education

RESEARCH REVIEWS Fortnightly round up from the leading medical journals

Calling the shots for hypertension

Will cardiovascular disease prevention mostly be delivered by subcutaneous injection in the future? With increasing numbers of people starting tirzepatide and glucagon-like peptide-1 (GLP-1) agonist injections for weight loss and diabetes, why not throw in something for blood pressure at the same time? Many struggle to take a tablet each day, and others may simply prefer a jab every 3-6 months. Enter zilebesiran, a "subcutaneously administered RNA interference therapeutic." A phase 2 study has found that, among patients already taking a single drug for hypertension, adding a single dose of zilebesiran (compared with placebo) significantly lowered systolic blood pressure after three months.

JAMA doi:10.1001/jama.2025.6681

Supplemental imaging for breast cancer screening

The BRAID trial is the first large scale randomised control trial of supplemental imaging techniques in women with normal mammograms and dense breast tissue. In all, 6305 women, recruited across 10 sites in the United Kingdom, received either abbreviated MRI, contrast enhanced mammography, or automated whole breast ultrasonography. The study was not designed to assess long term key outcomes of breast cancer specific mortality reduction or long term harms from overdiagnosis, but found that the two contrast enhanced techniques had higher rates of detection of invasive cancers than ultrasonography.

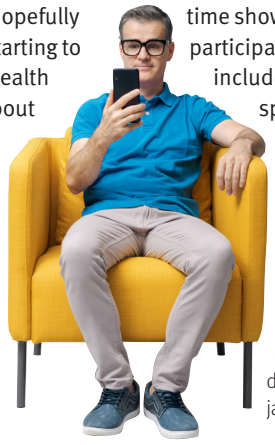
Lancet doi:10.1016/S0140-6736(25)00582-3

	Abbreviated breast MRI (n=2130)	Automated whole breast ultrasound (n=2141)	Contrast-enhanced mammogram (n=2035)
Recalled	206	85	197
Recall rate	9·7% (8·4 to 11·0)	4·0% (3·2 to 4·9)	9·7% (8·4 to 11·0)
Biopsied	105	32	89
Biopsy rate	4·9% (4·0 to 5·9)	1·5% (1·0 to 2·1)	4·4% (3·5 to 5·4)
Cancer detected	37	9	39
Cancer detection rate (arm) per 1000	16·0 (11·3 to 21·9)	4·0 (1·8 to 7·6)	17·4 (12·4 to 23·8)
Cancer detection rate (imaged) per 1000	17·4 (12·2 to 23·9)	4·2 (1·9 to 8·0)	19·2 (13·7 to 26·1)

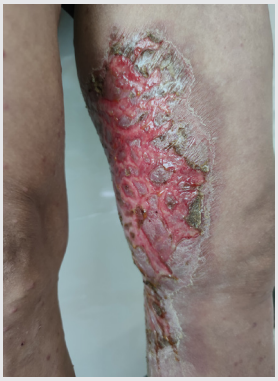
ADAPTED FROM TABLE 3 GILBERT FJ, ET AL. *LANCET* 2025;405:1935-44

Trends in sedentary behaviour

The amount of time people spend sitting down each day may have reduced, according to data from a nationally representative survey in the United States. The average sedentary time decreased from 7.1 hours per day in 2013-14 to 5.9 hours per day in 2017-20 and has stayed stable since then. Hopefully people are starting to take public health messages about sedentary behaviour seriously, rather than it being due to the question used to estimate sedentary time showing its age: participants are asked to include how long you spend each day playing cards yet doesn't ask how long is spent lying in bed scrolling through social media sites.



JAMA doi:10.1001/jama.2025.7220



CLINICAL PICTURE

A red ulcer on the leg

This man in his 50s presented with a six month history of a large, red, painless ulcer on his left leg; widespread nodular rashes; fatigue; anorexia without weight loss; and loss of sensation and paraesthesia all over the body. A biopsy specimen of the ulcer site was obtained. Fite-Faraco staining revealed acid-fast bacilli, confirming the diagnosis of leprosy. Leprosy is a chronic infectious disease that remains endemic in more than 140 countries.

Leprosy may cause permanent damage to the skin, peripheral nerves, muscles, and eyes, mediated by the bacteria's direct effects and by inflammation secondary to the immunological response to Mycobacterium leprae. This patient was treated with a multidrug combination of rifampicin (600 mg once monthly, supervised), clofazimine (50 mg daily and 300 mg once monthly, supervised), and dapsone (100 mg daily) for a year. The initiation in treatment was associated with transient swelling of the leg and aggravation of the skin lesions. A type 1 lepra

As-needed combination for mild asthma

Maintenance and reliever therapy has been rapidly rolled out since the BTS/NICE/SIGN asthma guideline was published in 2024. A new trial in people with mild asthma further supports this approach. Participants were randomised to receive either a combination budesonide-salbutamol or salbutamol inhaler for as-needed treatment. The study was stopped early when an interim analysis found severe exacerbation rates of 5.3% in the budesonide-salbutamol group compared with 9.4% in the salbutamol group (hazard ratio 0.54, 95% confidence interval 0.40 to 0.73). Although this study only recruited people with mild asthma, the inclusion criteria required that their symptoms were not well controlled and 10% reported having had a severe exacerbation in the year before enrolment.

New Engl J Med doi:10.1056/NEJMoa2504544

Learning from experience

When you want to achieve something the natural thing to do is to ask someone else how they managed it—whether it's passing an exam, running a marathon, or getting a 9% pay rise. Researchers used the same principle to devise a weight loss maintenance intervention where trial participants get support from mentors who have successfully lost weight as well as other people taking part in the study. From 287 people enrolled who had already managed to achieve at least 5% weight loss, weight regain was lower in those who were allocated to patient-to-patient treatment than in the standard care arm of the study after 18 months, but only by an average of less than 2 kg (0.77 kg v 2.37 kg respectively).

JAMA Intern Med doi:10.1001/jamainternmed.2025.1345

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

Cite this as: *BMJ* 2025;389:r1137

reaction—representing a delayed hypersensitivity reaction—was suspected and treated with a short course of prednisolone, gradually tapered down as his symptoms improved. After treatment, his systemic symptoms, widespread nodular rashes, and paraesthesia completely resolved, and the large ulcer healed with residual scarring.

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Patient consent obtained.

Cite this as: *BMJ* 2025;389:e082088

MINERVA From the wider world of research

Adolescent cardiorespiratory fitness and risk of cancer

Higher levels of cardiorespiratory fitness in late adolescence may offer protection against common cancers later in life. In a Swedish cohort of one million 18 year old men, those in the highest quartile of fitness had a 30% lower risk of cancer death compared with those in the lowest quartile (*Plos Med* doi:10.1371/journal.pmed.1004597). These findings were based on linkage of conscription records with national health and mortality registries. Unfortunately, lack of information on likely confounding factors, particularly cigarette smoking, makes interpretation difficult.

Cardiometabolic risk factors in pregnancy

The intrauterine environment exerts a lasting impact on cardiovascular health. A longitudinal study of mother-offspring pairs shows that the effects appear early in life (*JAMA Netw Open* doi:10.1001/jamanetworkopen.2025.9205). Children of mothers who were obese, had gestational diabetes, or experienced hypertensive disorders during pregnancy, had higher systolic and diastolic blood pressures and a steeper rise in blood pressure from age 2 to 18 than children of mothers without these risk factors.

Dysglycaemia and aortic stenosis

A large longitudinal study, originally intended to investigate apolipoproteins as cardiovascular risk markers, finds that blood glucose levels are linked to the incidence of aortic stenosis (*Heart* doi:10.1136/heartjnl-2024-325150). The risk increased progressively with higher fasting glucose levels. Over 25 years of follow-up, people with diabetes were more than twice as likely to develop aortic stenosis as those with normal glucose levels.

Diabetes and anaemia

Diabetes increases the likelihood of becoming anaemic. Over a 14 year follow-up, 42 000 participants in the UK Biobank study developed anaemia (*Diabetes Care* doi:10.2337/dc24-2535). Iron deficiency anaemia, vitamin B_{12} deficiency anaemia, and anaemia of chronic disease were three to five times more common in people with diagnosed diabetes than in those with normal glycaemia. Renal complications of diabetes, and decreased erythropoietin production, may be part of the explanation.

Exogenous testosterone

Myocardial infarction, ischaemic stroke, cardiac arrest, and ventricular arrhythmias are no more likely in people treated with exogenous testosterone than in a control group treated for glaucoma. An exhaustive analysis of half a million US health insurance records found no consistent differences between the two groups, except for a slight increase in venous thromboembolism risk among testosterone users (*Am J Epidemiol* doi.org/10.1093/aje/kwaf098).

Counting large numbers

Some quantities are too numerous to count directly and must be estimated using the notion of density. For example, knowing the number of red blood cells per ml and the circulating volume of blood, the total number of an individual's red cells can be reckoned at around 25 trillion. This approach works less well for tissues that lack homogeneity. The often quoted figure of 85 billion neurones in the human central nervous system may be wildly inaccurate (*Brain* doi.org/10.1093/brain/awae390).

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EASILY MISSED?

Early onset colorectal cancer

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CPD READING
0.5 HOURS

A 32 year old woman presented to her GP with a four week history of a prolapsing anal lump after defecation. She had a normal body mass index and a history of anxiety, irritable bowel syndrome, and haemorrhoids. She had no family history of bowel cancer. She was three months post partum with a baby born via forceps delivery with episiotomy. Her GP reassured her that her episiotomy wound was healing well and suggested her symptoms were secondary to possible rectal prolapse. She was given advice regarding postpartum pelvic floor exercises.

Over the next six months, the patient paid for a course of pelvic floor physiotherapy, with marginal improvement in her symptoms. She returned to her GP several times over the next year as her symptoms remained unresolved and was referred to a secondary care colorectal clinic for consideration of haemorrhoidal banding. After examination in the secondary care clinic, she was informed that there were no haemorrhoids and was discharged.

Two years later, she developed tenesmus with a change in bowel habit and mucus discharge per rectum. Her GP referred her urgently to secondary care for colonoscopy, where a suspicious rectal lesion was identified, and subsequent surgery confirmed the diagnosis of rectal cancer.

WHAT YOU NEED TO KNOW

- Early onset colorectal cancer refers to diagnoses of colorectal cancer in people under 50 years of age
- For younger people, incidence of colorectal cancer is increasing globally and this cancer is predicted to be the commonest cause of all cancer related death by 2030
- Rectal bleeding is the commonest reported symptom in younger people, and, compared with older people, these patients are more likely to present with advanced disease, which is located on the left side of their colon (rectal and sigmoid tumours)
- Younger people may experience delays in diagnosis if symptoms such as abdominal bloating or cramping and occasional rectal bleeding are incorrectly attributed to non-cancer diagnoses such as irritable bowel syndrome or haemorrhoids
- Investigate younger people by taking a thorough history, performing abdominal and digital rectal examinations, and carrying out blood tests and faecal immunohistochemical testing

What is early onset colorectal cancer?

Early onset colorectal cancer is defined as colorectal cancer in people under the age of 50 years.[1] US national registry data shows that, compared with older people, a higher proportion of patients with early onset colorectal cancer develop rectal cancer (42% of those under 50 years versus 24% of those over 65 years).[2]

Colorectal cancer diagnosed in individuals less than 50 years of age is more likely to be late stage compared with those diagnosed over the age of 50. This finding has been demonstrated in two US population based registry databases (47% in those <50 years old *v* 34% in those >50, odds ratio 1.81 (95% confidence interval 1.27 to 2.58))[3] and in a retrospective cohort study where, compared with those >50 years old, younger patients were more likely to present with stage III locally advanced cancer (relative risk ratio 1.37 (95% CI 1.34 to 1.41)) or stage IV metastatic disease (relative risk ratio 1.58 (1.53 to 1.63)).[4] Although a history of a first degree relative with colorectal carcinoma at any age may be associated with a reduced risk of developing late stage disease (30% risk of those with a first degree relative *v* 37% of those without, odds ratio 0.73 (95% CI 0.52 to 1.00)), when stratified by age, under 50 years remained a significant risk factor of late stage disease despite a first degree relative with colorectal carcinoma (odds ratio 1.92, P=0.00069).[3]

Approximately 75% of all new diagnoses of early onset colorectal cancer are sporadic (non-hereditary), with the remainder attributable to inherited conditions (of which Lynch syndrome is the most common).[5] Lifestyle patterns contribute to the development of sporadic early onset colorectal cancer, but emerging evidence suggests genetic susceptibility also contributes (box 1).

Early life exposure to environmental risk factors may contribute to rising incidence. Sugar sweetened beverage consumption, hyperlipidaemia, obesity, high fasting plasma insulin levels, diabetes, high alcohol consumption, low levels of physical activity, diets low in calcium and milk, early life exposure to certain bacteria and childhood antibiotic use have all demonstrated associations,[9-11] although no single factor plays a dominant role. There is substantial interest in the role of gut dysbiosis because of the complex interplay between high fat diets, obesity, antibiotics, and exposure to environmental chemicals that increase the bioavailability of nitrates (such as used in processed meat preservation, with higher exposure linked to higher risk).[12 13] It is possible that

Box 1 | Genetic factors of early onset colorectal cancer

- Genome-wide association studies have identified over 100 single nucleotide polymorphisms that are independently associated with colorectal cancer and have used these to devise a polygenic risk score[6 7]
- Subsequent validation studies have shown that, even among groups with the lowest risk factors, a high polygenic risk score confers almost three times the odds of developing early onset colorectal cancer[8]

these non-hereditary aetiologies are shared between early onset colorectal cancer and other gastrointestinal cancers arising in young adults.

How common is it?

In 2020, colorectal cancer ranked third worldwide in terms of incidence, but second in terms of mortality.[14] This is predicted to rise to first position by 2030, with the current annual rise in incidence in people aged under 50, as reported by GLOBOCAN 2020, a worldwide population database estimating cancer specific rates for 185 countries and territories.[14]

Early onset colorectal cancer makes up approximately 10% of all new colorectal cancer diagnoses.[15 16] This proportion is expected to increase; for example, in England between 1994 and 2015 there was a 51% increase in early onset colorectal cancer diagnoses.[17] Population level data from NHS Digital shows that the annual incidence of early onset colorectal cancer in 2015 was 1.3 per 100 000 in 20-29 year olds, 8.1 per 100 000 in 30-39 year olds, and 16.7 per 100 000 in 40–49 year olds.[17] There was no difference between men and women.

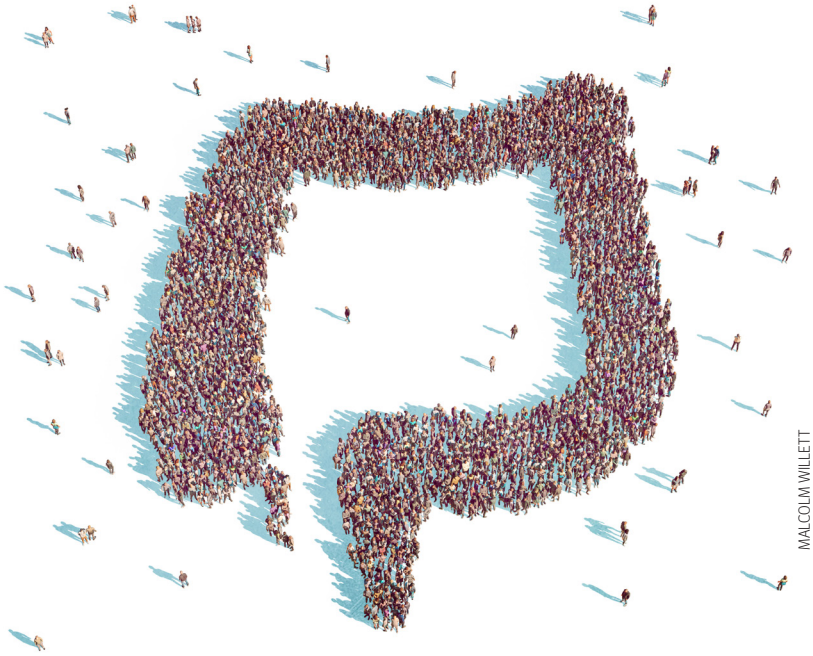
In other high income countries, including America, Australia, New Zealand, Canada, Korea, Taiwan, Germany, Denmark, Slovenia, and Sweden, the incidence of early onset colorectal cancer is increasing. Central European countries saw their incidence rise from 4.44 per 100 000 (95% uncertainty interval 4.22 to 4.68) in 1990 to 5.25 (4.47 to 6.14) in 2019.[18 19] This change mirrors the trend of increasing incidence of other gastrointestinal cancers (gastric, pancreatic, and gallbladder) in young adults.[20]

In upper middle income countries, specifically Mexico and China, the incidence of early onset colorectal cancer is rising more rapidly than in high income countries.[12] Registry data for low income countries are limited, but the evidence suggests increasing incidence of early onset colorectal cancer in South East Asia.[21]

In the US (40 out of 47 states), black people are twice as likely as white people to be diagnosed with early onset colorectal cancer, although this difference has reduced and the underlying aetiology remains unclear.[22]

Why is it missed?

Early onset colorectal cancer is easily missed because symptoms and signs are often non-specific. As in the case above, rectal bleeding may be explained by haemorrhoids, and abdominal pain or erratic bowel function may be attributed to irritable bowel syndrome or infection.



MALCOLM WILLETT

At all ages, consultation rates for relevant clinical symptoms or signs increase in the year before diagnosis.[23] Observational studies have reported that patients with symptomatic early onset colorectal cancer visited their GP three times or more before a referral was made for diagnostic testing.[24 25] In a cohort study examining 10 463 patients from the UK Clinical Practice Research Datalink database, only 3.3% of patients aged under 50 years visited their GP more than five times before diagnosis. In the same study, when compared with older age groups, people under 50 more frequently presented with non-specific symptoms on a single occasion and had a lower proportion of presentations with red flag symptoms.[26] In a mixed methods analysis of 273 patient accounts of the diagnostic barriers at primary care level in the UK, Australia, and New Zealand, 24% of patients attributed a delay in diagnosis to a missed diagnostic opportunity.[27]

Financial concerns may stop some people seeking medical attention and may prevent community doctors from referral to secondary care in healthcare systems with limited resources.[28] Furthermore, there are no universal screening programmes for early onset colorectal cancer globally; countries that do offer bowel cancer screening typically start at 50 years of age.[29]

Longer diagnostic intervals are associated with more advanced stage of cancer according to data from seven independent datasets from high income countries (Scotland, England, Canada, Denmark, and Spain).[30] In a UK retrospective cohort study of 4836 patients that used linked cancer, primary care, and secondary care registry data, the median interval from the patient first experiencing the symptom to first investigation was 131 days for colon cancer and 43 days for rectal cancer in patients aged under 45 years, compared with 65 days for colon cancer and 58 days for rectal cancer in people

Box 2 | Long term sequelae of early onset colorectal cancer diagnosis and treatment

- Treatment related
  - Dexterity loss during and after chemotherapy, resulting in difficulty in getting dressed, writing, and performing manual tasks[37 38]
  - Reduced mobility due to postoperative scarring affecting overall function and fitness
  - Problems related to life with a stoma—Avoidance of strenuous activity, need to have medical equipment at all times in case of bag leaks, longer term management of a parastomal hernia
- Lower career performance, loss of career trajectory, and loss of earning potential[16]
- Reduced fertility—Fertility preserving options such as egg/embryo freezing, sperm cryopreservation, and radiation shielding should be considered according to local eligibility criteria
- Sexual dysfunction—Patients with early onset colorectal cancer have an increased chance of being diagnosed with left sided colonic or rectal cancer. Surgery and chemotherapy may result in pelvic nerve damage (impotence, loss of libido) and carry a high chance of stoma formation (potential adverse effect on body image)
- Mental health impact—Negative impact on relationships, depression, and emotional exhaustion. In particular, the impact of a cancer diagnosis in younger years can lead to a longer period of health anxiety associated with follow-ups, surveillance for recurrent cancer, and worry should new abdominal symptoms develop

Box 3 | UK national guidelines for the use of faecal immunohistochemical test (FIT) to guide referral for suspected colorectal cancer in adults[38 39]

- Patients with any of the following clinical features of colorectal cancer:
  - Abdominal mass
  - Change in bowel habit
  - Iron deficiency anaemia
  - Rectal bleeding
  - Abdominal pain
  - Aged ≥60 years with anaemia even in the absence of iron deficiency
- FIT testing is not required before secondary care referral for people with a rectal mass, unexplained anal mass, or unexplained anal ulceration
- FIT is less sensitive in patients with iron deficient anaemia, who should still be considered for urgent referral despite a negative FIT

aged 55-64 years.[31] These data are corroborated by a recent systematic review and meta-analysis of 34 studies from across the world which reported a mean symptom duration of 6.4 (range 1.8-13.7) months from patient-reported symptom onset to diagnosis.[32] A Canadian analysis of prospectively collected data on 3344 patients observed a median patient-reported duration of symptoms before diagnosis of 141 days (95% CI 133 to 153) in younger patients, compared with 94 days (88 to 101) in older patients.[33]

Why does this matter?

A 2023 report showed an increase in colorectal cancer mortality rates in people under 50 years of 1.2% per annum between 2011 and 2020.[2] This compares with reductions of 0.5% per annum in 50-64 year olds and 2.9% per annum in those aged 65 and over. Stage at diagnosis is the most important predictor of survival from colorectal cancer: 90% five year survival with stage I disease versus 10% for stage IV metastatic disease.[15] Early stage (I/II) diagnosis results in a higher chance of curative surgery, improved survival outcomes, less need for adjuvant oncological therapies that carry significant morbidity, and lower rates of permanent stoma formation.[34]

Compared with older patients, patients with early onset colorectal cancer have a higher chance of being diagnosed with rectal cancer,[16] advanced disease (64% *v* 55% at stage III/IV),[17] and presenting as an emergency (27% *v* 17%).[35 36] Compared with patients of any age who present with colorectal cancer via non-emergency pathways, those who present as an emergency are more likely to have metastatic disease at diagnosis (49% *v* 21% at stage IV) and are less likely to be offered curative surgery (48% *v* 69%).[35]

Long term, patients who have early onset colorectal cancer may face substantial impairment as a direct consequence of their treatment, with a profound impact on their quality of life (box 2).

How is it diagnosed?

Early onset colorectal cancer can be challenging to diagnose. Assess for red flag features (see box 3). If present, perform a thorough clinical examination, including digital rectal examination, undertake baseline blood tests, and perform a stool test (faecal immunohistochemical test) to guide urgency of referral (box 4).

For patients under 50 presenting to their GP with solitary red flag symptoms, there is still a very low chance (<1%) that they will be diagnosed with early onset colorectal cancer.[25] In the UK and Europe, FIT is recommended as a means of risk stratification for patients with red flag symptoms (box 3), although the studies on which this guidance was based almost exclusively included adults over 50 years old.[39 40]

Quantitative FIT targets antibodies specific to human haemoglobin found within a stool sample and has replaced guaiac based faecal occult blood tests. FIT has a sensitivity of 97.7 (95% CI 95.0 to 99.1) or 92.2 (88.2 to 95.2) for colorectal cancer when using a cut-off of either >2 µg or >10 µg per g faeces, respectively, in adult patients of any age with red flag symptoms. The positive predictive value at these cut-offs is 8.9% and 16.2%, respectively.[41] However, data on the diagnostic accuracy of FIT in younger individuals are sparse. A recent meta-analysis of 236 440 symptomatic patients aged 40-49 years showed that a FIT >10 µg/g ("positive") increased the odds of colorectal cancer nearly 20-fold with a positive predictive value ranging from 2.7% to 6.8% and a negative predictive value of 99.5%.[42] While it is not completely clear if FIT performs identically across age groups, we believe there is a clear benefit in using this test to help stratify risk in symptomatic patients under 50 years of age.

A positive FIT result (FIT >10 µg/g) in the absence of symptoms is insufficient to warrant referral for urgent investigation, as this sits below the current FIT threshold of 80 µg/g used in the UK Bowel Cancer Screening Programme. In a recent study of a symptomatic primary care population, a predictive model that incorporated age, sex, mean corpuscular volume, platelet

Box 4 | Summary of key information to elicit during assessment (adapted from The Association of Coloproctology of Great Britain and Ireland guidelines[47])

When taking a history
- Presenting symptoms
  - Rectal bleeding
  - Change in bowel habit
  - Abdominal or anal pain
  - Weight loss
  - Unusual rectal discharge
  - Tenesmus
- Past medical history
  - Inflammatory bowel disease
  - Colorectal polyps
  - Obesity
- Social history
  - Alcohol intake (current and historic)
  - Smoking history (nicotine smoked or vaped)
- Family history
  - Colorectal cancer (first degree relative)
  - Genetic disorders, such as Lynch syndrome
  - Endometrial, ovarian, or stomach cancer

When examining a patient
- Abdominal mass
- Abdominal tenderness with no obvious mass

When performing a digital rectal examination
- Rectal or anal mass
- Blood on the glove
- Excess mucus

What tests should you order
- Blood tests
  - Full blood count (low haemoglobin, low mean corpuscular volume)
  - Haematinics (low ferritin)
  - Urea and electrolytes
  - Liver blood tests (low albumin)
- Stool tests
  - Faecal immunohistochemical test (FIT)
  - Faecal calprotectin (tests for gastrointestinal tract inflammation if cancer not expected)

How to safety net patients
- If treatment commenced for irritable bowel syndrome, constipation, diarrhoea, diverticulitis, haemorrhoids, or anal fissure, advise patients to return in 4-6 weeks if the clinical situation has not improved, or earlier if worsening or new symptoms

count, and faecal haemoglobin demonstrated superior diagnostic accuracy with a concomitant reduction in diagnostic investigations compared with faecal haemoglobin alone (at a FIT threshold >10 µg/g).[43]

The optimal test for diagnosis of colorectal cancer is colonoscopy regardless of age.[44] However, data from observational studies suggest that 2-7% of cases (60/797 within 36 months of test) may be missed.[45] This may be due to a variety of reasons, such as inadequate bowel preparation and subsequent poor mucosal visualisation, limitations on the day (including abandoning the procedure if it is too painful for the patient), the endoscopist missing detection of small cancers (particularly those in the right side of the colon), and if the scope withdrawal time is too quick.

EDUCATION INTO PRACTICE
- When patients under 50 years old present with bowel symptoms such as rectal bleeding, a change in bowel habit, or abdominal pain, how do you assess their risk of having bowel cancer?
- When do you consider the need for a FIT test in patients under 50 presenting with bowel symptoms such as rectal bleeding, a change in bowel habit, or abdominal pain?
- Consider the last time you assessed a patient under 50 with bowel symptoms. Did you perform a rectal examination and if not what was the reason for not doing so?

People with an underlying diagnosis of irritable bowel syndrome may find the test unacceptably painful due to visceral hypersensitivity. When referring people straight to colonoscopy, emphasise the need to follow instructions carefully ahead of the procedure, and for people with a tendency to be constipated advise them to consider following the low residue diet for longer than instructed, up to five days.

In the event of a negative colonoscopy, provide safety net advice and arrange follow-up for people who continue to have red flag symptoms.[46] If appropriate, and following review in secondary care, patients may undergo additional investigations.

How is it managed?

Primary care

In the UK, NICE recommends an urgent referral to secondary care for suspected cancer, ideally within two weeks, for all patients with suspected colorectal cancer, including those with suspected early onset colorectal cancer. Similar times for clinical assessment and referral are used for suspected cases of colorectal cancer in Australia, Canada, and the Nordic countries.[47 48]

In low and middle income countries the assessment and diagnosis of colorectal cancer is not well described. There remains under-reporting of cancer data in registries, and colorectal cancer screening programmes may not be fully developed.[49]

Secondary care

Current management of colorectal cancer is the same, irrespective of age of onset. The mainstay of treatment involves surgery, chemotherapy and radiotherapy, dependent on tumour stage, patient fitness, and shared decision making alongside patient preferences. Younger patients tend to receive more aggressive treatment regimens owing to initial physical fitness and later stage disease at presentation.[51] Radical surgical resection remains the standard of care and is associated with the highest chance of long term survival.

Competing interests: None declared.
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Find the full version with references at doi: 10.1136/bmj-2024-082452

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

We asked two patients with early onset colorectal cancer to reflect on their journeys, and asked for their input on our draft manuscripts. Based on their input, we have been able to present the difficulties people face at the initial diagnosis stage. Our patient co-author shared her story, modelled into the case vignette, and asked us to include additional information in the mental health section of this paper. She wished to highlight the high levels of health-related anxiety experienced after a diagnosis of early onset colorectal cancer.

EDITORIAL

Gaps in care of early onset colorectal cancer

Timely investigation needed in the wake of a rising incidence

Dame Deborah James, "Bowelbabe," transformed public health discourse by raising bowel cancer awareness. As the figurehead of Bowel Cancer UK's *Never Too Young* report,[1] she highlighted the rising incidence of early onset colorectal cancer and diagnostic challenges affecting patients under 50 years old.

According to one US retrospective cohort study of 258 024 patients with colorectal cancer from 1998 to 2011, 15% of patients were diagnosed <50 years old, and those diagnosed at this younger age were more likely to have locally advanced or metastatic disease.[2] Despite a largely stable or decreasing overall incidence of colorectal cancer in many high income countries, the incidence in people younger than 50 is rising in Asia, Australia, Europe, and North America.[2-4] In Europe, a registry study of 143.7 million people across 20 European countries shows there has been an increase in incidence of 8% per year in people aged 20-29 from 2004 to 2016.[3]

Most young people, however, will not have colorectal cancer, as demonstrated by a UK prospective case-control study, which estimated that fewer than 1.5% of patients <50 years old presenting to primary care with lower gastrointestinal symptoms are diagnosed with colorectal cancer.[6] These data highlight the challenge for primary care physicians when deciding which patients warrant onward referral for colonoscopy, balancing the risk of delayed diagnosis with the harms of unnecessary investigations.

Two education articles in *The BMJ* afford clinicians insightful perspectives on early onset colorectal cancer. In their Easily Missed article, Chambers et al review the data underlying the global burden of early-onset colorectal cancer, provide a practical framework for investigation,

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Incidence in people younger than 50 is rising in Asia, Australia, Europe, and North America

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and a case vignette to highlight diagnostic challenges.[7] In "What your patient is thinking" Johnson shares her perspective as a patient navigating a diagnosis of early onset colorectal cancer, focusing on the importance of empathetic communication from healthcare professionals.[8]

A key learning point is that about 75% of all new diagnoses of early onset colorectal cancer are in people without a family history of bowel cancer.[13] Clinicians should therefore refrain from thinking that those without a family history do not require assessment and consideration for investigation.

Diagnostic and care challenges

Symptoms of early onset colorectal cancer can be frustratingly vague, non-specific, and vary between individuals. Moreover, there is marked diagnostic overlap with non-cancer conditions.

Faecal immunochemical testing (FIT) is a common investigation used to stratify high risk patients and guide referral for colonoscopy. In a subgroup analysis of the NICE FIT study, which assessed 1103 symptomatic patients younger than 50 years old from NHS hospitals across England, a cut-off of 10 µg faecal haemoglobin per gramme of faeces had a positive predictive value of 6.8% for diagnosing colorectal cancer, more than double the 3% risk threshold for red flag referral recommended by NICE,[15] and negative predictive value of 99.7%.[16]

We echo Chambers et al's recommendations to offer younger patients with an unexplained change in bowel habit or with iron deficiency anaemia a FIT test.[17 18] In line with international guidelines, patients with persistent rectal bleeding and a normal FIT result should be considered for referral for sigmoidoscopy.[18] Patients with high risk symptoms, such as unexplained weight loss or a palpable rectal mass, should not have referral delayed while awaiting the outcome of FIT testing.[14 17 18]

Overall, the five-year survival for all patients with colorectal cancer, irrespective of age and stage of disease, is about 60%.[19] Despite the fact that younger patients are more likely to present with advanced disease,[2] many will undergo curative treatment or have palliative treatment with good initial response, meaning the impact of longer term effects and supportive needs are likely to be substantial. Similarly, late effects and long term sequalae of aggressive cancer treatments often affect those living beyond cancer for decades after treatment, including neuropathy, challenges related to stoma management, reduced fertility, and effect on mental health.[24]

Research into chemotherapy modification to help mitigate these treatment complications is warranted, as well as research into the potential benefits of physical activity and rehabilitation in this cohort.[25] For primary care, identifying supportive approaches to manage these care needs remains an evidence gap. For specialists, discussion around late effects is vital when counselling patients about treatment decisions. Across all care settings, Johnson's account[8] highlights that effective communication, offering information according to patient preference, remains paramount.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.r1121

WHAT YOUR PATIENT IS THINKING

Balancing empathy and information in cancer treatment

Georgina Johnson describes the compassion and support she received with a cancer diagnosis and getting the balance of information right

PRIYA SUNDRAM

CPD READING
0.5 HOURS

Being diagnosed with stage 3 bowel cancer at the age of 48 came as a huge shock. I'd started suddenly experiencing daily stomach cramps, and thinking it was irritable bowel syndrome, I contacted my GP. I was extremely lucky that the doctor I consulted about the cramps decided to request a faecal immunochemical test, despite my only having one symptom. I've heard of other bowel cancer patients whose GP sent them home with laxatives or antispasmodics. But my doctor decided to check just in case, and my results came back abnormal.

I was referred for a colonoscopy, but before my appointment I ended up in the emergency department with violent pain and bleeding. They found something in my bowel that they said might be a tumour and needed further investigation. I will never forget the kind way that the doctor broke the news to me. They were so gentle and caring, as I was clueless as to what was wrong with me. While I perched on the couch, the doctor sat on the floor to create a more relaxed atmosphere, and this helped.

My cancer team knew the exact amount of information to give me and at what stage to tell me

Balance of information

I recall the doctors assuring me they'd look after me and that I'd be OK, that they would hold my hand and help me get through it all. I'm so grateful for this as I'm sure their hearts must have sunk when they saw the tumour on my CT scan that day. While they knew the whole picture, they thought of the impact on me and told me only what I needed to know.

The day after my official diagnosis I had emergency surgery as the tumour was obstructing my bowel. I ended up with a stoma for more than six months and endured three months of chemotherapy with plenty of side effects. My cancer team knew the exact amount of information to give me and at what stage to tell me. This saved me from freaking out completely and from being totally overwhelmed by the bewildering amount of information my brain was already trying to process. But when I did need to have information, such as in the lead up to having chemotherapy or more surgery, it was good to have as much detail as possible to be prepared. I also appreciated the reassurance that it was normal to be experiencing the symptoms and feelings that I was.

Compassion equals trust

Just over a year on, I'm out the other side. My bowel is back to functioning perfectly and I am happily in remission. All the healthcare professionals that looked after me treated me with so much kindness and compassion that it reduced me to tears at times. They knew when to hug me if I felt overwhelmed and when to give me a gentle nudge to encourage and reassure me when I lost confidence in myself and my recovery. The empathy they showed me made my journey so much easier. It meant I could put all my trust in them and get through what was one of the hardest times in my life.

Cite this as: *BMJ* 2025;389:r817

WHAT YOU NEED TO KNOW

- During an initial cancer diagnosis, some patients prefer to receive only key information, so that they feel less overwhelmed
- Follow a patient's lead on how much information to give, and on when and how to provide it
- Showing compassion and kindness builds trust between health professionals and patients

EDUCATION IN PRACTICE

- How can you ensure you are sharing the right amount of information with patients during a diagnosis and/or treatment plan?
- What could you do to show your compassion for a patient?

STATE OF THE ART REVIEW

Current management of hypertrophic cardiomyopathy

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CPD READING
0.5 HOURS

This is a summary of Clinical Review Current management of hypertrophic cardiomyopathy. The full version can be read here: https://www.bmj.com/content/389/bmj-2023-077274

Hypertrophic cardiomyopathy is a common yet under-recognised structural heart condition. It has been defined as left ventricular wall thickness of ≥15 mm in any myocardial segment, not explained by alternate conditions leading to increased load, such as hypertension or aortic stenosis, or infiltration, such as amyloidosis. A diagnosis with less hypertrophy (≥13 mm) is possible in the context of a corroborating family history or positive genotype.[1] The clinical manifestations are heterogeneous, ranging from asymptomatic disease to sudden cardiac death and advanced disease necessitating heart transplantation.

Initial medical and surgical therapeutic interventions for hypertrophic cardiomyopathy were first described more than 60 years ago.[7] Advances in research during the past decade have ushered in a new era of highly effective and potentially disease modifying therapies, altering the treatment paradigm. Several promising treatments are now in varying stages of development. This review provides a critical analysis of the rapidly evolving and wide ranging therapeutic landscape in hypertrophic cardiomyopathy.

WHAT YOU NEED TO KNOW

- Hypertrophic cardiomyopathy is a common but under-recognised genetic structural heart condition characterised by left ventricular hypertrophy. Patients may present with obstructive disease, characterised by an elevated left ventricular outflow tract gradient, or non-obstructive disease
- Established medical and surgical treatment options for patients with hypertrophic cardiomyopathy and refractory symptoms can be effective in reducing outflow tract gradients and improving symptoms
- Stratification of the risk of sudden death is an important component of caring for patients with hypertrophic cardiomyopathy. Recommendations for implantable cardioverter-defibrillators are based on validated risk factors in combination with shared decision making
- Early identification is key to improving outcomes with advanced therapies, including cardiac transplantation

Epidemiology

Hypertrophic cardiomyopathy has a global presence with an estimated prevalence of 1 in 500. It has a similar prevalence in men and women.[8 9] Despite improvements in community awareness and advances in screening, an estimated 80-90% of cases remain undiagnosed.[10 11] Depending on the cohort studied, 30-60% of patients harbour genetic variants inherited as autosomal dominant traits, whereas no pathogenic variant is identified in around 40%.[12] Although overall mortality has decreased over the past several decades, sex, age, and race/ethnicity related inequalities in long term outcomes persist.[13] Women with the disease have higher rates of heart failure and mortality.[14]

Initial medical therapy

Obstructive disease

Assessment

Obstructive hypertrophic cardiomyopathy is characterised by left ventricular outflow tract (LVOT) obstruction, with a peak instantaneous Doppler echocardiography gradient of ≥30 mm Hg, although the predicted threshold at which this gradient becomes haemodynamically significant is ≥50 mm Hg at rest or with physiological provocation.[15] Echocardiography with provocative manoeuvres including Valsalva and exercise is important in determining the presence of obstruction, as only one third of patients with hypertrophic cardiomyopathy have outflow tract obstruction at rest.[16] The degree of LVOT gradients measured varies considerably depending on the patient's position, method of exercise, time of day, and volume status.[17 18]

Treatment

Figure 1 shows options for treatment of symptomatic obstructive hypertrophic cardiomyopathy. Initiation and titration of medical therapy in obstructive hypertrophic cardiomyopathy should focus on symptom management. To date, no data suggest that any current medical therapy improves survival. Similarly, no data support initiation of gradient reduction therapy in patients without symptoms.

An important initial step is a review of drug treatments that may worsen LVOT obstruction. These include many drugs prescribed for hypertension such as dihydropyridine calcium channel blockers (CCBs), angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and diuretics. Nitrates or phosphodiesterase type 5 inhibitors may reduce preload and promote vasodilation, worsening obstruction.[19] Use of these drugs should be limited if possible. Also, all patients should be counselled on lifestyle modifications including avoidance of dehydration, large or carbohydrate rich meals, and caffeine. Alcohol use has been shown to increase LVOT obstruction and should be minimised.[20-22]

Despite a paucity of randomised data, on the basis of data from series and crossover studies, non-vasodilating β blockers and CCBs remain the first line treatments for symptomatic hypertrophic cardiomyopathy.[22]

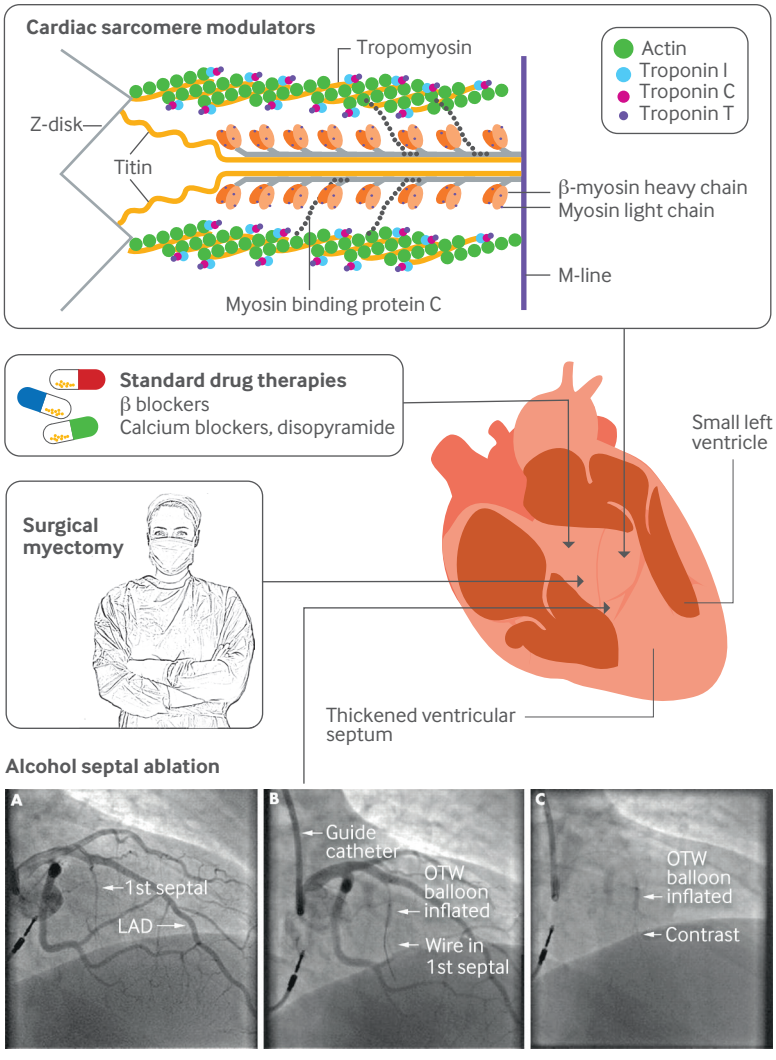

Fig 1 | Treatments for patients with symptomatic obstructive hypertrophic cardiomyopathy. Alcohol ablation image reproduced with permission from *Heart* 2006;92:1339-44

Patients who do not respond to initial medical therapy

Disopyramide, a class IA anti-arrhythmic with negative inotropic effects, has historically been the next choice in patients who do not respond to initial medical therapy. Disopyramide has been shown in retrospective studies to be safe and associated with an improvement in both LVOT gradient and symptoms when used in combination with β blockers or non-dihydropyridine CCBs. Use requires monitoring of the QTC interval and can be associated with anticholinergic symptoms.[30 31] As described below, increasing data suggest that cardiac myosin inhibitors are an appropriate second line therapy if first line agents are not successful at reducing symptoms.

Management of acute hypotension

In the absence of randomised data, recommendations for management of acute hypotension are based on physiological principles and expert consensus. Patients with obstructive hypertrophic cardiomyopathy and LVOT obstruction are less likely to tolerate haemodynamic changes associated with increased contractility or reduced preload and afterload. When these patients are admitted to hospital or undergoing surgical procedures, expeditious management of hypotension is important. Adequate preload should be maintained with appropriate fluid resuscitation. If vasopressors are required, an α blocker such as phenylephrine should be used. In a monitored setting, β blockers can be used in combination with vasoconstrictors to reduce contractility and prolong diastolic filling, improving LVOT obstruction.[38]

For patients who develop clinical evidence of volume overload, low dose diuretics can be cautiously started. Given the potential for preload reduction and resultant worsening of LVOT obstruction, the minimal effective dose should be targeted and ongoing use should be periodically reassessed.[39]

Non-obstructive disease

Many patients with non-obstructive hypertrophic cardiomyopathy have symptoms, with 8% in New York Heart Association (NYHA) class III or IV, and mortality rates are similar to patients with obstructive hypertrophic cardiomyopathy.[40] Limited evidence exists to guide medical therapy for these patients. Current management of dyspnoea in patients with non-obstructive hypertrophic cardiomyopathy is limited to diuretics for symptomatic heart failure.

Cardiac myosin inhibitors

The most meaningful recent progress in the treatment of hypertrophic cardiomyopathy has been the development of cardiac myosin inhibitors (CMIs). The first in class CMI is mavacamten, an orally administered selective inhibitor of cardiac myosin adenosine triphosphatase (ATPase). Inhibition of cardiac myosin ATPase results in reduced availability of myosin heads for engagement in actin-myosin cross bridging, a key interaction in cardiac contraction. This is thought to be effective because myocardial hypercontractility is a key component of the pathophysiology of hypertrophic cardiomyopathy.[46]

Important considerations with CMIs

Several considerations are important as CMI use increases. The potential for development of systolic dysfunction with potential for heart failure, although rare, requires frequent echocardiographic monitoring. Whether CMIs are associated with an increased rate of atrial fibrillation is not yet determined.

Invasive approaches to therapy

Obstructive disease

Invasive treatment with septal reduction therapy (SRT) is typically reserved for patients with NYHA III or IV symptoms and LVOT gradient ≥50 mm Hg who have not responded to medical therapy. It is associated with an improvement in symptoms in 90-95% of patients and a mortality rate of <1%.[59] Retrospective studies have suggested that patients with LVOT obstruction who undergo septal reduction have lower mortality than those who have medical treatment,[60 61] but as these are non-randomised the role of referral bias cannot be determined. Postoperative atrial fibrillation and increasing age are associated with worse short term outcomes.[62]

Catheter based alcohol septal ablation.[64] and septal myectomy have comparable rates of 30 day survival, sudden cardiac death, and long term survival in published studies, although no randomised controlled trial has ever been done.

The 2024 American Heart Association/American College of Cardiology (AHA/ACC) hypertrophic cardiomyopathy guidelines suggest CMIs, disopyramide, and SRT as potential options for patients with refractory symptoms despite maximal β or calcium channel blockade. When considering invasive therapy, a multidisciplinary and shared decision making approach with the patient is essential. Key factors that should be considered are the patient's specific anatomy, coexistent pathology, surgical risk, and comorbidities, as well as the centre's expertise and the patient's preference.

Non-obstructive disease

A small subset of patients with extensive apical hypertrophic cardiomyopathy, a small left ventricular cavity, and severely limiting symptoms may be considered for apical myectomy, done in a few highly specialised centres. Most patients with non-obstructive hypertrophic cardiomyopathy and refractory symptoms from heart failure despite treatment with guideline directed medical therapy should be considered for heart transplantation or advanced therapies if eligible.

Hypertrophic cardiomyopathy genetics

Genotype positive hypertrophic cardiomyopathy

Variants in genes that encode for myofilament proteins of the cardiac sarcomere are found in 30-50% of patients with hypertrophic cardiomyopathy.[70-74] These variants show autosomal dominant inheritance, variable expressivity, and age related penetrance. To date, variants in eight different sarcomeric genes have been identified as definitively causative of hypertrophic cardiomyopathy, and variants in several other genes show at least moderate evidence of pathogenicity.[75-77]

Gene elusive hypertrophic cardiomyopathy

The remaining 50-70% of patients with hypertrophic cardiomyopathy who meet clinical diagnostic criteria but do not possess identifiable pathogenic or likely pathogenic gene variants are characterised as "gene elusive." Increasingly, a polygenic contribution to hypertrophic cardiomyopathy is recognised in these patients.

Hypertrophic cardiomyopathy phenocopies

Importantly, every evaluation for hypertrophic cardiomyopathy should also reasonably exclude other non-sarcomeric causes of left ventricular hypertrophy, such as infiltrative or metabolic conditions (table 4, online). These conditions are typically referred to as "hypertrophic cardiomyopathy phenocopies" or "hypertrophic cardiomyopathy mimics" because of their phenotypic overlap with hypertrophic cardiomyopathy.

Identification of patients whose risk is high enough that an ICD will provide benefit outweighing the risks is imperative

Risk assessment for sudden death

Arrhythmic sudden cardiac death and heart failure represent the two most common modes of death related to hypertrophic cardiomyopathy, with an overall low annual mortality rate of 1.5-2%.[93] The decrease in hypertrophic cardiomyopathy related mortality, from 3-6% a year in early cohorts to the current 0.5% year,[95] has been attributed in part to the increasing identification of patients with hypertrophic cardiomyopathy at risk for sudden death with subsequent implantable cardioverter defibrillator (ICD) implantation.[95] Although ICDs save lives, they are not without complications,[96 97] so identification of patients whose risk is high enough that an ICD will provide benefit outweighing the risks is imperative.

Indications for consideration of ICD implantation vary between the US and European guidelines (fig 2). All guidelines recommend ICDs for patients with hypertrophic cardiomyopathy who have survived a cardiac arrest or haemodynamically significant ventricular tachycardia. Risk of sudden cardiac death is higher in children and has different risk predictors, so both guidelines recommend tailoring of risk stratification for children under 16 years old and repeated evaluations in both children and adults. Sudden cardiac death is less common in patients over 60 with hypertrophic cardiomyopathy, and individualised risk assessment is less well defined in this group.[84 101]

Specific factors that predict the risk of sudden death

Figure 2 shows specific risk factors identified to predict risk of sudden death in people with hypertrophic cardiomyopathy. Family history of sudden death in first degree relatives before age 40-50, long considered a marker of risk, has been validated in one study showing a similar rate of ICD interventions for those implanted for only this risk factor compared with those with other risk factors,[102] as well as in multivariable models of risk.[103] Personal history of non-vagal syncope is also predictive, particularly if recent. Episodes within six months are most predictive, whereas those further back than five years are not.[104]

Echocardiography will evaluate wall thickness, well described as a risk predictor, and left atrial size. LVOT obstruction has been identified as a predictor of sudden death in some but not all studies,[98 103 105] likely owing to the variability and ubiquity of resting gradient.[16-18] Whether treating LVOT obstruction decreases the risk of sudden cardiac death has not yet been determined. Left ventricular dysfunction, which for patients with hypertrophic cardiomyopathy is ejection fraction <50%, is present in 8% of patients with hypertrophic cardiomyopathy and is associated with adverse outcomes, particularly in those with sarcomeric variants.[106]

Cardiac MRI has more recently been identified as providing predictive information. Extensive fibrosis (typical threshold ≥15%) doubles the risk of sudden cardiac death in patients with no other risk factors, with

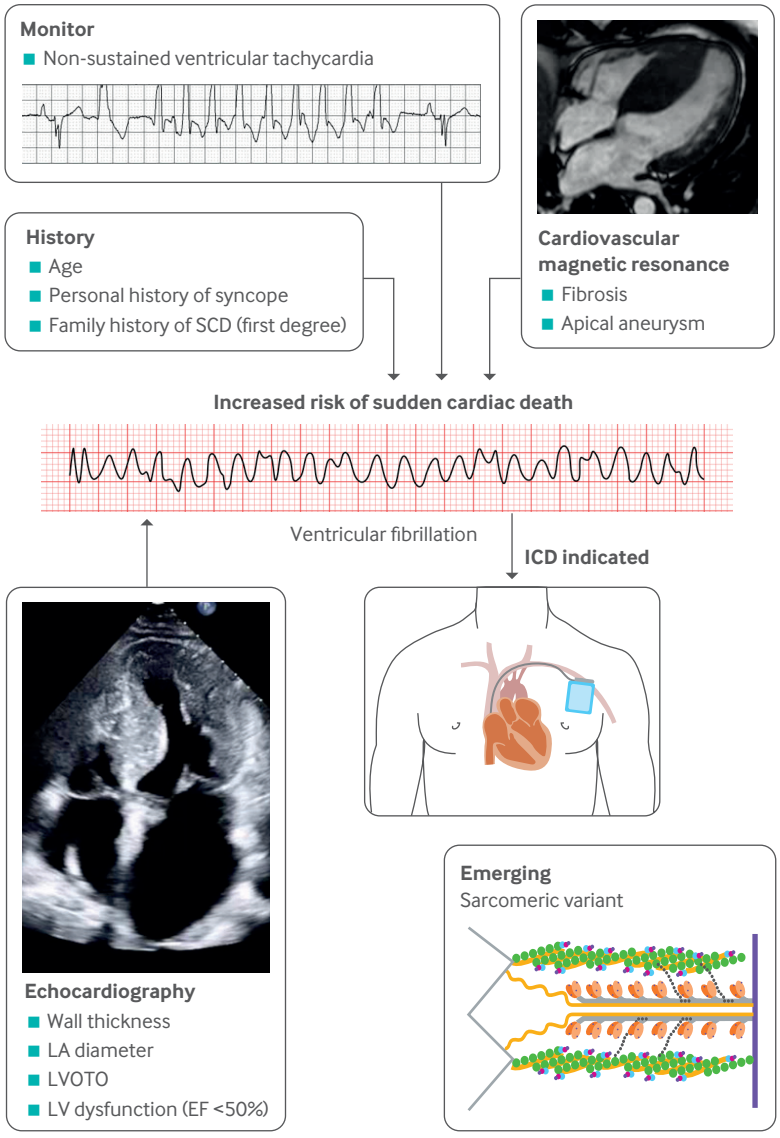

Fig 2 | Risk assessment for primary prevention of sudden cardiac death. EF=ejection fraction; ICD=implantable cardioverter-defibrillator; LA=left atrial; LV=left ventricular; LVOTO=left ventricular outflow tract obstruction; SCD=sudden cardiac death

an estimated risk for life threatening arrhythmia of 6% at five years.[107] Limited data suggest that left ventricular aneurysm may be associated with a high risk of life threatening ventricular arrhythmias and transplant.[108]

Non-sustained ventricular tachycardia seen on 24-48 hours of ambulatory monitoring is predictive of risk of arrhythmia. Both US and European guidelines use duration and rate cut-offs of three beats at 120 bpm to define risk, also noting that longer and faster runs likely carry more risk.

Management of atrial fibrillation

Atrial fibrillation is common in hypertrophic cardiomyopathy, being present in 5% at the time of diagnosis and developing in another 10-22% during follow-up.[112-114] Although most atrial fibrillation starts as paroxysmal, 42% of patients will go on to develop persistent atrial fibrillation. Data on association of atrial fibrillation with mortality in hypertrophic cardiomyopathy are mixed,[114 115] but patients with atrial fibrillation have more symptoms,[115] with greater functional limitation, particularly with progression to permanent atrial fibrillation.[113] As atrial fibrillation is poorly tolerated in hypertrophic cardiomyopathy, a rhythm control strategy is often preferred.[22]

Options for rhythm control include drugs or catheter ablation. Anti-arrhythmic drugs, including dofetilide and sotalol, have been found to be safe in small series of patients with hypertrophic cardiomyopathy, with effectiveness similar to the general population. Amiodarone has higher efficacy, but systemic toxicity limits its use.[117]

Anticoagulation

Thromboembolic risk in atrial fibrillation is higher for patients with hypertrophic cardiomyopathy, occurring in up to 27% of those with atrial fibrillation,[121] with a hazard ratio of 1.5 for a thromboembolic event compared with patients with atrial fibrillation without hypertrophic cardiomyopathy.[122] This risk is independent of the $CHADS_2VASc$ score, with many strokes seen in patients with hypertrophic cardiomyopathy with no traditional risk factors.[121] All patients with hypertrophic cardiomyopathy with clinical atrial fibrillation should thus receive anticoagulation. As in the general population, direct acting oral anticoagulants are preferred.[122]

Exercise in hypertrophic cardiomyopathy

For decades, vigorous exercise was recommended to be restricted for patients with hypertrophic cardiomyopathy, owing to concern that vigorous activity could precipitate life threatening ventricular arrhythmias.[126 127] Patients with hypertrophic cardiomyopathy are less active than other people, with a higher prevalence of obesity, anxiety, and reduced quality of life.[128 129] Recent data in both sedentary people and competitive athletes have challenged these assumptions.

Management of advanced heart failure in hypertrophic cardiomyopathy

A subset of patients (7-10%)[139] progress to experience advanced heart failure symptoms characterised by severe functional limitation and refractory heart failure symptoms in the absence of LVOT obstruction.[140] Recognition of advanced heart failure in hypertrophic cardiomyopathy remains challenging. Only 30% of patients with hypertrophic cardiomyopathy with heart failure will have a left ventricular ejection fraction <50% at presentation, with most patients having normal left ventricular ejection fraction with restrictive physiology.[140] Left ventricular dysfunction is uncommon, developing in 7.5% over 15 years, but once this occurs 35% progress to death, transplant, or mechanical assist device over median of 8.4 years [106]

Competing interests: See bmj.com.
Patient involvement: See bmj.com.
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Sexual assault referral centres provide high quality support

The study

Health and wellbeing of survivors of sexual violence and abuse attending sexual assault referral centres in England: the MESARCH mixed-methods evaluation

O'Doherty LJ, Carter G, Sleath E, et al

Health Soc Care Deliv Res 2024;12:1-168

CPD READING

0.5 HOURS

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Why was the study needed?

Sexual violence violates human rights and is a serious threat to a person's health and wellbeing across their life. In England and Wales, more than one million adults are sexually assaulted each year; 15% of girls and 5% of boys are sexually assaulted by the age of 16.

In a mixed methods study, researchers explored users' experiences of sexual assault referral centres and evaluated the care pathways they followed afterwards.

What did the study do?

The researchers analysed data from 335 survivors who accessed 21 sexual assault referral centres in England. The average age was 32 years, most were women (90%), and were white (85%).

What did it find?

Survivors went on to access a range of services. These were mostly voluntary organisations followed by independent sexual violence advisers, the police and criminal justice agencies, and the NHS.

Participants rated their experience of different services; they were mostly positive about sexual assault referral centres and the voluntary sector. Feedback was mixed about wider NHS services and the police and criminal justice service.

On entry to the study, most survivors (71%) had probable post-traumatic stress disorder (PTSD). This proportion was reduced one year later (but remained high, at 55%). Probable PTSD was highest among people with adverse childhood experiences, those with poor mental health before the sexual assault, and economic difficulties.

People who use sexual assault referral centres differ from survivors in the general population, the authors note. Many participants (44%) accessed the sexual assault referral centre within 10 days of the sexual trauma, and many (38%) had a forensic medical examination; most (77%) had four or more adverse childhood experiences.

The researchers interviewed 42 people from marginalised groups, such as those from ethnic minority groups, with insecure housing, or disabilities. Survivors found counselling beneficial but difficult to access because of long waiting lists and restrictions on the number of sessions they could have. Some saw mental healthcare as inappropriate and lacking in flexible options for those with complex trauma.

Why is this important?

This analysis provides evidence of good practice at sexual assault referral centres in England. They initiate pathways of care for many people after sexual assault, involve multiple agencies, and promote access to justice. They could therefore reduce the long term social, emotional, and physical harms of abuse.

Sexual assault referral centres offer excellent care, the researchers say, but are underused, partly owing to a lack of awareness among the public. Police forces signpost people to the service, but other areas (including primary care) lack awareness.

People with adverse childhood experiences, long term mental health problems, and economic disadvantage are particularly at risk of PTSD after sexual assault. These groups might need targeted support and access to counselling.

The researchers also carried out a review of 36 trials on psychological and social interventions. Among survivors of sexual violence, interventions such as cognitive behavioural therapy, eye movement desensitisation reprocessing, and newer treatments like trauma-sensitive yoga led to reductions in PTSD and depression. Other work highlighted the impact of how care was provided, and the value of offering choices of therapeutic support, a positive environment, and good rapport with the provider.

What's next?

The researchers will now work with policy makers to promote uptake of their findings. They suggest that services for people who have experienced sexual violence could be improved with:

- Raised awareness among the public about sexual assault referral centres
- Strengthened local partnerships between the NHS, police, and specialist statutory and voluntary sexual assault and abuse services
- Specialist training and support for NHS staff on trauma-informed care
- Tailored support for survivors with risk factors for PTSD
- Development of the role of independent sexual violence advisers to include more specialised advocacy for lesbian, gay, bisexual, or trans (LGBT+) survivors, and those with complex needs
- Greater choice and availability of interventions in NHS mental health 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

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CASE REVIEW

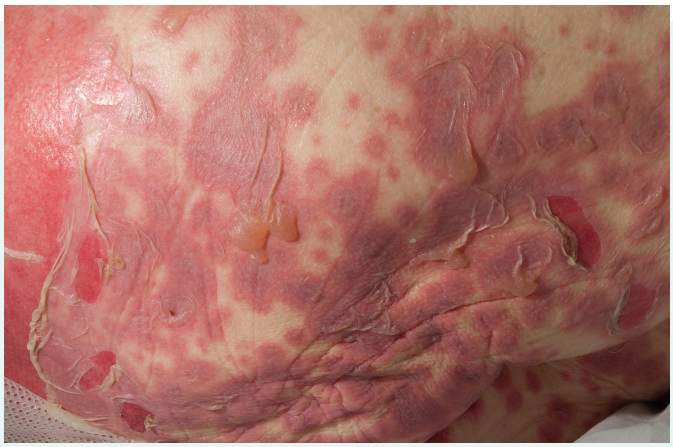
Progressive skin rash with eye and mouth involvement

A woman in her 80s, with Parkinson's disease, presented to the emergency department with a four day history of fever, malaise, gritty eyes, sore throat, and a progressive rash all over the body. She had no dermatological history. Six weeks previously, she had been prescribed sertraline owing to low mood. She had no known drug allergies.

Examination revealed dusky target lesions on her acral surfaces and widespread erythematous macules across her trunk and arms affecting >10% of the body surface area. There was lip ulceration, palatal ulceration, and conjunctival hyperaemia. The patient's vulva was not affected.

On admission, blood results showed a raised C reactive protein value (156 mg/L; reference range 0-12 mg/L), white cell count (12 $\times 10^9$/L; 4-11 $\times 10^9$/L), and neutrophil count (9.7 $\times 10^9$/L; 2.0-7.5 $\times 10^9$/L). Initial liver function tests were normal (albumin 39 g/L; 35-50 g/L). Glucose concentration was raised (7.9 mmol/L; 4-6 mmol/L). Urea, electrolytes, and bicarbonate levels were normal. Skin and mouth microbial swabs were negative. Blood cultures were negative and chest x ray was normal. A skin biopsy and ward admission were arranged.

Two days later, the erythematous macules rapidly progressed into dusky coalescent patches, with widespread flaccid blistering and epidermal detachment affecting >30% of the body surface area (figure). The patient's albumin level reduced to 25 g/L and C reactive protein value rose to 256 mg/L.



Dusky coalescent bullous lesions on the back, with patches of denuded epidermis occurring due to shearing forces (Nikolsky's sign)

1 What is the most likely diagnosis?
2 How should this condition be managed?
3 What are the complications of this condition?

Submitted by Mehak Chadha, Cleone Riad, Natasha Lee, and Angana Mitra

Patient consent obtained.

Cite this as: *BMJ* 2025;389:e083503

answers

CASE REVIEW **Progressive skin rash with eye and mouth involvement**

1. What is the most likely diagnosis?

Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) secondary to sertraline. SJS/TEN is a severe type IV hypersensitivity mucocutaneous reaction, which is driven by a cytotoxic T lymphocyte mediated response. SJS and TEN exist on the same disease spectrum. SJS encompasses epidermal detachment of <10% body surface area whereas TEN affects >30% body surface area; 10-30% is an overlap syndrome. The incidence of SJS/TEN is rare, at about 1-2 cases per million per year.

2. How should this condition be managed?

The British Association of Dermatologists provides guidance on managing the condition. For SJS/TEN triggered by a drug reaction, stop administering the drug immediately. It is important to suspect any new drug initiated within the previous eight weeks. All SJS/TEN cases should be managed by a multidisciplinary team, which should include general medicine, dermatology, ophthalmology, plastic surgery, urology/gynaecology, and dietetics. A high level of nursing care is required. Patients with >10% of body surface area affected should ideally be managed in an intensive care unit or in a specialist burns unit.

3. What are the complications of this condition?

A major complication of SJS/TEN is sepsis. Common pathogens are Staphylococcus aureus and Pseudomonas aeruginosa. Other complications include thermoregulatory dysfunction, insensible fluid losses, malnutrition, venous thromboembolism, scarring, visual impairment, mucosal strictures, and multiorgan failure. The psychological impact can be appreciable, with high rates of anxiety, depression, and post-traumatic stress disorder. Patients who are frail, with multimorbidity, are at greater risk of complications.

LEARNING POINTS

- SJS/TEN is a potentially fatal condition that should be considered in any presentation of an acute bullous eruption with epidermal sloughing and mucosal involvement, particularly in the context of drug initiation in the preceding eight weeks.
- If epidermal detachment is >10%, management should be undertaken in an intensive care unit, high dependency unit, or specialist burns unit.
- Multidisciplinary management is crucial and is primarily supportive.

PATIENT OUTCOME

See bmj.com.

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