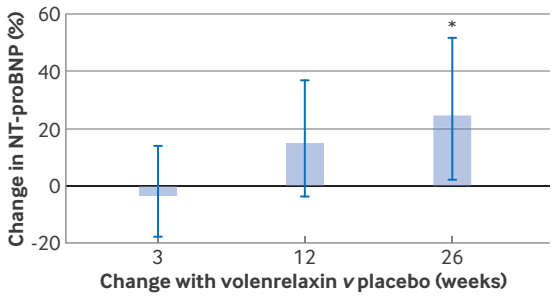
education

RESEARCH REVIEWS Fortnightly round up from the leading medical journals

Clopidogrel for coronary heart disease

Aspirin is the first choice antiplatelet therapy for people with stable coronary heart disease. However, an individual patient data meta-analysis of seven randomised trials has found that clopidogrel is more effective than aspirin for preventing major adverse cardiovascular or cerebrovascular events, with no increased risk of bleeding. Following the 28 982 patients for an average of 5.5 years, cardiovascular death, myocardial infarction, or stroke occurred less often in patients assigned to clopidogrel (2.61 events per 100 patient years) than in patients assigned to aspirin (2.99 events per 100 patient years, hazard ratio 0.86, 95% confidence interval (CI) 0·77 to 0.96).

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



Change in NT-proBNP *v* placebo (weeks). Error bars=95% confidence interval; *= P<0.05 for volenrelaxin v placebo

Time to stop relaxin

Another trial stopped early because of concerns that the intervention was causing harm is a phase 2 study exploring the use of relaxin for heart failure (the hormone relaxin, rather than the thing you do on the beach). Investigators randomised people with heart failure with preserved ejection fraction (HFpEF) and a recent heart failure decompensation to receive weekly injections of volenrelaxin—a long acting form of human relaxin—or placebo. Early findings showed that markers of congestion, including NT-proBNP levels, were higher in the volenrelaxin group compared with placebo (see figure), and although the study wasn't powered to detect the effect on heart failure hospitalisations or cardiovascular death, a trend towards worse clinical outcomes was seen with volenrelaxin.

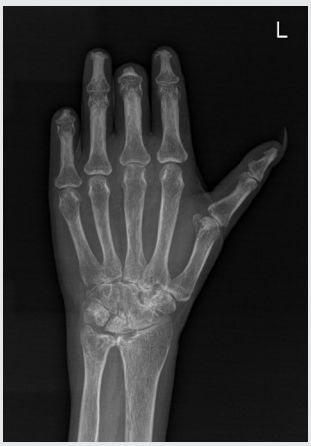
Nat Med doi:10.1038/s41591-025-03939-6

BORLAUG BA, ET AL. NAT MED 2025; HTTPS://DOI.ORG/10.1038/S41591-025-03939-6

Reducing harm in chronic coronary syndrome

Continuing a bad week for aspirin, a new trial set in France has found that starting aspirin for chronic coronary syndrome (eg, stable angina) in patients on long term anticoagulation does more harm than good. Death from any cause occurred in 58 out of 433 people (13.4%) in the aspirin arm of the study and in 37 out of 439 (8.4%) allocated to receive placebo, after a median follow-up of 2.2 years (adjusted hazard ratio 1.72, 95% CI 1.14 to 2.58). 10.2% in the aspirin arm and 3.4% in the placebo arm experienced major bleeding.

N Engl J Med doi:10.1056/NEJMoa2507532



CLINICAL PICTURE

Loss of fingertips

This woman in her 50s presented with bilateral digital shortening, sclerodactyly, and pallor of the fingertips. She described a 30 year history of progressive finger skin thickening and hardening, and Raynaud's phenomenon. She had a family history of connective tissue disease, had never smoked, had no respiratory symptoms, and had not previously sought medical care for her skin changes. Laboratory tests showed positive antinuclear and anti-Scl-70 antibodies, with weakly positive anti-Ro-52 antibodies. Results of an antiphospholipid screen were negative. Hand x ray imaging indicated marked acro-osteolysis of the distal and middle phalanges with marginal osteophyte formation (figure). She was diagnosed as having systemic sclerosis, and started on prednisone, methotrexate, hydroxychloroquine, and calcitriol. She also began treatment with beraprost sodium, a vasodilator and antiplatelet agent that is not licensed in the UK. She remained stable over a 14 month follow-up.

Acro-osteolysis is a radiographic sign of chronic digital ischaemia, typically seen in systemic sclerosis, psoriatic arthritis, Raynaud's syndrome, injury, or occupational

Ferritin thresholds for iron deficiency anaemia

It's easy to forget that reference ranges for laboratory investigations are a judgement call rather than some sort of universal truth. When diagnosing iron deficiency anaemia, increasing the cut off value for a normal ferritin to 45 ug/L (as recommended by the American Gastroenterological Association) would identify more people with true iron deficiency, but also subject more people to further diagnostic testing. Researchers examined ferritin levels in a large US cross-sectional cohort and estimated that the more liberal cut off (45 ug/L *v* 15 ug/L) would place an additional 3.3 million people into the category of having an iron deficiency anaemia. They also found that the median ferritin level in pre-menopausal women was 43 ug/L.

JAMA Intern Med doi:10.1001/jamainternmed.2025.2311

Digital wellbeing training

Healthcare professional wellbeing "can be modestly but meaningfully improved" by digital wellbeing training, conclude the authors of a new trial. The study enrolled 2315 healthcare professionals in Mexico and offered half of them a nine part course of two hour Zoom sessions and 13 weeks use of a wellbeing training app. Despite the positive findings, the study had no active control group, had relatively low levels of engagement (24.2% adhered to requested engagement levels), and the extent to which wellbeing was being affected by factors that should be addressed by employers (such as staffing levels) isn't described.

JAMA Intern Med doi:10.1001/jamainternmed.2025.3888

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

Cite this as: *BMJ* 2025;390:r1842

polyvinyl chloride exposure. It involves band acro-osteolysis or terminal tuft resorption of distal phalanges, occasionally affecting the middle phalanges. It is often associated with skin or nail changes including ulceration, nailfold capillary abnormalities, or subcutaneous calcinosis. Management is of the underlying disease, and treatment of pain and ischaemia with analgesics and vasodilators.

Haiye Ren; Hong-Lei Liu (hong-lei-liu@163.com), Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Patient consent obtained.

Cite this as: *BMJ* 2025;390:e083568

MINERVA From the wider world of research

Timing of antihypertensive medication

Six years ago, a trial from Spain reported that people taking antihypertensive medication at bedtime had better blood pressure control and only half the number of cardiovascular events when compared with people taking their drugs in the morning (*Eur Heart J* 2019 doi:10.1093/eurheartj/ehz754). Many commentators thought that the apparent benefits were implausibly large—a view which was supported by a later trial that found no advantage from nocturnal dosing (*Lancet* 2022 doi:10.1016/S0140-6736(22)01786-X). Settling any remaining doubt, a large trial in Canadian primary care finds that bedtime administration of antihypertensive medications has no beneficial effect on deaths or major cardiovascular events (*JAMA* doi:10.1001/jama.2025.4390).

Healing without scarring

Certain tissues, such as the uterine endometrium and the oral mucosa, usually heal without scarring. Experiments in mice and in human surgical specimens show that oral wounds are mainly infiltrated with anti-inflammatory cells, whereas wounds elsewhere attracted inflammatory immune cells and fibroblasts. The underlying molecular mechanisms involve a signalling pathway (known as the GAS6-AXL pathway) which regulates the balance between tissue regeneration and fibrosis (*Transl Med* doi:10.1126/scitranslmed.adk2101).

Vegetarian diets and cancer

In a longitudinal study of 100 000 Seventh-day Adventists in North America, risk of cancer among vegetarians was 10–20% lower than among non-vegetarians (*Am J Clin Nutr* doi:10.1016/j.ajcnut.2025.06.006). Reductions were largest for breast, colorectal, prostate, stomach, and lymphoproliferative cancers. The explanation may lie in a higher intake of fruits, nuts, and legumes, which are rich in protective phytochemicals, or in the absence of processed and red meats which are known to be associated with gastrointestinal malignancy.

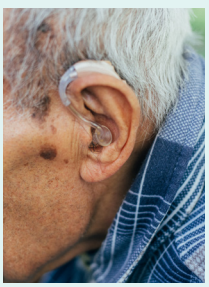
But it's worth noting that vegetarians also had a lower prevalence of obesity, and were less likely to smoke or drink alcohol.

Measles

Historical data from Switzerland show that, although deaths from measles declined during the early 20th century, morbidity remained high (*Am J Epidemiol* doi:10.1093/aje/kwaf167). It was only after the introduction of vaccination in the 1970s that complication rates dropped to low levels and measles ceased to be a seasonal disease. It's a compelling example of how vaccines have lightened the burden of infectious disease.

Hearing aids and dementia

Although hearing loss is associated with a higher risk of dementia, hearing aids may offer some protection. Findings from the Framingham Heart Study show that people under 70 with hearing loss who possessed hearing aids were less than half as likely to develop dementia as those with untreated hearing loss (*JAMA Neurol* doi:10.1001/jamaneurol.2025.2713). Hearing aids, however, didn't influence the incidence of dementia when hearing loss was first diagnosed after age 70.



Cite this as: *BMJ* 2025;390:r1841

Cardiovascular, kidney related, and weight loss effects of therapeutics for type 2 diabetes: a living clinical practice guideline

Full author details on bmj.com

Correspondence to: P O Vandvik per@magicevidence.org, T Agoritsas thomas@magicevidence.org

0.5 HOURS

Clinical question

What are the benefits and harms of medications for adults with type 2 diabetes at varied risks of cardiovascular and kidney related complications?

Recommendations

The guideline panel issued risk stratified recommendations regarding four prioritised medications for adults with type 2 diabetes (SGLT-2 inhibitors, GLP-1 receptor agonists, finerenone, and tirzepatide):

- Lower risk (three or fewer cardiovascular risk factors without established cardiovascular disease (CVD) or chronic kidney disease (CKD)): weak recommendation against SGLT-2 inhibitors or GLP-1 receptor agonists.
- Moderate risk (more than three cardiovascular risk factors without established CVD or CKD; or established CVD and/or CKD at lower risk of complications): weak recommendation in favour of SGLT-2 inhibitors or GLP-1 receptor agonists; and a weak recommendation against finerenone in adults with CKD.
- Higher risk (established CVD and/or CKD at higher risk of complications, or established heart failure): strong recommendation in favour of SGLT-2 inhibitors or GLP-1 receptor agonists; and a weak recommendation in favour of finerenone in adults with CKD.
- Across risk strata: weak recommendation in favour of tirzepatide in adults with obesity.

LINKED RESOURCES IN THIS *BMJ RAPID RECOMMENDATIONS* PACKAGE

- Nong K, Jeppesen BT, Shi Q, et al. Medications for adults with type 2 diabetes: a living systematic review and network meta-analysis. *BMJ* 2025;390:e083039. doi:10.1136/bmj-2024-083039[7]
- Rayner D, Shah D, Dai S, et al. Prognostic models for cardiovascular and renal outcomes in patients with type 2 diabetes: a living systematic review and meta-analysis of observational studies. *BMJ Med* 2025;4:e001369[8]
- González-Cruz DC, Moreno-Peña PJ, Garcia-Campa M, et al. Values, preferences, and treatment burden for initiation of GLP-1 receptor agonists, SGLT-2 inhibitors, tirzepatide and finerenone in adult patients with type 2 diabetes: a systematic review. [Pending submission to *BMJ*][9]
- MAGICapp – interactive, user-friendly platform providing recommendations, associated evidence summaries with risk-stratified benefits and harms for each candidate medication, and more detailed explanations regarding guideline methods and judgements: https://app.magicapp.org/#/guideline/noaRMj.

About this guideline and how it was created

Recommendations were informed by a linked living systematic review and network meta-analysis evaluating relative benefits and harms updated to 31 July 2024; and by linked systematic reviews addressing risk prediction models and values and preferences of adults with type 2 diabetes. Candidate therapeutics are prioritised based on availability of sufficient randomised trial data, relevance to a global audience, and likelihood of changing practice.This is the first version of the living guideline.

Why is the guideline needed?

In 2021, a previous *BMJ Rapid Recommendation* on sodium-glucose cotransporter-2 (SGLT-2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists for adults with type 2 diabetes provided risk stratified recommendations across five risk groups for cardiovascular and kidney outcomes.[3] Several limitations in the previously adopted risk stratification approach (summarised in MAGICapp), combined with a rapid evolution in evidence and available medications, has underscored the need for the current living practice guideline.

This guideline provides recommendations that are stratified by adults' risk of cardiovascular and kidney complications to allow clinicians to tailor care and optimise use of resources. The guideline also highlights uncertainties with respect to what evidence is needed to improve recommendations, patient care, and resource use in the future.

Our guideline in the context of current practice

At the inception of this living guideline in 2024, numerous professional societies in cardiology, nephrology, and endocrinology had incorporated cardiovascular and kidney related risk considerations and outcomes into their guidelines. Many professional societies recommended the use of SGLT-2 inhibitors and GLP-1 receptor agonists. Some societies made recommendations pertaining to finerenone. Guidelines incorporated varied risk stratification approaches and prognostic models for adults without established cardiovascular or kidney disease. Most guidelines incorporated recommendations for adults with established cardiovascular or kidney disease, but many did not consider the gradient of risk that exists

thebmj Visual summary

Rapid recommendation: Type 2 diabetes

Living clinical practice guideline on treatment

This graphic summarises risk stratified recommendations regarding prioritised medications for adults with type 2 diabetes. Recommendations are provided for adults at lower, moderate, and higher risk of cardiovascular and kidney complications. Subsequent iterations of the guideline will incorporate the latest available evidence and additional medications. MAGICapp displays the most recent version of the guideline and full content including evidence summaries and decision aids; major guideline updates will be published in *The BMJ*.

MAGIC app
See more details of recommendations and evidence base

Population

Recommendations apply to:

- ✔ All adults with type 2 diabetes regardless of ethnicity, sex, gender or comorbidities
- ✔ With or without cardiovascular or kidney disease

Who want to:

- ✔ Reduce the risk of major cardiovascular and kidney complications

and/or

- ✔ Achieve weight loss

Increased priority for many adults with obesity

May or may not apply to:

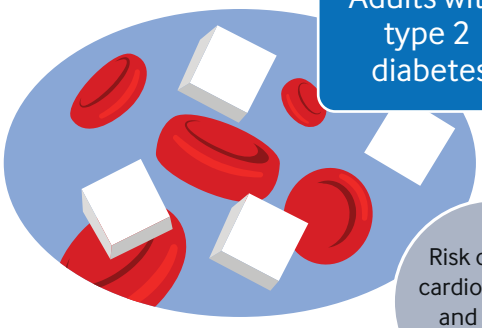
- ? People at either extreme of glycaemic control

Those with very strictly or poorly controlled HbA1c

Do not apply to:

- ✖ People with specific kidney-related conditions

Stratification



Adults with type 2 diabetes

Risk of major cardiovascular and kidney complications

No established cardiovascular or chronic kidney disease		Established cardiovascular disease and/or Established chronic kidney disease	
3 or fewer additional cardiovascular risk factors	More than 3 additional cardiovascular risk factors	Moderate risk of complications	Higher risk of complications
Lower	Moderate		Higher

Interventions

	Lower	Moderate	Higher
Strong recommendations in favour			SGLT-2 inhibitors GLP-1 receptor agonists
Weak recommendations in favour		SGLT-2 inhibitors GLP-1 receptor agonists Tirzepatide (Individuals with obesity)	Finerenone (Individuals with chronic kidney disease)
Weak recommendations against	SGLT-2 inhibitors GLP-1 receptor agonists	Finerenone (Individuals with chronic kidney disease)	

Summary of baseline risks for key cardiovascular and kidney outcomes across risk strata			
	Five year risk (per 1000 adults)		
	Lower risk	Moderate risk	Higher risk
All-cause death	20	60	240
Non-fatal myocardial infarction	30	70	110
Non-fatal stroke	30	40	90
Hospitalisation for heart failure	5	20	60-300*
Kidney failure	2	10	100

*Baseline risk was 60/1000 for adults with CKD and 300/1000 for adults with CVD.

within each disease category or the overlap in risks of complications between the disease categories. Many guidelines also provided recommendations pertaining to obesity, but few explicitly considered the comparative effectiveness of medications for weight loss. Furthermore, few guidelines reported risk stratified, absolute treatment effects for outcomes of benefit and harm; explicitly incorporated the values and preferences of adults living with type 2 diabetes; and adopted living models for summarising evidence regarding treatment effects and prognostic models to inform recommendations.

This living guideline prioritises the impact of medications on cardiovascular and kidney complications above effects on HbA1c and other markers of glycaemic control, given that complications are of considerable importance to patients and the growing evidence that intensive lowering of blood glucose does not correlate with large reductions in these complications.[13 14] We do, however, acknowledge that glycaemic control may remain an important consideration in treatment decision making for many patients.

This guideline adopts a relatively narrow focus in the wide array of management options for patients with type 2 diabetes. Recommendations therefore serve to complement rather than replace other local, national, or international practice guidelines.

Context for recommendations

These recommendations apply to all adults with type 2 diabetes, regardless of ethnicity, sex, gender, or comorbidities; and to adults with or without concomitant cardiovascular risk factors, cardiovascular disease (CVD), and/or chronic kidney disease (CKD). These guidelines do not apply to individuals receiving kidney replacement therapy or having received a kidney transplant, those with polycystic kidney disease, those with rare kidney diseases, and those with an estimated glomerular filtration rate (eGFR) below the threshold for safe use of a candidate medication (medication specific but typically <20 mL/min per 1.73 m^2) and not receiving kidney replacement therapy. The recommendations focus exclusively on available medications for diabetes management; non-pharmacological interventions are outside the scope of the guideline.

Assessing a patient's risk

In general, the higher the baseline risk for a given cardiovascular or kidney complication, the greater the benefit of treatment with a disease modifying agent. Recommendations provided are therefore stratified by the risk of such complications, classifying individuals as being at lower, moderate, or higher risk. In the absence of credible baseline risk estimates for other prioritised outcomes, risk stratification is currently limited to five patient-important outcomes (all-cause death, non-fatal myocardial infarction, non-fatal stroke, hospitalisation for heart failure, and kidney failure). The three defined risk strata represent a simple and pragmatic representation of the gradient of risk encompassed across patients with type 2 diabetes, and facilitate risk stratified recommendations.

Adults without established CVD or CKD are classified based on presence of cardiovascular risk factors. Those with three or fewer risk factors (excluding diabetes) are classified as being at lower risk for cardiovascular and kidney complications, and those with more than three are classified as being at moderate risk. These cardiovascular risk factors include (but are not limited to) poor glycaemic control, hypertension, dyslipidaemia, smoking or tobacco use, harmful alcohol use or other substance use, sedentary lifestyle, family history of premature CVD or CKD, and obesity.

Adults with established CVD or CKD are classified as being at either moderate risk or higher risk of complications. Adults with CKD may be classified based on eGFR and degree of albuminuria based on the KDIGO classification.[20]

For patients with established CVD, clinicians should rely on gestalt or one of several publicly available prognostic models to assess a patient's risk of cardiovascular and kidney complications. Decision makers should additionally consider the presence (or absence) of factors such as: history of myocardial infarction, coronary intervention, ischaemic heart disease, heart failure, cerebrovascular disease, peripheral vascular disease, or atrial fibrillation; older age; male sex; cardiovascular risk factors; and kidney function. For instance, an adult with a prior myocardial infarction with mild troponin elevation, no impairment in left ventricular function, no angina, and optimally controlled risk factors may be deemed to be at moderate risk, whereas another adult with a prior ischaemic stroke, peripheral vascular disease, and poorly controlled risk factors may be at higher risk for subsequent cardiovascular and kidney complications.

We provide a summary of baseline risks for key risk stratified cardiovascular and kidney outcomes across the proposed risk groups in the table. These baseline risks directly informed absolute effect estimates for medications and informed recommendations across the three risk strata.

Applicability to adults with diabetes and obesity

Approximately 90% of adults with type 2 diabetes are overweight or have obesity, emphasising the strong association between excess weight and diabetes.[20] Growing evidence supports the weight loss effects of candidate medications for diabetes, including GLP-1 receptor agonists and tirzepatide. The panel judged that weight loss is an important goal for many adults with diabetes and obesity. Recommendations therefore take into account the increased importance of this outcome for this subset of patients.

When providing class related recommendations (such as across GLP-1 receptor agonists), anticipated weight reduction may depend on the specific medication and the degree of obesity of the individual (with adults with higher body weights expected to benefit to a proportionally greater extent). In the absence of clear estimates of treatment effects on weight loss across varied body weights, a baseline weight of 90 kg was used to inform recommendations.

Combining medications

Most medications for which recommendations are provided can be used in combination (except for GLP-1 receptor agonists and tirzepatide, which have similar mechanisms of action). Clinicians and patients may choose to avoid combining candidate medications in certain contexts, including where the additive burden of administration or additive harms of treatment are substantial, or where additive benefits are not anticipated to be substantial. For example, adults taking multiple medications may choose to avoid adding another oral or subcutaneous treatment if the incremental benefit is small. Adults already taking medications with gastrointestinal side effects (such as metformin) may choose to avoid adding other drugs with similar side effects (such as GLP-1 receptor agonists) if the cumulative risk of gastrointestinal events exceeds anticipated benefits or is perceived as being too large a harm overall.

Recommendations

Below we summarise risk stratified recommendations, evidence regarding benefits and harms and their associated certainties, and rationales for judgments made by the panel.

Recommendations are stratified by adults' risk of cardiovascular and kidney complications

Adults at lower risk of cardiovascular and kidney complications

Adults with type 2 diabetes at lower risk are defined as those with three or fewer cardiovascular risk factors (not including diabetes) and without established CVD or CKD.

Recommendation 1: For adults at lower risk of cardiovascular and kidney complications, we suggest against using SGLT-2 inhibitors or GLP-1 receptor agonists (weak recommendation against)

Evidence—110 trials (86 803 participants) for SGLT-2 inhibitors and 109 trials (102 687 participants) for GLP-1 receptor agonists informed treatment effect estimates.

Understanding the recommendation—Given little or no benefit (high certainty evidence), risk of harms (genital mycotic infections for SGLT-2 inhibitors and severe gastrointestinal events for GLP-1 receptor agonists, both informed by moderate certainty evidence), and treatment burdens, the majority of adults were anticipated to be disinclined to accept SGLT-2 inhibitors or GLP-1 receptor agonists. A reasonable proportion of adults, however, were anticipated to be inclined to receive treatment in light of marginal cardiovascular and kidney benefits and the reversible nature of harms. The panel also considered possible longer term preventive benefits of initiating SGLT-2 inhibitors and GLP-1 receptor agonists early (for instance, to prevent progression to moderate or higher risk disease) balanced against concerns regarding potential harms, overtreatment, and pill burden from the patient perspective when formulating the recommendation. Variability in anticipated decision making justified a weak recommendation against both medication classes and emphasised the need for shared decision making.

Adults with obesity and type 2 diabetes may be more inclined to receive GLP-1 receptor agonists in light of the associated reduction in body weight (moderate certainty evidence for several medications within the class).

Adults at moderate risk of cardiovascular and kidney complications

Adults with type 2 diabetes at moderate risk are defined as having either more than three cardiovascular risk factors (not including diabetes) without established CVD or CKD; or having established CVD or CKD at lower risk of complications.

Recommendation 2: For adults at moderate risk of cardiovascular and kidney complications, we suggest in favour of using SGLT-2 inhibitors or GLP-1 receptor agonists (weak recommendation in favour)

Evidence—110 trials (86 803 participants) for SGLT-2 inhibitors and 109 trials (102 687 participants) for GLP-1 receptor agonists informed treatment effect estimates.

Understanding the recommendation—The cumulative cardiovascular and kidney benefits across outcomes (moderate to high certainty evidence) likely outweigh the risk of harms. A considerable majority of adults at moderate risk were anticipated to benefit and to be inclined to accept treatment. Anticipated variability in decision making, particularly between adults with the lowest baseline risks (who may be most disinclined) and highest risks (who may be most inclined) for complications within the group, justified a weak recommendation in favour and underscores the need for shared decision making.

The choice between SGLT-2 inhibitors or GLP-1 receptor agonists is contextual and is likely to vary based on individual attributes, context, and values. Adults with obesity are anticipated to place greater value on weight reduction and may be more inclined to consider GLP-1 receptor agonist initiation before considering SGLT-2 inhibitors.

Recommendation 3: For adults with CKD at moderate risk of cardiovascular and kidney complications, we suggest against using finerenone (weak recommendation against)

Evidence—Two trials (13 026 participants) informed treatment effect estimates.

Understanding the recommendation—Given little or no benefit (moderate to high certainty evidence), risk of harms (particularly severe hyperkalaemia, informed by moderate certainty evidence), comparatively limited clinical experience, resource considerations (including cost and access to therapy), and treatment burdens, the majority of adults were anticipated to be disinclined to accept therapy. Variability in anticipated decision making justified a weak recommendation against finerenone in this risk group and emphasised the need for shared decision making.

Adults at higher risk of cardiovascular and kidney complications

Adults with type 2 diabetes at higher risk are defined as having established CVD or CKD at higher risk of complications; or having established heart failure.

Recommendation 4: For adults at higher risk of cardiovascular and kidney complications, we recommend in favour of using SGLT-2 inhibitors or GLP-1 receptor agonists (strong recommendation in favour)

Evidence—110 trials (86 803 participants) for SGLT-2 inhibitors and 109 trials (102 687 participants) for GLP-1 receptor agonists informed treatment effect estimates.

Understanding the recommendation—Given the benefit on overall survival (high certainty evidence), important benefits on cardiovascular and kidney outcomes (moderate to high certainty evidence), and taking into account risk of harms (moderate certainty evidence) and treatment burdens, all or almost all higher risk patients with established disease were anticipated to be inclined to accept treatment; this justified a strong recommendation in favour. The panel also considered high certainty evidence of important benefits associated with SGLT-2 inhibitors for patients with established heart failure irrespective of diabetes status and agreed a strong recommendation in favour was in keeping with these established benefits.[23 24]

Adults with established heart failure may favour SGLT-2 inhibitors over alternatives. SGLT-2 inhibitors and GLP-1 receptor agonists can be combined.[21 22]

Recommendation 5: For adults with CKD at higher risk of cardiovascular and kidney complications, we suggest in favour of using finerenone (weak recommendation in favour)

Evidence—Two trials (13 026 participants) informed treatment effect estimates.

Understanding the recommendation—The survival and kidney benefits (moderate certainty evidence) offered by finerenone likely outweigh the risk of harms, uncertainties related to relatively limited clinical experience, resource considerations (including cost and access to therapy), and treatment burdens. Patients and clinicians are also likely to consider the availability of other medications with higher certainty evidence for cardiovascular and kidney benefits and safety (SGLT-2 inhibitors and GLP-1 receptor agonists). Taken together, a considerable majority of patients at higher risk were anticipated to accept therapy. Anticipated variability in decision making justified a weak recommendation in favour and underscores the need for shared decision making.

Adults across all risk groups, irrespective of likelihood of cardiovascular and kidney complications

Recommendation 6: For adults with obesity, we suggest in favour of using tirzepatide (weak recommendation in favour)

- Tirzepatide should not be given in combination with GLP-1 receptor agonists, but can be combined with SGLT-2 inhibitors and finerenone.
- When choosing between GLP-1 receptor agonists and tirzepatide, decision makers should weigh the higher certainty of cardiovascular and kidney benefits (offered by GLP-1 receptor agonists) against larger weight loss benefits (offered by tirzepatide).
- In adults at higher risk of cardiovascular and kidney complications, tirzepatide should generally not replace medications effective in reducing the risk of these complications. If replacing a GLP-1 receptor agonist with tirzepatide, initiation or continuation of an SGLT-2 inhibitor is indicated.

Evidence—Six trials (2252 participants) informed treatment effect estimates.

Understanding the recommendation—For adults with diabetes and obesity, the large reduction in body weight (relative to 90 kg baseline weight, mean of 8.63 kg weight loss; moderate certainty evidence) needs to be balanced against key uncertainties regarding effects on cardiovascular, kidney, and other outcomes (generally low or very low certainty evidence), risk of harms including severe gastrointestinal events (moderate certainty evidence), resource considerations (subcutaneous administration, access to therapy, and cost), and treatment burdens.

A large proportion of adults with obesity are likely to be classified as lower risk, with few or no other cardiovascular risk factors. Most of these individuals were anticipated to accept treatment with tirzepatide, given larger weight loss benefits relative to alternatives.

For patients with obesity at lower risk of cardiovascular or kidney complications, most adults were anticipated to choose tirzepatide over a GLP-1 receptor agonist, given superior weight loss effects.

For adults with obesity at moderate or higher risk of cardiovascular and kidney complications, decision making requires more nuance. A weak recommendation in favour is in place for SGLT-2 inhibitors or GLP-1 receptor agonists for all adults at moderate risk, irrespective of obesity status. A strong recommendation in favour is in place for both medications for higher risk individuals, given high certainty of benefit on key cardiovascular and kidney related outcomes. This leaves the residual question of how tirzepatide, with superior weight loss effects but currently uncertain cardiovascular and kidney benefits, should be positioned in the treatment of obese adults in either risk strata. For adults prioritising initiation of tirzepatide over GLP-1 receptor agonist therapy due to larger weight loss effects, initiation or continuation of an SGLT-2 inhibitor is indicated.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

The guideline panel included two patient partners with diabetes. The perspectives and contributions of the two patient partners involved were actively solicited and encouraged throughout the guideline process and were crucial in informing the values and preferences underlying recommendations.

Competing interests: None declared.

Cite this as: *BMJ* 2025;390:e082071

Find the full version with references at doi: 10.1136/bmj-2024-082071

Medications for adults with type 2 diabetes

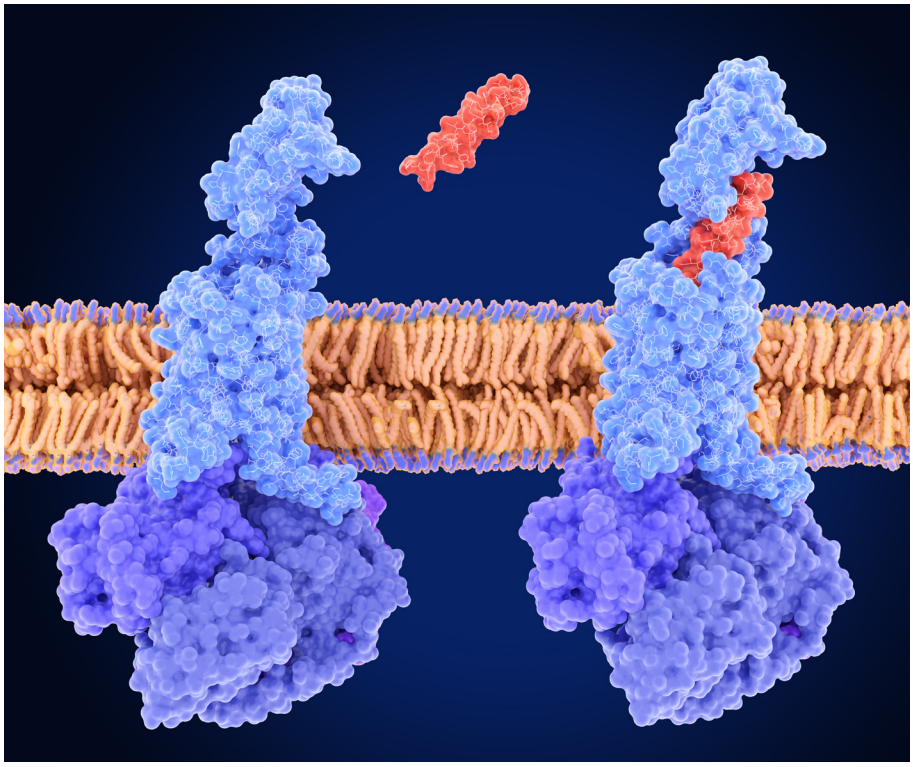
Nong K, Jeppesen BT, Shi Q, et al

Cite this as: *BMJ* 2025;390:e083039
Find this at doi: 10.1136/bmj-2024-083039

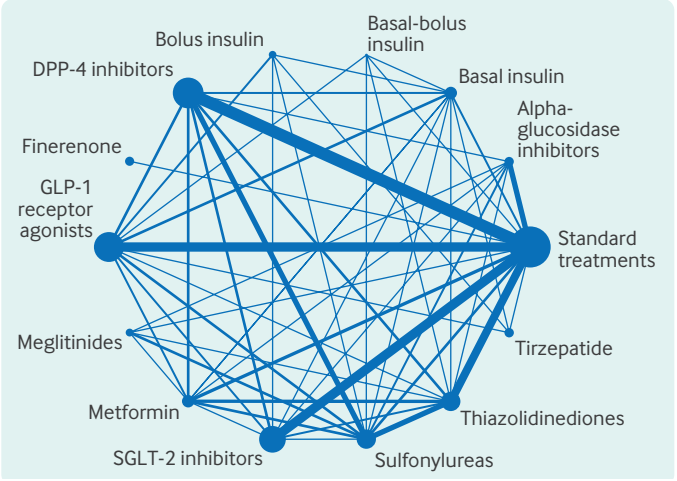
Study question What are the key benefits, risks, and uncertainties of glucose-lowering and emerging disease-modifying medications for adults with type 2 diabetes, based on up-to-date evidence?

Methods This living systematic review evaluates the comparative add-on effectiveness of medications for type 2 diabetes relative to standard treatment (current regimen) and to other medications using network meta-analysis, with certainty of evidence rated using the GRADE approach. The current iteration is updated to 31 July 2024, with updates planned at least two times a year from time of initial publication.

Study answer and limitations This review includes 869 randomised controlled trials with 493 168 adults living with type 2 diabetes and compares benefits and harms of 13 drug classes (63 drugs) across 26 patient-important outcomes. Regarding benefits, moderate to high certainty evidence confirms the well established cardiovascular and kidney benefits of sodium-glucose cotransporter-2 (SGLT-2) inhibitors, glucagon-like peptide-1 receptor agonists (GLP-1RAs), and finerenone (latter for patients with established chronic kidney disease). Magnitude of treatment effects depends on the baseline risk of cardiovascular and kidney events occurring in the absence of treatment; risk-stratified absolute effects are summarised using an interactive tool (https://matchit.magicevidence.org/250709dist-diabetes/#!/). The most effective drugs in reducing body weight were tirzepatide (mean difference (MD) −8.63 kg (95% confidence interval −9.34 to −7.93), moderate certainty) and orforglipron (MD −7.87 kg (−10.24 to −5.50), low certainty), followed by eight other GLP-1RAs (high to moderate certainty). Regarding drug-specific harms, SGLT-2 inhibitors increase genital infections (odds ratio (OR) 3.29 (95% CI 2.88 to 3.77), high certainty) and ketoacidosis due to diabetes (OR 2.08 (1.45 to 2.99), high certainty), and probably increase amputations (OR 1.27 (1.01 to 1.61), moderate certainty); tirzepatide and GLP-1RAs probably increase severe gastrointestinal events (most increased risk with tirzepatide: OR 4.21 (1.87 to 9.49), moderate certainty); finerenone increases severe hyperkalaemia (OR 5.92 (3.02 to 11.62), high certainty); and thiazolidinediones increase major osteoporotic fractures and probably increase hospitalisation for heart failure. Sulfonylureas, insulin, and dipeptidyl peptidase-4 inhibitors probably increase the risk of severe hypoglycaemia. Low or very low certainty evidence exists regarding treatment effects on other diabetes-related complications including neuropathy and visual impairment. Despite interest in the issue, there is uncertainty about whether GLP-1RAs may reduce dementia (OR 0.92 (0.83 to 1.02), low certainty).



Tirzepatide drug molecules and glucagon-like peptide-1 transmembrane receptors



Network plot for all included studies. Medications were grouped by their classes. Each node represents a medication class with node size reflecting the sample size of the treatment arm. The line between nodes represents the direct comparison between two medication classes with the thickness reflecting the number of trials. GLP-1 = glucagon-like peptide-1; SGLT-2 = sodium-glucose cotransporter-2; DPP-4 = dipeptidyl peptidase-4

What this study adds This study provides the best summary of existing evidence regarding the effects of medications on patient-important outcomes for adults with type 2 diabetes, including SGLT-2 inhibitors, GLP-1RAs, finerenone, and tirzepatide.

Funding, competing interests, and data sharing
Funding by 1.3.5 Projects for Disciplines of Excellence West China Hospital, Sichuan University (Grant No ZYYC24001). Six co-authors reported industry-related financial conflict of interests. No additional data available.

Study registration PROSPERO number: CRD42022325948. A more detailed protocol is available at https://data.aliveevidence.org/records/q02rv-km486.

EDITORIAL

Management of type 2 diabetes

Empowering choice in the pharmacological management of type 2 diabetes

The living rapid recommendations guideline by Agarwal and colleagues[2 3] provides recommendations for adults with type 2 diabetes on medications that offer cardiovascular or renal benefits—specifically sodium-glucose cotransporter-2 (SGLT-2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, tirzepatide, and finerenone—taking into account individual cardiovascular and kidney disease risk, the likelihood of treatment-related harm, quality of the supporting evidence, and patient preferences.

P. MARAZZI/SPL

Role of risk stratification

In recent years, treatment decisions for diabetes have shifted beyond glycaemic control, to emphasising comprehensive assessment of cardiovascular risk, alongside the presence and severity of cardiovascular and chronic kidney disease. This approach is already reflected in recommendations from organisations such as the European Society of Cardiology, which advises using tools such as SCORE2-Diabetes to estimate an individual's 10 year risk of fatal and non-fatal cardiovascular events based on their clinical profile.[4]

People in a higher risk category for cardiovascular disease are anticipated to derive greater benefit from treatments that modify this risk, which can inform discussions on treatments, taking into consideration benefits, side effect profile, and quality of evidence from available studies. This rapid recommendations guideline provides an evidenced framework for joint clinical decision making and offers a pragmatic approach on consideration of risk of cardiovascular disease and chronic kidney disease, which expands on the existing published guidelines. Given the wide variation in cardiovascular and kidney outcomes among individuals with diabetes, risk stratification is essential in guiding therapy in modern diabetes care.

This guidance marks a shift from focusing primarily on glycaemic control

Importance of glycaemic control

This guidance marks a shift from focusing primarily on glycaemic control and managing cardiovascular risk in parallel, to prioritising the reduction of cardiovascular and renal complications when applying diabetes therapeutics. This is illustrated by the cautious inclusion of finerenone, a non-glucose lowering agent recommended for higher risk patients with chronic kidney disease, highlighting its cardiovascular and renal benefits. Nevertheless, HbA1c remains a valuable marker with a well established link to microvascular complications.[7-9] Similarly, early glycaemic control predicts microvascular complications,[10] and the current practice of an intensive multifaced intervention for diabetes carries a legacy effect on the expected rate of microvascular complications and mortality from cardiovascular events[8]; therefore, early control, including glycaemic control, remains a targeted intervention.

However, intensive glycaemic targets in clinical trials with the use of older diabetes therapies such as insulin and secretagogues (sulphonylureas) may carry potential risks. For example, over the 3.5 years of the ACCORD trial mortality increased with aggressive HbA1c lowering (<6.0%), although certain subgroups—those with a haemoglobin glycosylation index less than 0.44, age below 61 years, and not obese—did benefit and showed an overall 2.3% reduction in absolute mortality.[11] In the nine year follow-up there was no difference in overall mortality after returning to conventional management.[12] This suggests that long term intensive glycaemic management may reduce or have a neutral effect on cardiovascular events, and continuing to examine the relationship of newer diabetes therapeutics resulting in diabetes remission and the likelihood of cardiovascular events will be important.

Poor glycaemic control continues to contribute to complications such as neuropathy, retinopathy, malaise, urinary incontinence, malnutrition, and functional decline.[15] Therefore, managing glycaemia in parallel with cardiovascular and renal risk factors remains essential, particularly for complications less affected by newer therapies.[16 17] Overall, the new recommendations may be most applicable to patients with HbA1c values between 6.5% (48 mmol/mol) and 8% (64 mmol/mol), in line with the evidence base supporting these guideline interventions.

In the future, guidelines could be further refined by assigning weightings to specific comorbidities—such as cardiovascular disease, chronic kidney disease, and obesity—and by accounting for characteristics such as gender, duration of diabetes, and baseline HbA1c, which may modify risk categorisation. The impact of treatment combinations could also be explored.[18]

Aikaterini Theodoraki, consultant physician in endocrinology and diabetes, Chelsea and Westminster NHS Foundation Trust, London, UK
aikaterini.theodoraki@nhs.net

Cite this as: *BMJ* 2025;390:r1726

Find the full version with references at http://dx.doi.org/10.1136/bmj.r1726

Reducing unnecessary imaging in ankle and foot trauma

Tahara D Bhate,[1 2] Varunaavee Sivashanmugathas,[3] Saleem Varachhia,[4 5] Lucas B Chartier[1 6 7]

Full author details on bmj.com

Correspondence to: L Chartier Lucas.Chartier@uhn.ca

This article is part of a series of Education articles based on recommendations from international Choosing Wisely campaigns. The BMJ thanks Wendy Levinson and Karen Born at Choosing Wisely for valuable advice and supporting the selection of topics. Choosing Wisely had no input into the peer review process or editorial decision.

CPD READING

0.5 HOURS

The Ottawa foot and ankle rules, widely known as the Ottawa ankle rules, are a clinical decision tool developed in 1992 to improve care for patients with foot and ankle trauma. The rules are intended to reduce unnecessary radiation exposure from diagnostic imaging for patients and to reduce emergency department wait times and healthcare costs. During 30 years of validation and implementation studies, the Ottawa ankle rules have been shown to have sensitivity approaching 100%[1] for assessing ankle and foot trauma, and to reduce use of radiography by up to 30%.[2 3] However, utilisation of the rules remains low across the world, including in Canada where they were first developed.

The clinical problem

Before the Ottawa ankle rules were introduced, obtaining foot and ankle radiographs was considered standard care for evaluation of acute ankle trauma. However, clinically significant fractures (defined as those with osseus fragments greater than 3 mm, and reflecting the need for immobilisation) were identified in only 15% of radiographs.[4] The Ottawa ankle rules help clinicians to identify low risk foot and ankle injuries. They state that ankle and/or foot radiographs are indicated only if there is pain in the ankle (malleolar) or midfoot region following blunt ankle trauma and:

- Patients are unable to weight bear both immediately after their injury and at time of assessment (for four steps) or
- If they have tenderness at any of four anatomically defined areas on palpation in addition to ankle (malleolar) or midfoot pain (figure).[5]

The initial validation and implementation studies for the Ottawa ankle rules, including a one year trial in eight community and academic hospitals across Canada, showed a reduction in radiograph rates of 30-40% with a fracture sensitivity rate of 100%.[3-6] This was associated with a statistically significant decrease in emergency department length of stay of 36 minutes (P<0.001), fewer subsequent physician visits (7% *v* 20%, P<0.001), and fewer days off work (3 days *v* 5 days, P<0.001), with the 5% of patients receiving follow-up radiographs being consistent between groups that received radiographs in the emergency department and those that did not.[6] Subsequent cost analysis estimated cost savings per visit totalling up to $3m (1993 dollars) per 100 000 patients, inclusive of the cost of radiographs and the economic impact of other benefits.[7]

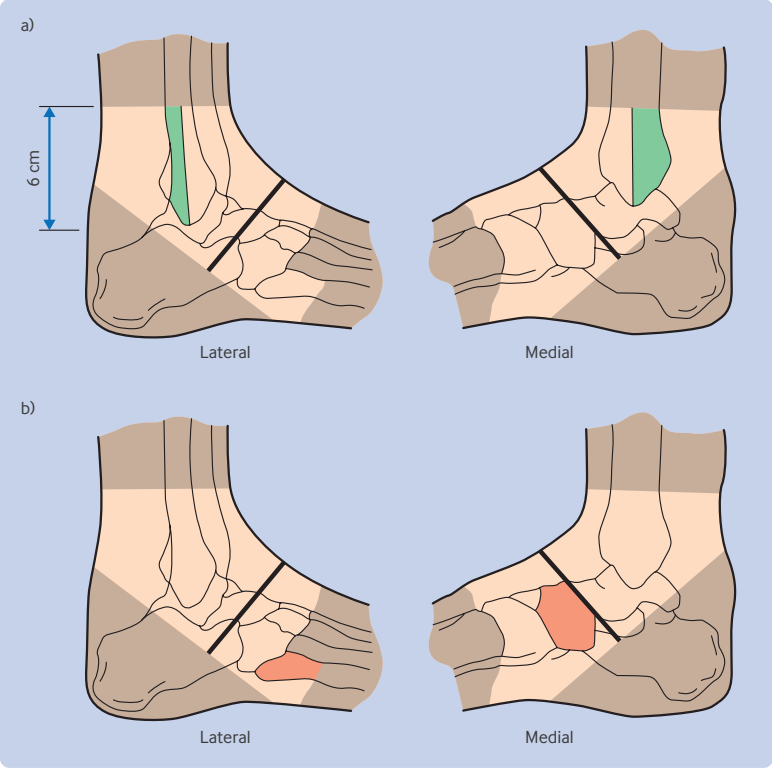
The Ottawa ankle rules were rapidly disseminated in some locations, with 91-99% of 1769 emergency department physicians surveyed in the UK, Spain, France, the US, and Canada familiar with them by the early 2000s.[8] They have been the focus of Choosing Wisely campaigns in Canada,[9] and were recommended in the 2016 guidelines from the National Institute for Health and Care Excellence (NICE) on non-complex fracture management in the UK.[10] However, based on a scoping literature review of data (table 1, bmj.com) and the authors' clinical experience, the practice of ordering imaging for most acute foot and ankle injuries persists.

WHAT YOU NEED TO KNOW

- The Ottawa ankle rules are a clinical decision tool that helps clinicians determine the need for foot and/or ankle radiography
- Validated internationally across thousands of patients, the Ottawa ankle rules' sensitivity for fractures is reported at >96%, with no clinically significant (>3 mm) missed fractures in studies with sensitivities below 100%
- Implementation of the Ottawa ankle rules remains suboptimal in many areas, despite the substantial savings this can bring in terms of reduced ordering of radiography, reduced patient length of stay, and associated reduction in healthcare costs
- Adopting a shared decision making approach with patients that encompasses education and discussion of appropriate return indications prior to discharge may help to allay concerns about patient satisfaction and medicolegal risks
- Successful and sustained implementation of the Ottawa ankle rules is likely to require approaches beyond individual clinician education, including patient engagement and institution support leveraging both technology and the interprofessional team

Evidence for change

In the 10 years following introduction of the Ottawa ankle rules, international validation and implementation studies consistently demonstrated their safety and efficacy. A 2003 meta-analysis on the performance of the Ottawa ankle rules (27 studies, n=15 581) found a pooled sensitivity of 98% (95% confidence interval, CI, 96.3 to 99.3) for ankle radiographs, 99% (95% CI, 97.3 to 100) for foot radiographs, and 96.4 (95% CI, 93.8 to 98.6)



Visual summary of the Ottawa ankle rules. (a) Anatomical criteria for ordering ankle radiographs. (b) Anatomical criteria for ordering foot radiographs.
(a) Ankle radiographs are indicated if a patient is having pain in the malleolar zone (green) and is either unable to weight bear both immediately after injury and at time of assessment (for four steps), or has tenderness on palpation to the posterior edge (over 6 cm) or tip of either malleolus.
(b) Foot radiographs are indicated if a patient is having pain in the midfoot zone (red) and is either unable to weight bear both immediately after injury and at time of assessment (for four steps) or has tenderness on palpation to base of the 5th metatarsal (shown in the lateral view) or the navicular (shown in the medial view).
Adapted from: Stiell IG, Greenberg GH, McKnight RD, et al. Decision rules for the use of radiography in acute ankle injuries refinement and prospective validation. *JAMA* 1993;269:1127-32

for combined foot and ankle radiographs[2]; the pooled false negative rate was 0.3% (47/15 581). International validation studies continued, with an updated systematic review in 2016 that looked at an additional 21 studies, and found only three that reported a sensitivity less than 100% (ranging from 92% to 99%), with none of those three studies reporting any clinically significant missed fractures.[1] In addition, while many of the implementation studies do not report on follow-up, the original multi-site trial in eight Canadian hospitals (n=12 777) found 0.5% (7/1301) of patients who did not receive initial radiography had fractures diagnosed on subsequent radiographs.[3] However, only one of those patients had the Ottawa ankle rules correctly applied, with the rules not used in two cases, and improper palpation documented in the others.[3] All patients received six month follow-up and healed without delay or complication.[3]

In studies that used chart audits spanning 2008 to 2021, the percentage of radiographs performed that would have been deemed unnecessary under the Ottawa ankle rules ranged from 20% in Gold Coast, Australia[22] and 23.3% in an emergency department in Malta[23] to 37.8% in a tertiary hospital in South Australia.[24] The largest such study, in Ankara, Turkey,[25] found 36% of radiographs (n=792) in patients with acute foot and ankle injuries were unnecessary based on the Ottawa ankle rules. Furthermore, a case series analysis of 7706 acute ankle injuries in Ontario, Canada, showed an increase of 3% in radiographs per year between 2001 and 2007, when controlling for the number of cases positive for fractures.[26]

Providing clinicians with education about the Ottawa ankle rules has been shown to improve rates of implementation, with a corresponding decrease in unnecessary radiography requests. In settings with previously high baseline rates (92-100%) of ankle and foot radiography for patients presenting with minor foot and ankle trauma, education of clinicians about the Ottawa ankle rules correlated with a decrease in the percentage of radiographs ordered—a decrease of 31.8% in a hospital in São Paulo, Brazil,[27] 45.6% in a hospital in Nairobi, Kenya,[21] and 59% in selected emergency departments in Oman.[28]

Barriers to change

Familiarity with the Ottawa ankle rules varies geographically. Overuse of radiographs persists in several countries where lack of awareness may be a contributing factor (table 1, see bmj.com).[21 27]

Still, evidence suggests that knowledge alone may not be enough for sustained practice change. The 2011 Ontario case series analysis described above, showing a 3% rise in radiographs (controlled for rates of fracture positive x rays) over seven years,[26] and a 2005 postal survey of 262 randomly selected emergency physicians from the membership list of the Canadian Association of Emergency Physicians[30] showed that only 42.2% reported using the Ottawa ankle rules as a basis for decisions about radiography, despite 99.2% reporting familiarity with them.[30]

In our experience, perception of patient expectations is one of the most influential drivers of clinician behaviour, and potentially even more so in the context of prolonged wait times and increasingly busy emergency departments. A 2012 cross-sectional questionnaire survey in an emergency department in the UK showed that 58% of patients presenting with minor injuries expected a radiograph as part of their care.[31] In an intensive implementation study of the Ottawa ankle rules in Canada, 78% of care providers in emergency departments stated that patient expectations influenced their management.[32]

The fear of medicolegal repercussions owing to missed fractures has also been raised in light of patients' expectations for accurate diagnosis.[11 32] The absence of large numbers of missed fractures with the potential for poor patient outcomes, across tens of thousands of patients over 30 years of studies, is highly reassuring.[1 2] However, as with all clinical decision aids, the Ottawa ankle rules are not intended to substitute for clinical judgment and an appropriate physical examination.

Discussions with patients

- A lot of people expect an x ray when they twist their ankle or hurt their foot, but it is not always needed
- Based on studies with thousands of patients internationally, we can tell with a high degree of certainty if you have a broken bone, by pressing on a few specific areas during our assessment
- If the areas we press on are not tender, the chance that you have broken a bone (fracture) is less than a 3 in 1000 (0.3%), and we would therefore advise against an x ray, as this can only be used to identify an injury to the bone, and will not be helpful in the case of a sprained/twisted ankle
- Unnecessary x rays confer some risk in terms of radiation, and the increased wait time will impact both you and other patients, without any additional benefit or improved outcome
- If we do not perform an x ray when we first see you (based on our physical examination) and your injury fails to improve as expected, you can receive an x ray later. In the very rare case where a broken bone is identified later, studies show no reported cases of the delay in diagnosis causing any harm or affecting the chance of a full recovery

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

This paper was reviewed by an external patient reviewer who suggested edits related to better understanding of drivers of patient expectations, and more detailed suggestions to guide patient-clinician conversations. Additional references and discussion were added to address these concerns, as well as a more robust discussion on mitigating and managing delayed diagnosis of injury.

EDUCATION INTO PRACTICE

- How often do you apply the Ottawa ankle rules in practice? If the answer is rarely, consider using them intermittently to start, reflecting on how the patient encounter goes, and trying different approaches to the discussion.
- Are most radiographs at your institution ordered at triage? How might you implement a joint education or quality improvement project with the nursing team to implement the Ottawa ankle rules at triage?

How should we change our practice?

Shared decision making

Clinicians' perception that their patients will leave dissatisfied if they do not undergo radiography is a strong motivator for their behaviour. However, in a large prospective study of the Ottawa ankle rules (n=6398), when patients who did not receive radiographs were followed up after discharge (n=342/494, 69% eligible patients) and compared with a random sample of those patients who did receive radiographs, no difference was seen in overall satisfaction between the two groups, which also had similar rates of seeking additional care, and later obtaining imaging.[32] This suggests that patient expectations may be more amenable to discussion and shared decision making than clinicians might assume. We have suggested some key messages clinicians might wish to explore in consultation with patients (box).

Making patient facing educational materials, such as brochures and posters, available during a patient's visit to the emergency department has proved successful in other Choosing Wisely campaigns and projects. These can be based on the key messages highlighted in the box.

Clinical judgment and follow-up

The Ottawa ankle rules have a false negative rate of 0.3%.[2] The rules were never intended as a substitute for clinical judgment or an appropriate and thorough physical examination of the injured area, including assessment for ligamentous injury. Correct application of the rules is important, and particular attention should be paid to palpating the correct areas for tenderness, including the entire distal 6 cm of fibula,[6] as identified in the figure.

Institution support

The impact of large scale educational programmes on the use of the Ottawa ankle rules has been mixed, with one study showing sustained practice change after 12 months,[38] and another, using a "train the trainer" model, not leading to meaningful practice change.[39] However, those studies were done before the Choosing Wisely era and clinicians may be more receptive today to education and messaging around investigation overuse.[40]

Point-of-care tools

An alternative to traditional education programmes is leveraging technology, specifically smartphone based point-of-care tools. The Ottawa Rules smartphone app, which contains numerous clinical practice guidelines developed by the emergency medicine group based in Ottawa, Canada (who developed the Ottawa ankle rules), had 48 349 app sessions recorded among 42 225 app users worldwide between November 2018 and May 2019.[41] Technology availability and infrastructure may limit the use of this type of point-of-care application, but the international uptake of this programme is encouraging and potentially represents a more accessible option for education than establishing standalone institution wide educational programmes. Another option is point-of-care clinical decision supports based on electronic medical records, with forced function acknowledgment of the Ottawa ankle rules.[42]

Triage

A systematic review found that nurse initiated triage protocols utilising the Ottawa ankle rules reduced patient length of stay in the emergency department by 34.5 minutes on average (95% CI -54.2 to -14.8; P<0.0001), with the proportion of radiographs ordered by nurses significantly less than that of physicians based on routine practice (odds ratio 0.36, 95% CI, 0.22 to 0.59, P<0.0001), and no instances of overlooked fractures reported.[43] Two randomised controlled trials showed similar benefits in length of stay in the emergency department, with no missed fractures, and with generally positive feedback from triage nurses.[29 44]

Competing interests: None declared.

Cite this as: *BMJ* 2025;390:e084845

Find the full version with references at doi: 10.1136/bmj-2025-084845

WHAT YOUR PATIENT IS THINKING

Facing a smear test after my trauma

CPD READING
0.5 HOURS

Ruth Ajayi shares her experience of cervical screening after a traumatic childbirth, and how healthcare professionals could offer more compassionate, flexible care

PRIYA SUNDRAM

When it comes to smear tests, if my vagina could speak it would be screaming, "I do not want to go, leave me alone." When I am with someone I trust, being naked feels natural. I do not think about how my body looks or feels. But lying half naked in a medical room, legs in stirrups, with strangers watching, touching, is nothing like that. For some people, like me, it can feel terrifying, shaming, and deeply uncomfortable.

My fear started after I gave birth to my daughter. My pregnancy, labour, and the time after were very hard. My health visitor later told me I was experiencing birth trauma and post-traumatic stress disorder. During labour, childbirth, and the postnatal period in hospital, I felt powerless. People touched my body and made decisions without asking me first. I was shouted at, and felt coerced. I spoke up, but no one listened.

A screening letter that broke me

Some years later, I received a letter inviting me for a smear test. As soon as I read it, I panicked. Flashbacks came quickly. I remembered being naked in the operating theatre, legs apart as they inserted a catheter. The theatre was packed, leaving me powerless, exposed, and humiliated. The thought of lying back again, with someone inserting a speculum to collect cells, filled me with dread and made me feel powerless again.

I decided not to book the appointment. Someone called me to follow up, but no one asked me why I didn't want to book the appointment. Instead, I was made to feel like a disobedient child for saying no to the request. Finally, a nurse from the practice called and I shared my experience. She listened kindly but kept focusing on why getting the smear test done was important. I knew I could not face it. I might have changed my mind if she had provided trauma informed care and worked with me to find ways to make the smear test less traumatising and more empowering for me.

Better screening options

This year, I discovered Tiger UK—Together Improving Gynae Experiences and Research. It is a network for anyone passionate about improving gynaecology experiences, including healthcare professionals, researchers, and people with lived experience. I was excited about what they were doing, and I wanted to be involved.

It was through Tiger that I learnt about at home cervical screening trials in the UK. I was ecstatic when the government announced that the option of home testing kits be offered to women who do not participate in the cervical screening programme. This will allow women to collect a sample themselves and post it to the laboratory. I am very pleased to have the opportunity to explore this option with my GP.

ruthajayi40@gmail.com

Cite this as: *BMJ* 2025;390:r1439

WHAT YOU NEED TO KNOW

- Patients with a history of trauma may find smear tests, or the prospect of them, to be retraumatising
- If possible, offer choices around smear tests, including self-sampling kits, having a same sex clinician, or offering time to discuss concerns first
- Respect the patient's decision to decline and avoid making patients feel guilty or forced

EDUCATION IN PRACTICE

- How could you ensure that patients have the opportunity to talk about their concerns before offering cervical screening?
- What practical adjustments could you offer patients to help them feel safer during intimate examinations?

ADDITIONAL INFORMATION

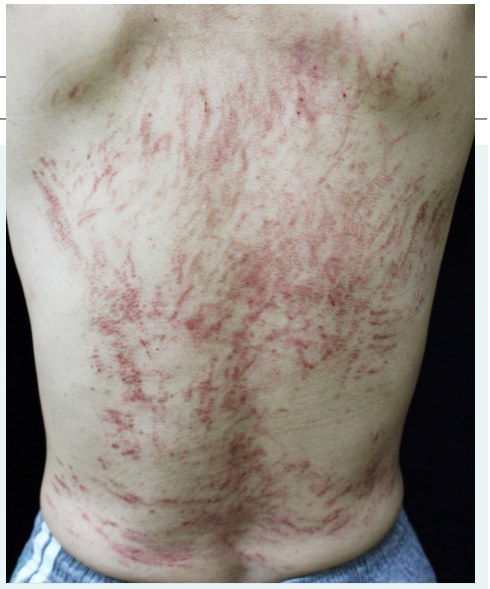
- Cancer Research UK. HPV self-sampling could help 1m more women get cervical screening. https://news.cancerresearchuk.org/2024/07/17/hpv-self-sampling-could-help-1m-more-women-get-cervical-screening/
- Cancer Research UK. A trial looking at a new blood test to help diagnose cancer earlier (SYMPLIFY) https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-a-new-blood-test-to-help-diagnose-cancer-earlier-symplify
- SARSAS. The impact of trauma and cervical screening. https://www.sarsas.org.uk/the-impact-of-trauma-and-cervical-screening/#:~:text=Communicate%20with%20your%20body%20about,force%20your%20body%20to%20go
- TIGER UK. Together Improving Gynae Experiences and Research. https://linktr.ee/tigeruk?utm_source=linktree_profile_share&ltsid=1479a9c4-8148-4656-9404-37ef2dcaed0d

CASE REVIEW

Whip-like rash on the trunk

A woman in her 50s presented with a 10 day history of daily high grade spiking fever (39°C), accompanied by arthralgia involving multiple joints, sore throat, and itchy rash on the chest and back. Skin lesions manifested as multiple red-to-brown, linear plaques resembling whip marks (known as flagellate dermatosis), which persisted during the afebrile period (figure). The patient was initially treated at another hospital, where blood and urine cultures were unremarkable. Fever of unknown origin was considered and broad spectrum antibiotics were commenced five days after the onset of symptoms.

The patient was referred to our institution, where laboratory investigations showed leucocytosis (18.03×10^9/L with 88% neutrophils), increased inflammatory markers (erythrocyte sedimentation rate 44 mm in first hour, C reactive protein 121.7 mg/L), slightly raised transaminases (aspartate transaminase 53 U/L, alanine transaminase 87 U/L), and hyperferritinaemia (›20 000 ng/mL). Antinuclear antibody titres and the autoantibodies rheumatoid factor, anti-CCP, anti-Ro, anti-La, and anti-dsDNA autoantibodies were within normal ranges. Abdominal sonography showed splenomegaly (12.4 cm). Bone marrow biopsy revealed no evidence of haematological malignancy. Repeat blood, urine, and stool culture yielded no growth. There was no serological evidence of active or recent infection with cytomegalovirus, Epstein-Barr virus, hepatitis A virus, hepatitis B virus, or hepatitis C virus. Her fever and symptoms persisted despite the use of broad spectrum intravenous antibiotics.



Whip-like rash on the back

1 What are the differential diagnoses?

2 What is the most likely diagnosis?

3 How would you manage this patient?

Submitted by Sheng-Wen Liu, Chien-Ping Chiang, Chih-Tsung Hung, and Feng-Cheng Liu

Patient consent obtained.

Cite this as: *BMJ* 2025;389:e083472

answers

CASE REVIEW **Whip-like rash on the trunk**

1. What are the differential diagnoses?

Flagellate dermatosis can be seen with reactions induced by bleomycin, shiitake mushroom ingestion, jellyfish envenomation, dermatomyositis, and adult onset Still's disease (AOSD).

2. What is the most likely diagnosis?

AOSD, which is a systemic autoinflammatory disorder that typically manifests as a triad of daily spiking fever, arthralgia, and an evanescent rash. The estimated prevalence of AOSD is 3.9 per 100 000 people, with a mean age of onset of 46 years. The pathogenesis of AOSD involves the activation of an aberrant inflammatory response, which can be triggered by an infection in genetically predisposed individuals.

3. How would you manage this patient?

The goal of treatment is to achieve and maintain clinically inactive disease, defined as the absence of symptoms and normalisation of erythrocyte sedimentation rate or C reactive protein. In the absence of evidence from a randomised controlled trial, NSAIDs are recommended only for symptomatic management of fever and arthralgia. Although short term corticosteroid drugs might be considered at the onset of disease and gradually tapered off, an interleukin 1 or interleukin 6 inhibitor should be initiated as early as possible to avoid the prolonged use of corticosteroid drugs.

Macrophage activation syndrome, which occurs in as many as 15% of AOSD cases, is a life threatening complication with reported mortality rates ranging from 10% to 41%. Patients should be actively screened and closely monitored because macrophage activation syndrome can develop at any stage of the disease. Macrophage activation syndrome should be suspected when there is a shift in fever pattern from spiking to persistent, accompanied by splenomegaly, cytopenias, raised or rising serum ferritin, abnormal liver function tests, hypertriglyceridaemia, and evidence of intravascular coagulation.

LEARNING POINTS

- AOSD is a rare systemic autoinflammatory disease of unknown cause. Diagnosis relies on clinical features and exclusion of infections, malignancies, and autoimmune diseases.
- Typical signs include spiking fever, arthralgia, salmon pink rash, and raised inflammatory markers (C reactive protein, erythrocyte sedimentation rate, and ferritin). Persistent pruritic flagellate rashes can also appear and show characteristic histopathology.
- Treatment includes corticosteroid drugs and early interleukin 1 or interleukin 6 inhibitors, with close monitoring for macrophage activation syndrome.

PATIENT OUTCOME

See bmj.com.

CPD READING 0.5 HOURS

You can record CPD points for reading any article. We suggest half an hour to read and reflect on each.

LEARNING MODULE

Articles with a "learning module" logo have a linked BMJ Learning module at learning.bmj.com.