

education

FROM THE JOURNALS Edited highlights of weekly research reviews

No thanks, I'm sweet enough

I wonder how much coffee gets drunk by academics as they try to grind out another research paper? Should author coffee consumption—or addiction—be disclosed on research papers about the health benefits of coffee? This prospective cohort study, where no coffee drinking interests were declared, finds moderate consumption of unsweetened and sugar sweetened coffee was associated with a lower risk of death over a median follow-up period of seven years.

Data from the UK Biobank was used, which meant the authors could adjust for possible confounders such as education level, deprivation, physical activity, and even tea and milk consumption. But residual confounding and other methodological limitations mean this study still can't prove that it's all down to the coffee. Perhaps a randomised control trial is needed, but I'm not sure it's ethical to make people drink sugary coffee, let alone coffee with artificial sweetener—which in the current study wasn't associated with the same survival benefit.

• *Ann Intern Med* doi:10.7326/M21-2977

Worrying stats for sats

A retrospective cohort study based in the US sheds further light on pulse oximeter bias associated with race and ethnicity, this time in patients hospitalised with covid-19. Occult hypoxaemia is when the true arterial blood oxygen saturation levels are less than 88%, but the pulse oximeter is still giving a reading of 92-96%. In the 1216 patients who had concurrent pulse oximeter and arterial oxygen levels measured, occult hypoxaemia was identified in 3.7% of samples from black and Asian patients, versus 1.7% of samples from white patients.

The chances of patients having at least one incidence of occult hypoxaemia during their admission were remarkably high: 30.2% in Asian patients, 28.5% in black patients, and 17.2% in white patients. An accompanying editorial says that this is a fixable problem—the technology exists to make more accurate, non-racist pulse oximeters—but, unless practitioners and those responsible for healthcare systems push for change, things will likely stay as they are.

• *JAMA Intern Med* doi:10.1001/jamainternmed.2022.1906

(CAR) T blanche

The *New England Journal of Medicine* has enthusiastically kicked off a new article series called "Science behind the Study," declaring that few things are more exciting than a potential new treatment for an incurable illness. Reading through the first article in the series reminded me that there

are few things I find more difficult to understand than gene therapy. The new treatment is chimeric antigen receptor (CAR) T cell therapy, which was used in two patients with metastatic prostate cancer, leading to a response in one: a partial regression of visceral metastasis that was sustained at six months.

• *N Engl J Med* doi:10.1056/NEJMoa2119662

Blocking programmed death

Next on the journal's new treatments round-up comes an immunotherapy for rectal cancer that works by the promisingly named mechanism of programmed death 1 (PD-1) blockade. Around 5-10% of rectal adenocarcinomas lack DNA mismatch repair enzymes, and are therefore less responsive to chemotherapy and radiotherapy. However, PD-1 blockade has previously shown promising results in those with mismatch repair deficient metastatic disease.

This new phase 2 study recruited 12 patients with mismatch repair deficient stage II or stage III rectal cancer and gave them dostarlimab, an anti-PD-1 monoclonal antibody, every three weeks for six months. All 12 patients had complete remission, sustained at follow-up, between six and 25 months later: no evidence of tumour was found on magnetic resonance imaging, positron emission tomography, endoscopy, biopsy, or digital rectal examination. None of the patients has needed chemotherapy, radiotherapy, or surgery, and none has experienced severe adverse events. This is a small study from a single site, with relatively short follow-up, but, with such dramatic results, it's not surprising it made the headlines.

• *N Engl J Med* doi:10.1056/NEJMoa2201445

Bariatric surgery and cancer risk

A retrospective cohort study of over 30 000 patients with a body mass index of over 35 found that those who had bariatric surgery had a lower risk of obesity associated cancers and cancer related mortality.

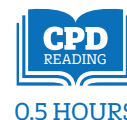
After 10 years, 2.9% of those who had bariatric surgery and 4.9% of matched controls had a diagnosis of obesity associated cancer: that gives a hazard ratio of 0.68. Possible selection bias (differences in those who come forward for or who could access bariatric surgery) and healthy user bias (healthier lifestyles during the follow-up period in those who undergo surgery) seem to raise big questions over the degree to which bariatric surgery itself lowers these risks. It seems that—as with coffee drinking—we may need further evidence from randomised trials.

• *JAMA* doi:10.1001/jama.2022.9009

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What is the role of minimally invasive surgical treatments for benign prostatic enlargement?



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This is one of a series of occasional articles that highlight areas of practice where management lacks convincing supporting evidence. You can read more about how to prepare and submit an Education article on our Instructions for Authors pages: www.bmj.com/about-bmj/resources-authors/article-types

Benign prostatic enlargement (BPE), also called benign prostatic hyperplasia, is a common cause of lower urinary tract symptoms in men over 50. Increased frequency or urgency of urination, nocturia, difficulty starting urination, or dribbling at the end of urination, are common symptoms.¹ BPE is characterised by growth of glands and smooth muscle parts of the prostate and is separate from prostate cancer. In later stages, it can result in bladder outlet obstruction with complications including urinary retention, infection, and possibly impaired renal function.

Initially, if no complications are evident, patients are advised conservative measures such as reducing the amount of fluid intake in the evening, and medications, including α blockers and 5- α reductase inhibitors.² Surgical ablation to reduce the physical obstruction caused by BPE is an option if symptoms do not improve, patients experience side effects (for example, orthostatic hypotension, which can occur with α blockers, or sexual adverse events with 5- α reductase inhibitors) or do not prefer to take medications long term.

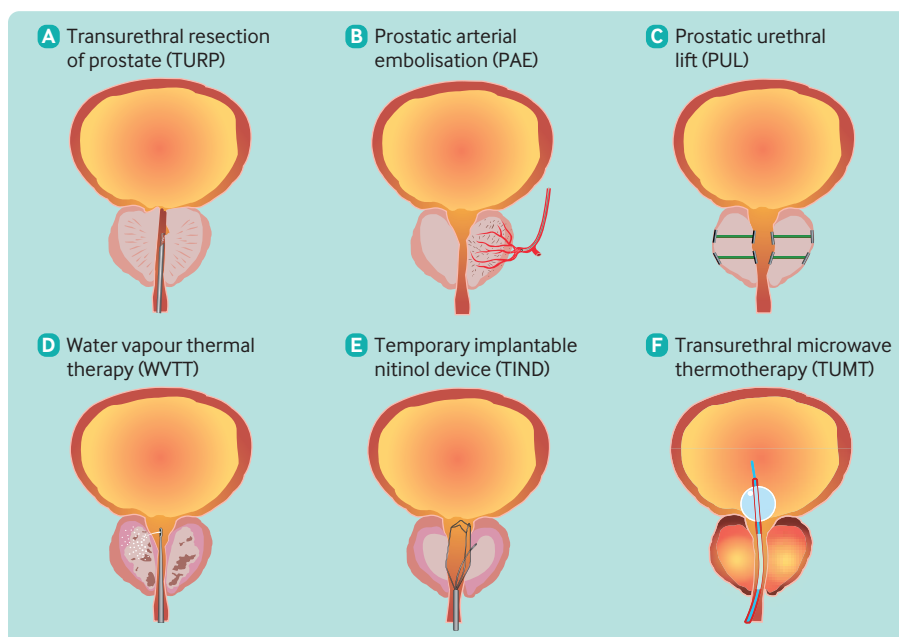


Fig 1 | Main treatment modalities used in minimally invasive procedures and traditional surgery. a) Transurethral resection of the prostate (traditional surgery)—a resectoscope is inserted through the urethra to remove prostatic tissue using a wire loop. **b)** Prostatic arterial embolisation—microspheres are released into the prostatic artery causing tissue ischaemia. **c)** Prostatic urethral lift—hooks are placed that pull the urethral wall, expanding on the inner lumen. **d)** Water vapour thermal therapy: a jet of water vapour triggers prostatic necrosis. **e)** Temporary implantable device—a cage-like device expands the lumen of the urethra, causing necrosis to the adjacent prostatic tissue. **f)** Transurethral microwave thermotherapy—a transurethral probe irradiates heat to the prostatic tissue causing necrosis

Transurethral resection of the prostate (TURP) is the mainstay of surgical treatment.² This involves shaving off inner sections of the prostate with an electric loop under direct vision of a cystoscope (fig 1a). TURP requires general (or spinal)

anaesthesia and usually catheterisation and admission to hospital at least overnight. It can result in complications such as blood loss which requires transfusion (5%), dilutional hyponatraemia (TUR syndrome) (2%), urinary tract infection, and problems with erections (up to 10%) and retrograde ejaculation (65-75%).^{2,3} Technical advances such as improved visualisation and the use of bipolar rather than monopolar electrocautery have reduced these complications.³

Minimally invasive surgical therapies have been developed that use intravenous sedation and avoid having to admit patients to hospital. Figure 1 depicts these procedures. Guidelines differ in their recommendations for these procedures⁴⁻⁶

WHAT YOU NEED TO KNOW

- New minimally invasive surgical treatments for benign prostatic enlargement that do not use spinal or general anaesthesia are available for patients experiencing lower urinary tract symptoms
- Some of these procedures may offer similar improvement in symptoms as traditional surgery, with fewer adverse events, but the evidence is of low to very low quality, short term, and insufficient
- Refer patients whose condition does not improve with conservative measures and medications to a urologist to discuss surgical options, considering benefits and possible complications, effect on sexual function, and need for retreatment

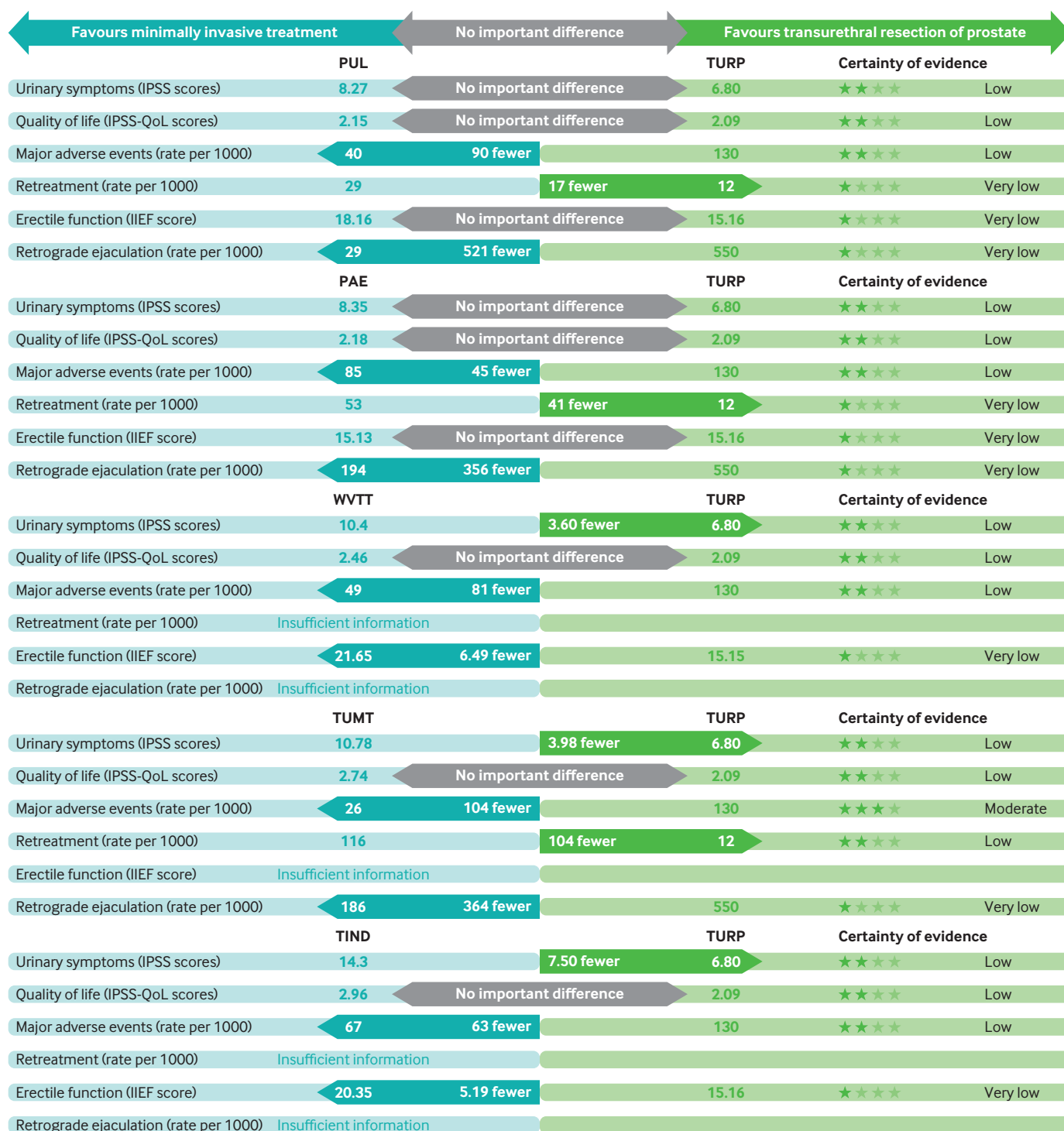


Fig 2 | Summary of the main evidence from a systematic review with network meta-analysis on minimally invasive treatments in patients with lower urinary symptoms attributable to benign prostatic enlargement compared with transurethral resection of the prostate. IPSS=International Prostate Symptom Score. IPSS-QoL: IPSS scoring on quality of life. Insufficient information: PAE=prostatic arterial embolisation; PUL=prostatic urethral lift; TIND=temporary implantable nitinol device; TUMT=transurethral microwave thermotherapy; TURP=transurethral resection of the prostate. WVTT=water vapour thermal therapy; The trials for TIND and WVTT were very short term and did not provide adequate data for comparison with other interventions. We considered a threshold of 3 points for IPSS, 1 point for IPSS-QoL, and 5 points for IIEF-5 based on the literature

(table 1, see bmj.com). Other procedures, such as aquablation, are sometimes labelled as “minimally invasive” owing to their surgical approach, but they typically require general or spinal anaesthesia and are not covered in this article.

TURP remains the most frequently used procedure, but use of minimally invasive treatments, predominantly prostatic urethral lift (PUL), has nearly doubled over the past decade according to studies in the US and Australia.^{7 8}

The array of options to choose from can be confusing for clinicians and patients. It is uncertain if minimally invasive treatments are safe and effective compared with TURP, and which of these might be the best.

What is the evidence of uncertainty?

Minimally invasive treatments result in broadly similar or less improvement in urinary symptoms and quality of life compared with TURP in men with BPE having moderate to severe symptoms as per a Cochrane network meta-analysis published in 2021 (27 randomised controlled trials, 3017 patients)^{9,10} (fig 2). Among minimally invasive procedures, PUL and prostatic artery embolisation (PAE) are likely to be more effective in reducing urinary symptoms. The evidence is limited and of low to very low certainty.¹¹

Major adverse events may be fewer (45-100 fewer events per 1000) compared with TURP (130 events per 1000). Evidence is insufficient on the effects of minimally invasive procedures on sexual outcomes including erectile and ejaculatory function. These have not been systematically assessed, for example, in a well defined group of sexually active patients to be randomised. Reporting was limited to a subset of sexually active patients, which raises concerns about selection bias and comparability. Retreatment rates with TURP tend to be lower overall (12 per 1000) compared with minimally invasive therapies. Higher retreatment rates were reported with transurethral microwave therapy (TUMT).^{9,10}

Most studies have important methodological limitations and were rated at high risk of bias. A fairly large number of trials have assessed TUMT (n=16) and PAE (n=7), but much less evidence is available on the latest additions, namely PUL (n=2), water vapour thermal therapy (WVTT) (n=1), and temporarily implanted nitinol devices (TIND) (n=1). Trials of WVTT and TIND compare these interventions with a sham procedure (a form of surgical placebo) rather than any active treatment. Most of the data are short term. Follow-up data of the trials on WVTT and TIND are limited to three months, leaving it uncertain how patients fared long term and if and when they were retreated in some form.

We also identified three trials assessing the effects of intraprostatic botulinum A toxin injections, another minimally invasive procedure, as an alternative to oral medications. This treatment seems to provide little to no symptomatic relief based on the limited evidence available.¹²⁻¹⁴

These procedures may have lower costs related to anaesthesia and inpatient care, but data are insufficient to suggest if they are more cost effective than TURP.^{15,16}

Is ongoing research likely to provide relevant evidence?

We searched ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform (ICTRP) in October 2021 for ongoing trials assessing minimally invasive treatments. We identified 14 ongoing randomised trials (table 2, see bmj.com). Ten studies compare these surgical treatments among each other; most of them (n=6) focus on PAE, and one investigates a new device (Zenflow). Four trials compare minimally invasive surgical therapies with medications, thereby exploring their use as first line treatment offered upfront instead of at least a trial of medications.

Most of these trials are at an early stage of recruitment, or their status is unclear. Based on details provided in their protocol registration, we are unsure if these studies will provide conclusive results.

EDUCATION INTO PRACTICE

- How would you communicate the benefits and harms of each minimally invasive intervention to a patient with BPE?
- How would you elicit the patient's values and preferences on the available options to ensure shared decision making?

What should we do in light of the uncertainty?

Consider conservative measures such as a reduction of fluids with diuretic effect (caffeinated and alcoholic beverages), reduced fluid intake prior to the period of greatest symptoms (night time or working hours), and medications. The onset of action of different treatments varies. We suggest monitoring treatment response and patient satisfaction over subsequent months. If these options fail to provide relief of symptoms or patients experience side effects, offer referral to a urologist to discuss surgical procedures.

TURP is the mainstay of surgical treatment. Minimally invasive therapies are usually performed by a urologist or, in the case of PAE, by an interventional radiologist. These can be office based procedures or completed in an ambulatory surgical theatre. These procedures require specialised equipment, expertise, and training.

When discussing surgery, assess the patient's perceived burden of symptoms, his understanding of the success rate of a given procedure and potential complications, as well as his willingness to accept other surgical interventions at a later date (ie, retreatment) if the first is unsuccessful.¹⁸ Discuss his concerns, for example, with regard to the preservation of sexual function after the procedure. Inform patients of benefits and harms of each procedure compared with TURP, highlighting the lack of evidence and important uncertainties surrounding claims of lower incidence of sexual adverse events with some of these procedures (see box 'What patients need to know' at bmj.com).

Competing interests: None declared.

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HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Two male patients with lower urinary tract symptoms resulting from benign prostatic enlargement (one of them considering surgery) reviewed this manuscript prior to submission. They provided input that helped to improve the presentation of data and reduce medical jargon. They also provided feedback on how the treatments, and their benefits and harms, can be better presented.

Type 2 diabetes: summary of updated NICE guidance



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Further information about the guidance, a list of members of the guideline development group, and the supporting evidence statements are in the full version on [bmj.com](https://www.bmj.com).

The National Institute for Health and Care Excellence (NICE) last updated the drug treatment section of the type 2 diabetes guideline in 2015. Since then, further evidence on drug treatment from randomised trials investigating the effects of glucose lowering drugs on cardiovascular outcomes has emerged, prompting a further update. This article summarises the most recent recommendations on drug treatment of type 2 diabetes from the NICE guideline.¹ This rapid update focuses on evidence of cardiovascular outcomes, with a full update of the section now under way. Key changes to current practice include new recommendations for the use of sodium-glucose co-transporter 2 (SGLT2) inhibitors in adults with type 2 diabetes who have chronic heart failure or established atherosclerotic cardiovascular disease or who are at high risk of developing cardiovascular disease.

SGLT2 inhibitors have both cardiovascular and renal benefits

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Committee members involved in this guideline update included lay members who contributed to the formulation of the recommendations summarised here.

WHAT YOU NEED TO KNOW

- When assessing or reviewing adults with type 2 diabetes, include an assessment of the person's cardiovascular status and cardiovascular risk
- Assess the lifetime risk of cardiovascular disease in people with type 2 diabetes aged <40 years, instead of 10 year cardiovascular risk
- Offer adults with type 2 diabetes who have chronic heart failure or atherosclerotic cardiovascular disease a sodium-glucose transport protein 2 (SGLT2) inhibitor with proven cardiovascular benefit
- Consider an SGLT2 inhibitor in adults with type 2 diabetes who do not have chronic heart failure or atherosclerotic cardiovascular disease but who have an increased cardiovascular risk
- If an SGLT2 inhibitor is indicated and no glucose lowering drugs are already being taken, it should be prescribed in combination with metformin as soon as metformin tolerability is confirmed
- Check and address modifiable risks for diabetic ketoacidosis before starting treatment with an SGLT2 inhibitor

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Committee's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are in the full version of this article on [bmj.com](https://www.bmj.com).

Choosing drug treatment

The 2015 guideline recommendation listed several factors to consider when choosing drug treatment, including the effectiveness of drug treatments in terms of metabolic response. The updated recommendation has expanded this point to include cardiovascular and renal protection based on evidence from randomised trials showing that SGLT2 inhibitors have both cardiovascular and renal benefits. The Guideline Committee has also emphasised shared decision making in relation to choosing drug treatments, considering the person's preferences, needs, and individual clinical circumstances (such as contraindications or concerns about weight).

Assessing cardiovascular risk

Although all people with type 2 diabetes are considered at increased risk of cardiovascular disease, the recently published randomised controlled trials focused on two groups at higher cardiovascular risk: people with established atherosclerotic cardiovascular disease and those at greater risk of developing cardiovascular disease (termed "higher cardiovascular risk" below). The cardiovascular risk score QRISK2 is recommended in current NICE guidance² for assessing cardiovascular risk in people with type 2 diabetes and is used widely in practice. However, QRISK2 does not reflect lifetime cardiovascular risk; therefore, additional risk factors should be considered for people aged under 40 years with type 2 diabetes, who may have increased risk for cardiovascular disease and mortality³ (see box 1 for details).



- Assess the person's cardiovascular status and risk to determine whether they have chronic heart failure or established atherosclerotic cardiovascular disease or are at high risk of developing cardiovascular disease.

First line drug treatment

In line with the 2015 guideline, the updated guideline recommends metformin as first line drug treatment for all adults with type 2 diabetes. It makes new recommendations to offer an SGLT2 inhibitor with proven cardiovascular

Diabetes medicines

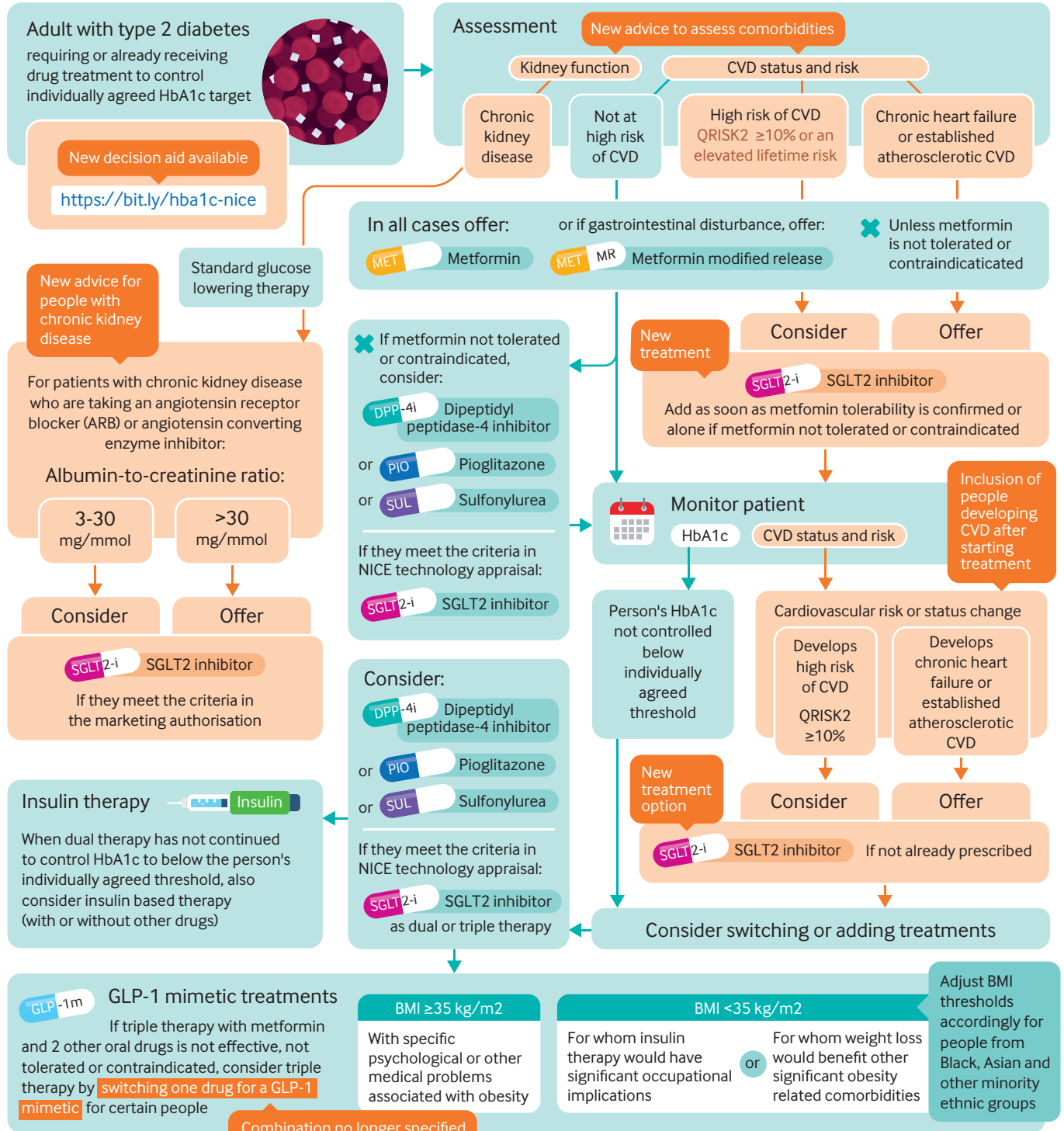
Drug treatments for adults with type 2 diabetes

Rescue therapy
For symptomatic hyperglycaemia, consider:
 Insulin or  A sulfonylurea

Review when blood glucose control has been achieved

The 2021 update to the NICE guidance on diabetes (<https://www.nice.org.uk/guidance/ng28>) adds assessment of cardiovascular disease (CVD) and kidney disease. It also includes advice on when to offer SGLT-2 inhibitors. This graphic shows a summary of the medicines now recommended, highlighting the new additions

Orange boxes show changes between updated (2021-22) and previous (2015-18) NICE guidance



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Box 1 | Definitions for atherosclerotic cardiovascular disease and high risk of developing cardiovascular disease

Atherosclerotic cardiovascular disease

Includes coronary heart disease, acute coronary syndrome, previous myocardial infarction, stable angina, previous coronary or other revascularisation, cerebrovascular disease (ischaemic stroke and transient ischaemic attack), and peripheral arterial disease

High risk of developing cardiovascular disease

Defined as adults with type 2 diabetes who have:

- QRISK2 cardiovascular risk score >10% in adults aged ≥40 years or
- Elevated lifetime risk of cardiovascular disease (defined as the presence of ≥1 cardiovascular risk factor* in someone aged <40 years)

* Cardiovascular disease risk factors: hypertension, dyslipidaemia, smoking, obesity, family history (in a first degree relative) of premature cardiovascular disease

Box 2 | Checking for risk of diabetic ketoacidosis when prescribing SGLT2 inhibitors

Diabetic ketoacidosis (DKA) is a rare but potentially serious or fatal complication of type 2 diabetes. All known risk factors for DKA should be considered before starting SGLT2 inhibitor treatment. Some risk factors for DKA are non-modifiable (such as a person having had a previous episode of DKA)

Any modifiable risk for DKA should be addressed before starting treatment with an SGLT2 inhibitor, for example:

- Alcohol intake above recommended UK threshold
- Use of illegal drugs
- Use of other medicines
- Concurrent illness, injury, or planned surgery
- Very low carbohydrate or ketogenic diet

So, for example, before starting treatment with an SGLT2 inhibitor, adults with type 2 diabetes should be advised to discuss with a healthcare professional if they are on, or plan to start, a very low carbohydrate or ketogenic diet. It may be necessary to delay or suspend treatment until the diet has been changed or completed

benefit in addition to metformin to those with chronic heart failure or established atherosclerotic cardiovascular disease, and to consider this treatment for those at high risk of developing cardiovascular disease. The Guideline Committee noted that, although all SGLT2 inhibitors were effective and cost effective, there was greater certainty associated with the cardiovascular benefits of empagliflozin, canagliflozin, and dapagliflozin at the time of publication. The guideline uses the term “SGLT2 inhibitor with proven cardiovascular benefit” to enable prescribers to choose an appropriate SGLT2 inhibitor for each person, while allowing the recommendation to remain current even if additional evidence or new SGLT2 inhibitors become available.

The SGLT2 inhibitor should be started as soon as metformin tolerability is confirmed to reduce clinical inertia and optimise cardiovascular benefit. For those at higher cardiovascular risk who cannot take metformin, the recommended first line treatment is monotherapy with an SGLT2 inhibitor. These recommendations are summarised in the infographic, which highlights changes to the guideline alongside those recommendations that remain unchanged. Risk of diabetic ketoacidosis should be considered before prescribing an SGLT2 inhibitor, as outlined in box 2.

- Based on the cardiovascular risk assessment for the person with type 2 diabetes:
 - If they have chronic heart failure or established atherosclerotic cardiovascular disease, offer an SGLT2 inhibitor with proven cardiovascular benefit in addition to metformin
 - If they are at high risk of developing cardiovascular disease, consider an SGLT2 inhibitor with proven cardiovascular benefit in addition to metformin.

Reviewing drug treatment

The 2015 guideline recommended reassessing a person's needs and circumstances at each review and to think about whether to stop any medicines that are not effective. The update has added a separate recommendation to emphasise important aspects of medicines optimisation during a review including considering adverse effects, adherence with treatment, and checking that doses and formulations are appropriate, as well as revisiting diet and lifestyle advice. In addition, the Guideline Committee agreed that it is important to think about stopping medicines that do not have useful clinical impact unless there is likely cardiovascular and renal benefit from continued treatment, and whether switching rather than adding drugs could be effective to prevent people taking multiple drugs unnecessarily.

Adding an SGLT2 inhibitor at any stage after first line treatment has been started

The update recommends that people who are at higher cardiovascular risk or whose cardiovascular risk increases over time and who are already taking glucose lowering drugs should have the same access to the cardiovascular benefit of SGLT2 inhibitor as those starting first line treatment. A shared decision about switching treatments or adding an SGLT2 inhibitor should be made at the review.

Treatment options if further interventions are needed

The existing recommendations about what further glucose lowering drugs may be added or switched to as dual or triple therapy remain unchanged from the 2015 guideline (a DPP-4 inhibitor, pioglitazone, or sulfonylurea) and apply to people at all levels of cardiovascular risk. In addition, for people at lower cardiovascular risk an SGLT2 inhibitor could be added at this stage (if they meet the access criteria set out in the existing relevant NICE technology appraisals for the SGLT2 inhibitor). Insulin remains an option in the pathway when people have reached the point of requiring triple therapy.

Competing interests: See bmj.com.

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Find the full version with references at <http://dx.doi.org/10.1136/bmj.o775>

GUIDELINES INTO PRACTICE

- How will you work with your organisation to ensure that clinical practice is in line with the new recommendations for SGLT2 inhibitors in adults with type 2 diabetes and heart failure, atherosclerotic cardiovascular disease, or higher cardiovascular risk?
- When prescribing an SGLT2 inhibitor, what measures do you take to ensure it is prescribed safely and that the person is aware of the risk of diabetic ketoacidosis?

WHAT YOUR PATIENT IS THINKING

Learning to live in a body at war with itself



0.5 HOURS

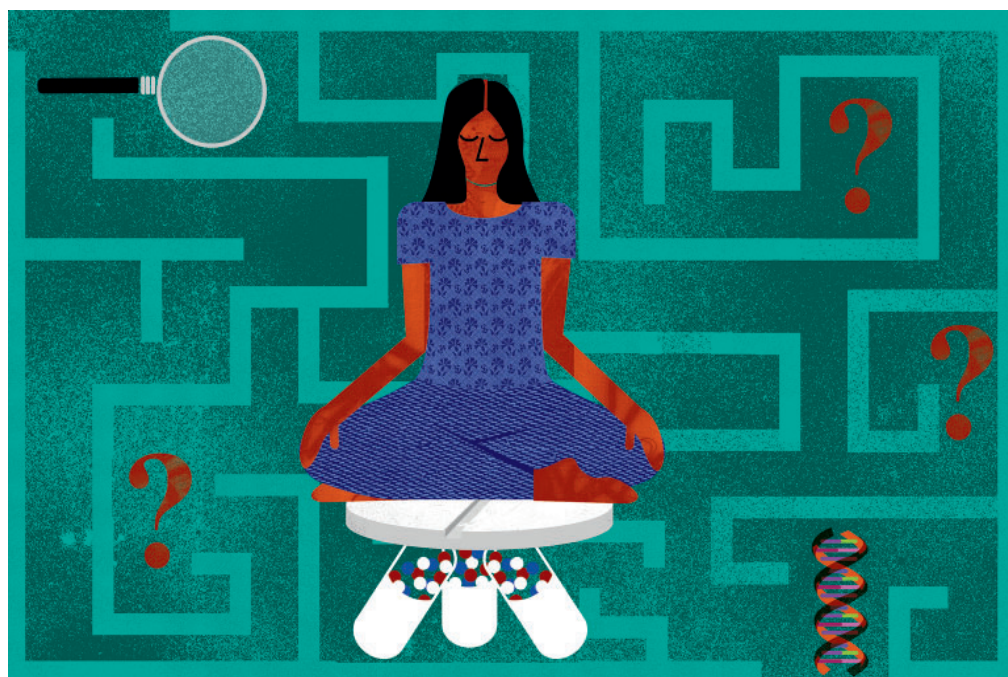
Presha Kardile explains how health professionals could have better helped her prepare for life ahead after a diagnosis of lupus

WHAT YOU NEED TO KNOW

- Coming to terms with the diagnosis of a chronic illness and learning to live with it are ongoing processes that can bring relief as well as dread
- One-to-one counselling, support groups, and alternative therapies can help patients adjust to their new normal
- Having mental health support, in which both patients and their caregivers can voice concerns and address misconceptions, is important in helping accept the changes brought on by a chronic illness diagnosis

EDUCATION INTO PRACTICE

- How could you ensure that your patients feel supported during diagnosis of a chronic illness?
- How might you incorporate an ongoing conversation about mental wellbeing into long term management of a condition?
- How can you inform and educate your patients on the types of mental health support available during a new diagnosis?



ROSE LLOYD

I started having symptoms in my early 20s that were initially dismissed as irritable bowel syndrome. My health worsened over the course of a year, with hair loss, severe fatigue, and joint pain adding to an ever increasing list of strange symptoms. As a last resort I had several antibody tests which eventually led to a diagnosis of systemic lupus erythematosus (“lupus”). This brought with it a sense of relief after years of misdiagnoses, but also filled me with dread about the future.

After starting treatment, I focused on beating the disease so I could get back to normal. It took a while for me to realise that this approach did not make sense, as there was nothing external attacking my body. By trying to beat my condition, I was fighting against my own overactive immune system. This helped me accept my diagnosis and focus on moving forward.

Learning to adjust

I experienced a profound grief while letting go of the life I had lived. I tried to find the courage to face the tsunami of changes to come. These included learning to adjust to new medications that would leave me immunocompromised, and living in social isolation with an increased dependency on my care giver. These unwelcome changes deeply affected my mental health.

Support for my mental health was, and still is, crucial in ensuring a smoother transition to my new normal. A psychologist helped me manage my fear of taking the hoard of medications that I was suddenly expected to take every day. They helped me cope with the devastating realisation, as a young person, that I would potentially need to be on medication for the rest of my life.

By trying to beat my condition, I was fighting against my own overactive immune system

Finding support

Daily mindfulness practices help me manage my pain. These practices are tailored to the needs of people who experience chronic pain, and they are practically achievable, considering that the intensity of the pain varies each day and can manifest itself in different parts of the body. I found a support group for people with chronic pain, which focused on acknowledging pain and the suffering that comes with it, rather than trying to put a positive spin on it. This helped me cope with my isolation and added to my existing support network. I also attended several online alternative therapy workshops that used art, dance, movement, and music as forms of expression. These introduced me to practices and resources that used my existing hobbies to help me cope with my new reality and support my mental wellbeing.

It took an incredible amount of research to find these groups and the courage to take the first step to seek help. It would have helped if, early on in my diagnosis, my healthcare professionals had shared the types of mental health support available. Being given a list of vetted resources would have helped me and my care givers navigate the uncertainty without the additional pressure of finding groups and individuals I could trust.

Competing interests: None declared.

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CASE REVIEW A woman with white deposits in her eye

A woman in her 80s was referred to the glaucoma department with a three week history of discomfort in the right eye. Four years earlier she underwent bilateral cataract surgery. At this presentation, the intraocular pressure (IOP) in her right eye was elevated, at 40 mm Hg (normal IOP range ≈ 5-21 mm Hg).

Visual acuity in both eyes was stable, at 20/20 without correction. When a glaucoma drug was administered to the right eye in clinic, the IOP decreased to 29 mm Hg. Slit lamp examination showed a defect in the nasal portion of the patient’s visual field (fig 1, fig 2).

- 1 What is the most likely diagnosis?
- 2 How does it typically present?
- 3 How is this managed?

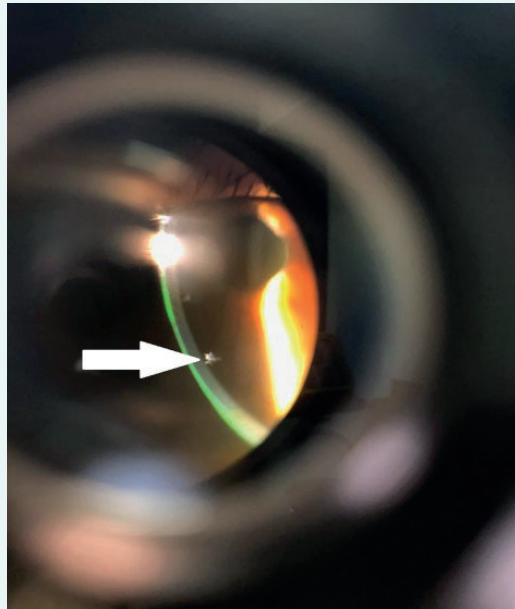


Fig 1 | Slit lamp image of right eye showing fibrillary white material on the pupillary border of the iris and in the anterior chamber (arrow)

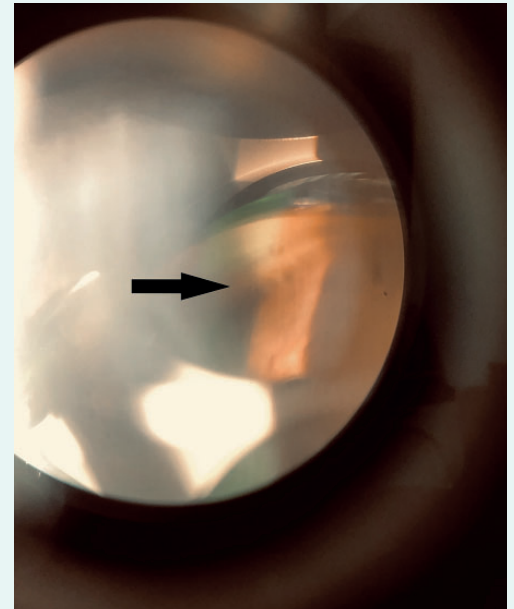


Fig 2 | Slit lamp image of right eye showing fibrillary white material in drainage system (arrow)

Submitted by Abraham Nirappel, Nandita Anand, David Solá Del Valle, and Allison Soneru
 Patient consent obtained.
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CASE REVIEW A woman with white deposits in her eye

1 What is the most likely diagnosis?

Pseudoexfoliation glaucoma—the most common subtype of secondary open angle glaucoma. This condition is characterised by accumulations of white fibrillary material in the eye’s drainage system (fig 1, fig 2), which can result in elevated IOP and damage to the optic nerve. The patient’s visual field defect is consistent with glaucomatous damage. Pseudoexfoliation glaucoma is known to be linked to a mutation in the LOX1 gene.

2 How does it typically present?

White fibrillary material accumulates on the lens or pupillary border of the iris, which can cause high IOP, vision changes (eg, halos, blurry vision), eye pain, and discomfort. High IOP can lead to

3 How is this managed?

Refer patients with suspected raised IOP to ophthalmology as early as possible. Topical glaucoma drugs are most commonly used to treat all types of glaucoma, including pseudoexfoliation glaucoma. Follow-up is usually every 1-6 weeks initially, depending on the level of IOP elevation, and every 4-6 months once the IOP is stable. Patients with a persistently elevated IOP are likely to require surgery.

PATIENT OUTCOME

The patient was advised to use a glaucoma drop (dorzolamide-timolol) twice daily in her right eye. At clinic follow-up a month later the IOP had decreased to 20 mm Hg and the discomfort had resolved. **LEARNING POINT** • Refer patients with any signs of raised IOP to ophthalmology as early as possible.



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MINERVA

Bruising with pancreatitis—but not as you know it

A woman in her early 40s was admitted to the surgical department with severe pancreatitis. Two weeks later she developed tender indurated ecchymoses to the upper thighs and was referred to the dermatology department. Computed tomography of the abdomen and pelvis showed large retroperitoneal collections indicating a diagnosis of Fox's sign. In this infrequently reported sign, severe necrotising pancreatitis leads to retroperitoneal haemorrhage tracking along the iliopsoas fascia. There is development of ecchymoses inferior to the inguinal ligament with a well demarcated upper border. This is a rare cutaneous manifestation of severe pancreatic inflammation and necrosis and should alert clinicians to severe or worsening pancreatitis, and mandates intra-abdominal imaging.

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Patient consent obtained.

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If you would like to write a Case Review or Spot Diagnosis for Endgames, please see our author guidelines at <http://bit.ly/29HCBAL>

Electrocardiogram in pericarditis

Widespread ST elevation on electrocardiogram (ECG) is generally thought to support a diagnosis of pericarditis. But since the pericardium is electrically silent, any changes on ECG probably imply concurrent myocardial involvement rather than simple pericarditis. In a series of patients seen at an Italian hospital, ECG changes were present in a quarter of those with pericarditis. Although they were associated with raised levels of troponin, they weren't linked to a greater risk of arrhythmias or a worse prognosis (*Heart* doi:10.1136/heartjnl-2021-320443).

Symptoms after radiotherapy for breast cancer

Patient and physician ratings of four symptoms (pain, pruritus, oedema, and fatigue) were compared in 10 000 people who had received radiotherapy for the treatment of breast cancer. Physicians underestimated all these symptoms—by as much as 51% in the case of oedema. Failure to identify symptoms was more common if the patient was younger or from an ethnic minority (*JAMA Oncol* doi:10.1001/jamaoncol.2022.0114).

Dementia after traumatic brain injury

Risk of dementia is increased by around 50% after major traumatic brain injury (defined as a diagnosis of traumatic intracranial haemorrhage and a hospital

stay of at least three days), according to a nationwide investigation from Finland. Adjustment for education, smoking, alcohol consumption, physical activity, and hypertension weakened this association. Minor traumatic brain injury had no effect on subsequent risk of dementia (*Neurology* doi:10.1212/WNL.000000000200290).

Creutzfeldt-Jakob disease

Human prion diseases are progressive and invariably fatal. At present, no effective therapy exists, but a monoclonal antibody against cellular prion protein offers a glimmer of hope. Given intravenously to six patients with Creutzfeldt-Jakob disease, the treatment was free of adverse effects and measurable concentrations of antibody were achieved in cerebrospinal fluid and brain tissue. It is not yet possible to say whether it alters the course of the disease (*Lancet Neurol* doi:10.1016/S1474-4422(22)00082-5).

Vegetarian diets in childhood

A longitudinal study of 9000 children aged 6 months to 8 years at recruitment and followed over three years finds that those who ate a vegetarian diet had similar body mass indices, height for age, serum ferritin, 25-hydroxyvitamin D, and serum lipid measurements to children who ate a diet that contained meat. Children eating a vegetarian diet were slightly more likely to be underweight but no association was seen with overweight or obesity (*Pediatrics* doi:10.1542/peds.2021-052598).

Risk of dementia is increased by around 50% after major traumatic brain injury

Topical nitroglycerin for arterial cannulation in children

Nitroglycerin relaxes smooth muscle and might facilitate arterial cannulation in children by increasing the internal diameter of the vessels and preventing vasospasm. A systematic review of the topical application of nitroglycerin in neonates and children found only two relevant randomised controlled trials. Although both trials reported that nitroglycerin patches increased the likelihood of successful cannulation and reduced procedure time, patient numbers were too low for these findings to be considered definitive (*Arch Dis Child* doi:10.1136/archdischild-2021-323757).

Delirium and dementia

Follow-up of 13 000 patients confirms that an episode of delirium carries a poor prognosis. All patients were over 65 and free of dementia at the time of the incident episode of delirium. Over the next five years, the cumulative incidence of dementia was estimated to be greater than 30%. Risk of dementia rose with increasing age and with worsening socioeconomic deprivation (*J Neurol Neurosurg Psychiatry* doi:10.1136/jnnp-2022-328903).

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