaluated three to six months after starting treatment.[33]

Case denouement

As we discussed risks and benefits of different preventive treatment options, the patient mentioned a remote history of nephrolithiasis that contraindicated a trial of topiramate. Using a shared decision making model, we agreed on a trial of erenumab for prevention. For acute treatment, we recommended a trial of a rimegepant.

At a follow-up visit four months later, she had five headache days per month, which were milder than previously, and responded well to rimegepant.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

We invited two patients who receive care for migraine at the University of Vermont Medical Center to provide feedback on this paper. Their comments regarding clarity of the tables and resolution of the case have been incorporated into this final version. We thank NLG and AR for their time and helpful input.

EDUCATION INTO PRACTICE

- In which situations would you consider prescribing gepants or ditans for acute migraine treatment?
- Based on reading this article, do you consider CGRP-targeted treatments as first line for preventive treatment of migraine? How do cost and access concerns affect your answer?

Competing interests: RB receives compensation for services as an associate editor for *Neurology*; ER receives compensation for services as the viewpoint and online editor for *JAMA Internal Medicine*.

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Community perinatal mental health teams reduced women's risk of mental illness relapse

The study

Community perinatal mental health teams and associations with perinatal mental health and obstetric and neonatal outcomes in pregnant women with a history of secondary mental health care in England: a national population-based cohort study

Gurol-Urganci I, Langham J, Tassie E, et al

The Lancet Psychiatry, 2024;11:174-82

CPD READING

0.5 HOURS

NIHR | National Institute for Health and Care Research

NIHR Alerts are summaries of NIHR-funded research with novel findings and implications for practice. They are intended for health and care professionals, commissioners, researchers and members of the public.

To read the full NIHR Alert, go to: https://tinyurl.com/32xmpw75

Why was the study needed?

Women who have previously had severe mental illness, such as bipolar disorder or severe depression, are at increased risk of relapse after giving birth. A 2016 review showed that many (37%) women with bipolar disorder relapsed after childbirth. Other research suggests that women with a history of mental illness are more likely to give birth prematurely (10%) than other women (7%).

Community perinatal mental health teams were launched in England in 2016 to improve access to mental healthcare for pregnant women. The teams aim to prevent and treat episodes of mental illness during pregnancy and after birth. The service offers psychological interventions, medication advice, help with bonding with the baby, and emergency referrals to appropriate clinicians. However, there is little research that evaluates the service.

What did the study do?

This study assessed whether access to community perinatal mental health teams reduced the risk of relapse after birth among women with a history of mental illness. The researchers also looked at pregnancy outcomes.

The study was based on the records of women with a history of mental health illness who gave birth in England from 2016 to 2018. Almost half (31 276) had access to community perinatal mental health teams; the others (39 047) did not. Participants had been in contact with a secondary mental health service in the 10 years before their pregnancy. Women who gave birth to more than one baby were excluded.

What did it find?

The main outcome was the number of women who had a relapse requiring a psychiatric hospital admission or being seen by the crisis resolution team in the year after birth. Researchers found that in areas where community perinatal mental health teams were available:

- More women accessed mental healthcare (32%) than in areas without teams (26%)
- Fewer women relapsed (3.6%) than in areas without teams (4.5%).

Fewer women had a preterm birth (10.1%) in areas where the service was available than in areas without teams (11.1%). However, the researchers also found that in areas where community perinatal mental health teams were available:

- Stillbirth and infant death were slightly more common (0.5% births) than in areas without teams (0.4%)
- More babies had low birthweight (7.2%) than in areas without teams (6.6%).

Overall, there was no difference in adverse pregnancy outcomes in areas with or without community perinatal mental health teams.

Why is this important?

This study provides evidence that community perinatal mental health teams increase access to mental healthcare and reduce the risk of relapse. Greater access to these teams across the UK could improve mental health outcomes for women during pregnancy and after birth. Community perinatal mental health teams are unique to the UK and the researchers say that other countries could benefit from similar services.

There is no simple explanation for the increased risk of stillbirth, child death, and low birthweight babies in areas with access to teams. The researchers suggest that mental health could sometimes have been prioritised over physical health in women with a history of mental illness.

The researchers caution that the study considered women's potential access to community perinatal mental health teams; it did not look at whether they actually accessed the service.

What's next?

The researchers suggest that closer working between community perinatal mental health teams and other maternity services could improve care for pregnant women with a history of mental illness.

Mental health services have expanded and are now more embedded in maternity services.

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

Cite this as: *BMJ* 2025;390:r918

Supporting my child with her medical care

This author describes attending her child's frequent medical appointments, and how interactions between child, carer, and healthcare professional evolve over time

You are the doctor, my child is the patient, and I am neither; but I live this experience wedged between you both. You are the expert in this condition, I am the expert in my daughter until she can be expert for herself, her voice until she has one of her own.

Where it begins

My child is 2, and our conversation goes over her head. I ask the questions I need answers to, even the scary ones. I don't realise this at the time, but these appointments are some of the easier ones. I can filter out what I think she doesn't need to know right now, and translate for her using *our* normal words into a narrative she can understand. I keep control of our world, letting in as much or as little of the "bad stuff" as I feel she can manage. She has received a diagnosis of arthritis, aged 2. She may or may not grow out of it. I will live this with her; I would prefer to live it for her instead.

Growing understanding

My child is 8. She has pain, she feels different from her friends. I can ask you, the health professional, a few things, but not the things I really want to know because she is good at listening now. She is cross: she does not want a sticker—she knows this doesn't change anything. I had to persuade her to come today—she would rather have stayed in school. When I drop her back to school she does not want to go in because the other children will ask her where she has been. I cannot go in and answer for her. It is not easy for her to say, "I have arthritis," because they learnt about arthritis at school and it was something that happens to old people.

PRIYA SUNDRAM

CPD READING
0.5 HOURS

Importance of the welcome

My child is 12. When you come to call us from the waiting room, she is already assessing your demeanour to decide if you are kind or not. She has met so many health professionals over the years. She is absorbing the tone of your voice, the speed at which you turn to lead the way to your clinic room, whether you linger to share a joke. I am internally begging you to linger and share a joke, to smile at us both, to let her know it will be OK. I know how busy you are. She is observing your expression—she knows you have the results of her scan. I am crossing my fingers that you will relay whatever news you have in words that are not too ominous. She doesn't want you to have a "sympathetic" face because that would mean that it is not good news. I know that on the way home I will have to take apart everything you say and make it OK for her. She will remember all of it, and chew over the words and phrases you have used.

Stepping into adulthood

My "child" is 17. She doesn't like it when I make small talk with you. She made me promise not to. I feel awkward but I keep my promise because otherwise she may refuse to come. She may cry on my shoulder on the way home depending on how today goes. There is so much I need to tell you, so many questions I need to ask about how she has been, but this is her appointment, so I stay quiet. I am urging you silently to engage her somehow. She is more than her disease and the best appointments are when you ask her about herself, her aspirations, her school day, her favourite subject, maybe tell her something about yourself, make her laugh. This is when my shoulders can drop a little and I can breathe for a bit. She needs to know you are human too.

Cite this as: *BMJ* 2025;390:r1818

WHAT YOU NEED TO KNOW

- Parents and carers see more of their child's lived experience than anyone else, thus can provide insight to guide holistic care and support
- Consider offering parents and carers an opportunity to speak to you alone, so that the child does not hear their worries or concerns
- Parents and carers may need reassurance and support in gradually stepping back as their child shifts to managing their own healthcare

ADDITIONAL INFORMATION

CCAA Kids with Arthritis. Supporting children and families living with juvenile idiopathic arthritis (JIA). www.ccaa.org.uk

EDUCATION IN PRACTICE

- How do you ensure that children, young people, and their family members feel welcome and safe when they meet you for the first time?
- How do you support the children and young people in your care to gradually take control of their own healthcare appointments?

CASE REVIEW

Raynaud's phenomenon and telangiectasias

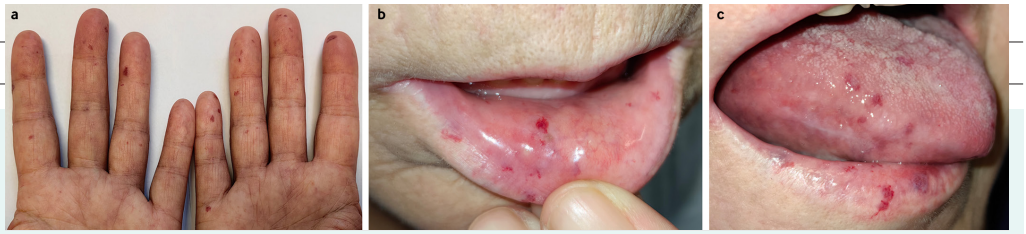

Fig 1 | Telangiectasias observed on the patient's palms (a), lower lip (b), and tongue (c)

A woman in her 60s visited her GP with a two year history of red rashes on her hands and tongue, along with episodes of her fingertips turning white when exposed to cold. She had not previously sought medical care because the symptoms were mild. However, her symptoms had worsened in the past winter. She was diagnosed with Raynaud's phenomenon and referred to our rheumatology department. She had no history of digital ulcers, skin tightening, joint pain, swelling, muscle weakness, heartburn, reflux, dysphagia, dyspnoea, or epistaxis, and no relevant family history.

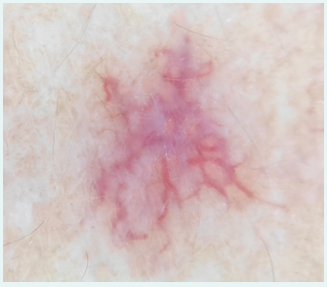

Fig 2 | Dermatoscope image showing a mat-like pattern of telangiectasia

Physical examination revealed numerous telangiectasias on the palms, lower lip, tongue, and face—all of which blanched with applied pressure (fig 1). Dermatoscopic examination showed that these telangiectasias were composed of interwoven, branching vessels (fig 2). Nailfold videocapillaroscopy revealed the presence of giant capillaries (apical diameter ≥50 µm) and pericapillary microhaemorrhages. There was no evidence of puffy fingers, sclerodactyly, proximal skin thickening, pitting scars, or calcinosis.

Full blood count, erythrocyte sedimentation rate, C reactive protein, liver enzymes, creatine kinase, and creatinine levels were unremarkable. Antinuclear antibodies were positive with a titre of 640 by indirect immunofluorescence with a centromere pattern. Further serological testing revealed high titre anti-centromere antibodies. High resolution computed tomography of the chest showed no evidence of interstitial lung disease. Echocardiography and pulmonary function testing revealed no abnormalities.

1. **What are the differential diagnoses?**
2. **What is the most likely diagnosis?**
3. **How would you manage this patient?**

Submitted by Wanyi Lin, Chenhan Jia, Hanlin Yin, and Liangjing Lu
Patient consent obtained.
Cite this as: *BMJ* 2025;390:e084088

answers

CASE REVIEW **Raynaud's phenomenon and telangiectasias**

1 What are the differential diagnoses?

Telangiectasias arise from five principal causes: congenital, trauma, hormonal, primary cutaneous, and systemic connective tissue diseases with cutaneous manifestations.

2 What is the most likely diagnosis?

Systemic sclerosis sine scleroderma, a subtype of scleroderma that is seen in approximately 8% of people with systemic sclerosis.

Telangiectasias are common indicators of microvascular changes in systemic sclerosis, with a prevalence of approximately 75%. Telangiectasias in a scleroderma-like pattern are round, well demarcated, and appear as mat-like vessels on dermatoscopic images; typically observed on the hands, lips, and inside the mouth.

Systemic sclerosis sine scleroderma is defined by the absence of skin thickening despite other diagnostic features. The 2013 American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) classification criteria for systemic sclerosis have a scoring system used for diagnosis. Cases with a score greater than nine are considered to be systemic sclerosis.

3 How would you manage this patient?

The management of vascular damage in systemic sclerosis primarily relies on vasodilation. Dihydropyridine-type calcium channel blocker drugs, particularly oral nifedipine, are recommended as the preferred therapy for systemic sclerosis related Raynaud's phenomenon. Phosphodiesterase 5 inhibitor drugs represent therapeutic options.

LEARNING POINTS

- Systemic sclerosis is a chronic autoimmune connective tissue disease defined by autoimmunity, fibrosis, and vasculopathy, and is classified into limited cutaneous, diffuse cutaneous, and sine scleroderma subtypes based on skin involvement.
- Systemic sclerosis should be strongly suspected in patients presenting with Raynaud's phenomenon and telangiectasias, which might affect the hands, lips, or oral mucosa.
- Multidisciplinary management is crucial in systemic sclerosis, emphasising immunosuppressive and anti-fibrotic therapies for skin and lung involvement, vasodilator drugs for vascular complications, and vigilant monitoring for internal organ involvement.

PATIENT OUTCOME

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