

education

FROM THE JOURNALS Edited highlights of Richard Lehman's blog on <http://bmj.co/Lehman>

Uselessness: a key outcome for diabetes drugs

I'm an old man and I have long since said all I want to about drugs for diabetes. I'll just commend to your attention two of the latest abstract summaries from the world's most prestigious journal:

"Among patients with type 1 diabetes who were receiving insulin, the proportion of patients who achieved a glycated haemoglobin level lower than 7.0% with no severe hypoglycaemia or diabetic ketoacidosis was larger in the group that received sotagliflozin than in the placebo group. However, the rate of diabetic ketoacidosis was higher in the sotagliflozin group." Q: In that case, why would you use sotagliflozin in type 1 diabetes?

Next: "Among patients with type 2 diabetes with or without previous cardiovascular disease, the incidence of major adverse cardiovascular events did not differ significantly between patients who received exenatide and those who received placebo." Q: Why not give them placebo then?

• *New Engl J Med* doi:10.1056/NEJMoa1708337

• *New Engl J Med* doi:10.1056/NEJMoa1612917

Reconsidering respiratory labels

One key to progress in medicine is to reconsider diagnostic labels. "Asthma" used to mean breathlessness generally, crudely divided into cardiac asthma and pulmonary asthma. Nowadays we just cling to the latter, but isn't it time to let go? I'm glad to see an article on the *Lancet* website arguing for just that.

"We suggest that the only way we can make progress in the future is to be much more clear about the meaning of the labels used



Return of reflux

"Laparoscopic anti-reflux surgery was associated with a relatively high rate of recurrent gastroesophageal reflux disease requiring treatment, diminishing some of the benefits of the operation." What's your idea of a "relatively high rate" in this situation? Relative to what? Actually, in this Swedish follow-up study lasting a mean of 5.6 years, recurrence of symptoms only occurred in 17.7% of patients, and the majority of these opted for medical treatment, therefore the overall proportion of the total cohort who underwent further surgery was less than 3%.

• *JAMA* doi:10.1001/jama.2017.10981

for asthma and to acknowledge the assumptions associated with them. Airways diseases should be deconstructed into traits that can be measured and, in some cases, modified (ie, treatable traits), and which are set in the context of social and environmental factors and extrapulmonary comorbidities."

The authors are fond of eosinophils as the current fashionable marker, but I'm not so sure. The point is that we keep flexibility in our diagnostic thinking, and don't go too far up any one mechanistic byway.

• *Lancet* doi:10.1016/S0140-6736(17)30879-6

Removing axillary nodes in early breast cancer surgery

Here's a 10 year survival study of women who underwent localised resection and radiotherapy for T1-2 breast cancer. If 1-2 metastases were found in the sentinel nodes, they were randomised either to sentinel node resection only or to complete axillary node resection. Got that? It took me a couple of goes. Survival was actually slightly better in the women who had sentinel node removal alone. They also presumably had a lower incidence of lymphoedema, though disappointingly I can't see any mention of that in the paper.

• *JAMA* doi:10.1001/jama.2017.11470

Diagnostic reasoning: an endangered skill?

If you're interested in lifelong learning and being a good diagnostician, do try to get hold of this article. If you're not interested in lifelong learning and being a good diagnostician, consider a different career. And yet we do so little as a profession to encourage a deep exchange of skills across a lifetime in medical practice. Arabella Simpkin's snapshot of how diagnostic thinking is taught to junior residents at Massachusetts General Hospital is inspiring, but only hints at what should be going on from entry into medical school up to the point where we hang up our stethoscopes.

• *Ann Intern Med* doi:10.7326/M17-0163

Corticosteroids for sore throat

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This *BMJ Rapid Recommendation* article is one of a series that provides clinicians with trustworthy recommendations for potentially practice changing evidence.



What is the role of a single dose of oral corticosteroids for those with acute sore throat? In this article an expert panel makes a weak recommendation in favour of corticosteroid use, using the GRADE framework according to the BMJ Rapid Recommendation process. These recommendations are based on a linked systematic review (see p 437) triggered by a large randomised trial published in April 2017. This trial reported that corticosteroids increased the proportion of patients with complete resolution of pain at 48 hours.

Acute sore throat is defined as pain in the throat for less than 14 days. Acute sore throat could be caused by pharyngitis, nasopharyngitis, tonsillitis, peritonsillar abscess, or retropharyngeal abscess. Some patients with sore throat also experience headache, fever, muscle stiffness, cough, and general malaise.

Acute sore throat is common, but only a minority of patients will visit their general practitioner.¹

Acute sore throat is a self limiting disease and typically resolves after 7-10 days in adults and 2-7 days in children.⁷ Most infections are of viral origin; only a few are caused by a bacterial infection. About 2% of patients initially presenting

HOW THE RECOMMENDATION WAS CREATED

Our international panel—including general practitioners, general internists, paediatricians, an otorhinolaryngologist, epidemiologists, methodologists, statisticians, and people with lived experience of sore throat—decided the scope of the recommendation and the outcomes that are most important to patients. After a systematic review on the benefits and harms of corticosteroids,¹⁶ and a systematic search for evidence about patients' values and preferences (appendix 1 on bmj.com), the panel met to formulate a recommendation. No person had financial conflicts of interest; intellectual and professional conflicts were minimised and managed (appendix 2 on bmj.com).

The panel followed the BMJ Rapid Recommendations procedures for creating a trustworthy recommendation,^{26 27} including using the GRADE approach to critically appraise the evidence and create recommendations (appendix 3 on bmj.com).²⁸

with sore throat will have a mononucleosis infection caused by an Epstein-Barr virus, which could prolong the duration of symptoms.⁸

Some patients experience unacceptable morbidity and inconvenience, and miss school or work due to recurrent sore throat.⁹ Pain is a common reason for work or school absence. Complications of sore throat are rare: about 0.2% of patients with tonsillitis will develop a peritonsillar abscess.¹⁰

The diagnosis of an acute sore throat is based on signs and symptoms.

Most guidelines recommend paracetamol or ibuprofen as the first choice treatment.¹³ The use of corticosteroids is mentioned in few, and is generally discouraged. Antibiotics are probably not helpful for pain relief in an episode of acute sore throat caused by viruses, but may help those with a bacterial infection.^{14 15}

The evidence

The linked systematic review (page 437) reports the effects of corticosteroids when added to standard care in patients with acute sore throat.¹⁶ Figure 1 (overleaf) gives an overview of the trials included.

The panel identified eight patient-important outcomes needed to inform the recommendation: complete resolution of pain, time to onset of pain relief, pain severity, need for antibiotics, days missed from school or work, recurrence of symptoms, duration of bad or non-tolerable symptoms, and adverse effects. The included studies reported on all patient-important outcomes, except for duration of bad or

WHAT YOU NEED TO KNOW

- International guidance varies about whether to use corticosteroids to treat acute sore throat, but a trial published in April 2017 suggested that corticosteroids might be effective
- We make a weak recommendation to use a single dose of oral corticosteroids in those presenting with acute sore throat after performing a systematic review of the new evidence in this rapid recommendation
- The recommendation is weak because corticosteroids did not help all patient reported outcomes and patients' preferences varied substantially
- Steroids somewhat reduced the severity and duration of pain by one day, but time off school or work was unchanged. Harm seems unlikely with one steroid dose. The treatment is inexpensive and likely to be offered in the context of a consultation that would have taken place anyway

Population



This recommendation applies to almost all patients with sore throat:

- ✓ Children 5 years and older and all adults
- ✓ Severe and not severe sore throat
- ✓ Emergency and primary care settings
- ✓ Patients with a viral or bacterial sore throat
- ✓ Patients who receive immediate or deferred antibiotics

However the recommendation is **not** applicable to patients with:

- ✗ Infectious mononucleosis
- ✗ Immunocompromising conditions
- ✗ Sore throat following surgery or intubation
- ✗ Children under 5 years old

Comparison

Short course of steroids

1-2 doses of oral Dexamethasone (or equivalent dose of alternative corticosteroid) + standard care

Adults: 10 mg
Children: 0.6 mg per kg
+ Standard care
+ Analgesics
+/- Antibiotics

or

No steroids

Standard clinical care, which typically includes analgesics, and may include antibiotics

Standard care
+ Analgesics
+/- Antibiotics

Favours steroids

Favours no steroids

Strong

Weak

Weak

Strong

We suggest a course of steroids. Discuss with patients in shared decision making.

Comparison of benefits and harms

	Favours steroids	No important difference	Favours no steroids	
Events per 1000 people				
Complete pain resolution (24h)	224	124 more	100	★★★★ Moderate
Complete pain resolution (48h)	608	183 more	425	★★★★ High
Mean time to resolution (hours)				
Complete pain resolution	33.0	11.1 fewer	44.0	★★★★ Low
Events per 1000 people				
Symptom recurrence or relapse	34	No important difference	65	★★★★ Moderate
Antibiotics prescription	468	96 fewer	564	★★★★ Low

Preferences and values

The panel believes that there is a great variability on how much reduction in pain severity or time to complete pain resolution each patient would consider important. Shared decision making may help establish what matters most to each patient.

Serious adverse events

One-dose administration of steroids is not likely to cause serious adverse events. Very low quality evidence exists for extremely rare but serious adverse effects following higher doses or longer courses of steroids (up to 30 days).

Multiple doses

Risks may outweigh benefits when cumulative doses of steroids are given for multiple episodes of sore throat. To mitigate this issue, clinicians could administer the medication in the office if possible, or prescribe only one dose per visit.

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DATA SOURCES

Use this information to gauge how similar your patients' conditions are to those of people studied in the trials

NUMBER OF TRIALS

10

NUMBER OF PATIENTS

1426

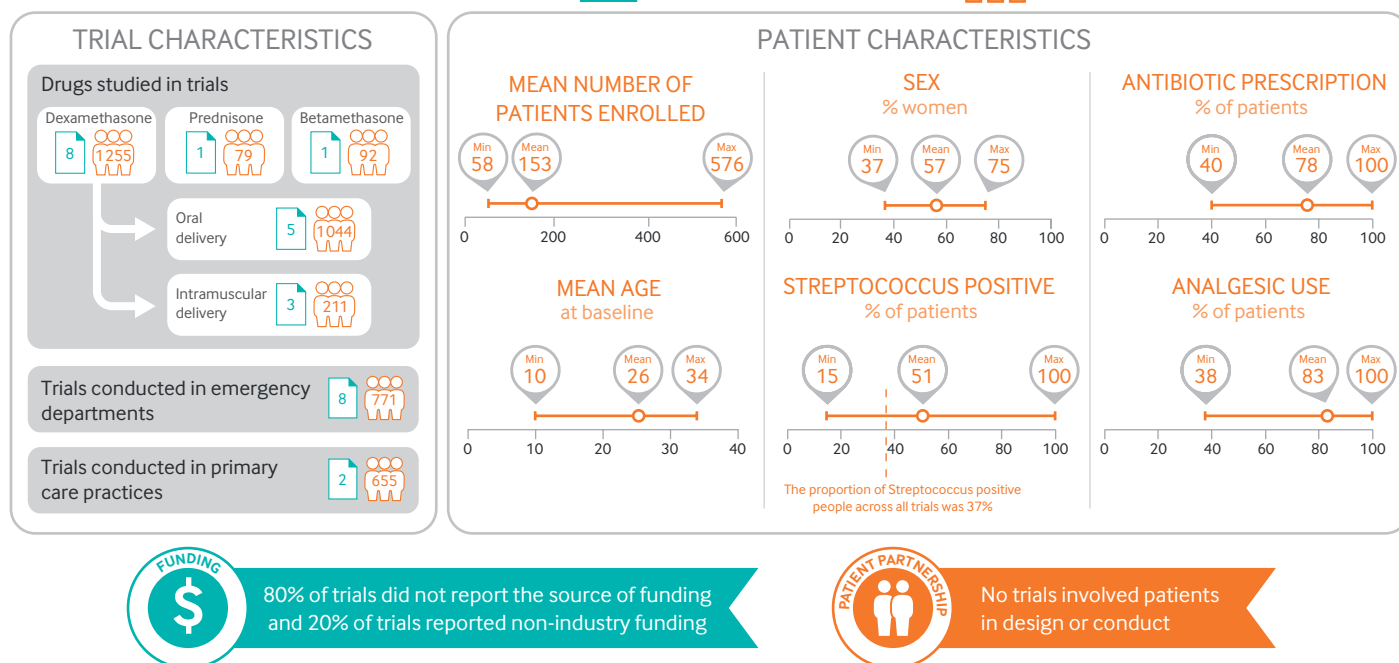


Fig 1 | Characteristics of patients and trials included in systematic review of effects of corticosteroids on acute sore throat

non-tolerable symptoms. Regarding pain, the panel appraised the likelihood of complete resolution of pain at 24 hours and 48 hours, as well as the mean time to complete resolution of pain and the mean time to onset of pain relief.

Although most of the studies (80%) were conducted in emergency departments, they accounted for 54% of all patients enrolled across studies. The remaining 46% were enrolled in the studies conducted in primary care settings, and the panel was therefore confident that the evidence was applicable to them as well. Most of the studies focused on adults only (60%). The studies that focused only on children (three studies, 2% of all the patients enrolled in the studies) did not include children younger than 5 years old, and thus the recommendation does not apply to younger ages.

Since the randomised controlled trials focused on patients who did not have recurrent episodes of sore throat, the panel was less confident of the applicability of the evidence to such patients, and the recommendation therefore does not apply to them. Similarly, the panel did not consider patients with sore throat after surgery or intubation, nor immunocompromised patients.

Understanding the recommendation

The recommendation for using corticosteroids made by the panel was weak because of the modest reduction of symptoms and the large variability in patient preferences.

The panel is confident that the recommendation applies to almost all patients with acute sore throat: children 5 years and older and adults, severe and not severe sore throat, patients who receive immediate antibiotics and those who receive deferred antibiotics, patients with a viral

or bacterial sore throat, and patients who seek care in the emergency department as well as those who attend primary care.

Absolute benefits and harms

Although the evidence indicates that the treatment works on average, it did not reduce the severity of pain dramatically and failed to improve several other patient-important outcomes.

Considering the evidence and its certainty, the panel was confident that:

- Corticosteroids increase the chance of complete resolution of pain at 24 and 48 hours, reduce the severity of pain, and shorten the time to onset of pain relief (GRADE high to moderate quality evidence)
- Corticosteroids are unlikely to reduce recurrence or relapse of symptoms or days missed from school or work (GRADE moderate quality evidence)
- A single dose of corticosteroids is unlikely to cause serious adverse events
 - The randomised trials did not report any major event attributable to single dose corticosteroids (GRADE moderate quality evidence)
 - The panel also considered evidence from observational studies that used higher doses of steroids. A cohort study of private insurance claims assessed adverse events in 327 452 adults who received an outpatient prescription of corticosteroids.¹⁸ There was a small absolute increase in the rate of sepsis, venous thromboembolism, and fracture in the first 30 days

EDUCATION IN PRACTICE

- How do you currently approach giving advice for those with acute sore throat? Do you consider offering corticosteroids?
- The recommendation for corticosteroid use is weak. What information could you share with your patient to help reach a decision together?








PRACTICAL ISSUES		
	Steroids	No steroids
 MEDICATION ROUTINE	One (or two) dose of steroids, taken as pill(s) or intramuscular injection(s) May require concomitant antibiotics, and/or over-the-counter pain relievers	
 TESTS & VISITS	May need additional visits if symptoms do not resolve or worsen	
 ADVERSE EFFECTS	Serious adverse events are unlikely with one-dose steroids. There may be risks with repeated doses across multiple episodes of sore throat, or through self medication May require concomitant antibiotics, and/or over-the-counter pain relievers	
 EMOTIONAL WELL-BEING	May cause transient sleep disturbance and excitability, although infrequently with one-dose steroids	
 PREGNANCY & NURSING	Dexamethasone crosses the placenta, and is generally avoided during pregnancy. There is, however, probably no risk of malformation	
 COSTS & ACCESS	Inexpensive, available by prescription	
 FOOD & DRINK	May increase appetite, particularly in children	

Fig 2 | Practical issues about use of corticosteroids to treat acute sore throat

- (GRADE low quality evidence). The panel agreed that such events seemed unlikely with single dose steroids
- Similarly, among paediatric populations, indirect evidence from a meta-analysis of 44 randomised trials did not report any major adverse events in patients with conditions requiring a short course of corticosteroids (such as asthma, bronchiolitis, croup, wheeze, and pharyngitis or tonsillitis)²⁰
 - There are no differences in the relative effects of corticosteroids (when compared with usual care) between primary care settings and emergency departments

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Five people with lived experience of sore throat were full panel members. These panel members identified important outcomes, and led the discussion on values and preferences. They agreed that while small reductions in pain severity and time to complete pain resolution were important to them, these values may not be shared by all patients; they expected moderate to great variability in how much importance other patients would place in small reductions in pain.

- It is unlikely that new information will change interpretation for outcomes that are high to moderate quality of evidence.

The panel was less confident about whether:

- Corticosteroids reduced antibiotic use, due to a lack of improvement or worsening of symptoms in patients not prescribed antibiotics immediately when consulting the physician (GRADE low quality evidence)
- Corticosteroids reduced the average time to complete resolution of pain (GRADE low quality evidence).

Values and preferences

The weak recommendation for corticosteroids reflects a high value on a modest reduction of symptom severity and the time that it takes to achieve such improvement, and a substantial and important increase in the chance of complete resolution of pain at 48 hours.

The panel, including the patient representatives, felt that the values and preferences are likely to vary greatly across patients, which justifies a weak recommendation. For example, achieving complete pain resolution 12 hours earlier may be of little importance for patients who feel less busy in their daily life, have higher tolerance to pain, or whose symptoms are not so severe.

The weak recommendation for corticosteroids also reflects the concerns that the panel had with acceptability. Specifically, how acceptable is it to treat a condition that is usually not severe and is self limiting with a drug that many patients, practitioners, and other stakeholders know is almost always used for more severe diseases.

A systematic search identified two studies with relevant information on patients' values and preferences (see appendix 1 on bmj.com). Neither of the studies provided additional data that had not been raised by the panel members: the panel had identified appropriate patient-important outcomes and considered the variability in patient values and preferences regarding sore throat management.

Practical issues, costs, and resources

Figure 2 outlines the key practical issues for patients and clinicians discussing adjunct steroids for sore throat, which are also accessible along with the evidence as decision aids to support shared decision making in MAGICapp. Steroids are typically given as 10 mg dexamethasone (or adapted to weight for children: 0.6 mg/kg, up to a maximum dose of 10 mg), typically taken as pill or intramuscular injection.

The risks may outweigh the benefits when larger cumulative doses of corticosteroids are given to patients who experience multiple episodes of sore throat.

The treatment is inexpensive and likely to be offered in the context of a consultation that would have taken place anyway. Nevertheless, it remains uncertain whether it may increase the proportion of patients visiting a doctor to get a prescription of corticosteroids.

Competing interests: See bmj.com.

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● RESEARCH, p 437

Is gabapentin effective for women with unexplained chronic pelvic pain?

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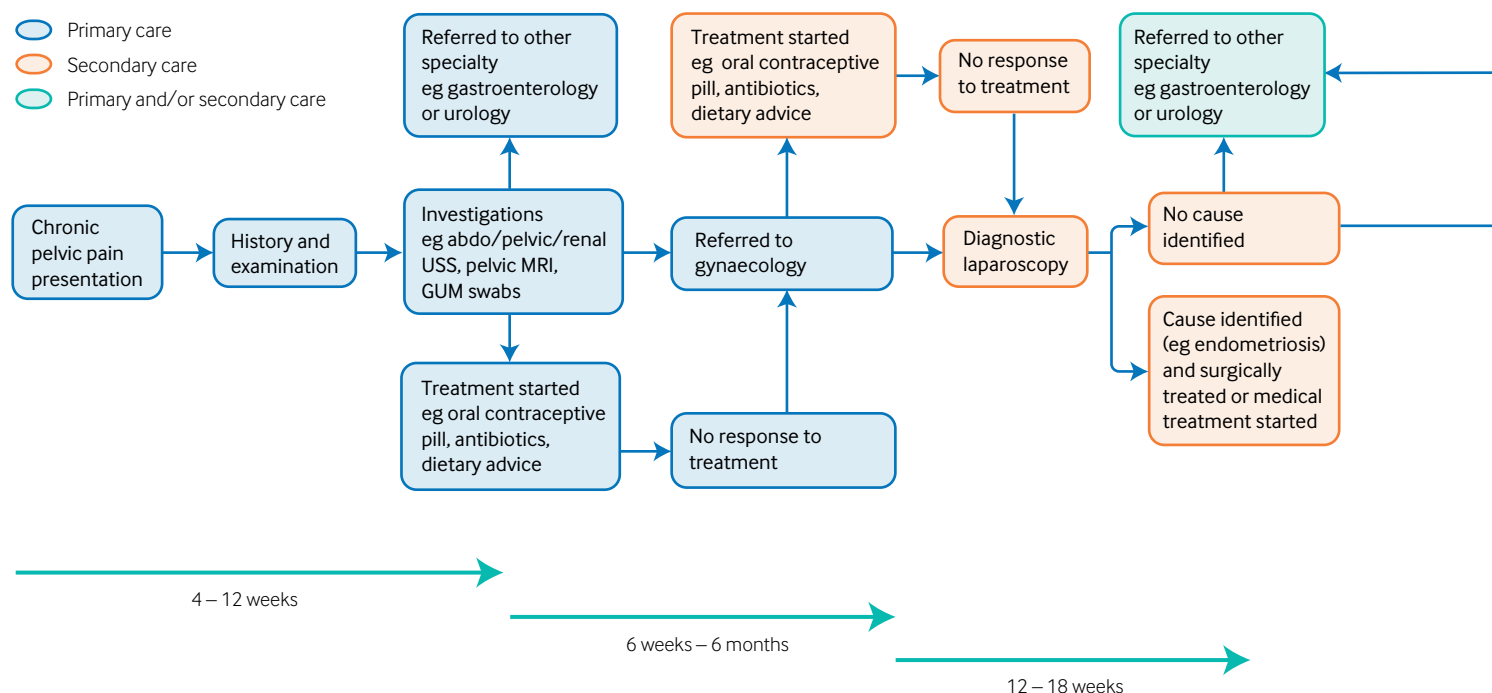
WHAT YOU NEED TO KNOW

- Up to half of all women with chronic pelvic pain in secondary care have no obvious underlying pathology
- For pain relief, a combination of drugs, physiotherapy, and cognitive behavioural therapy can be tried
- There is no strong direct evidence to support the use of gabapentin for women with chronic pelvic pain, and uncertainty remains regarding its safety, and clinical and cost effectiveness

Chronic pelvic pain in women is a common presentation in primary care. Pain persists or recurs over at least six months¹ and can be distressing, affecting physical function, quality of life, and productivity.² Nearly 38 per 1000 women are affected annually in the UK. Global estimates range from 2.1% to 24% of the female population.^{3,4}

Endometriosis, adenomyosis, adhesions, pelvic inflammatory disease, irritable bowel syndrome, bladder pain syndrome, nerve entrapment, and musculoskeletal pain are among the common causes.^{4,5} These are often identified by screening for pelvic infection (eg, *Chlamydia trachomatis*), pelvic imaging (eg, ultrasound, magnetic resonance imaging), and diagnostic laparoscopy.¹ Some 40%–55% of women with chronic pelvic pain in

secondary care appear to have no obvious underlying pathology based on clinical history, examination, and investigations.^{4,6} Management of this group of women is challenging and there are few established gynaecological treatments. The Royal College of Obstetricians and Gynaecologists recommends a combination of pharmacological interventions, physiotherapy, and cognitive behavioural therapy.¹ Often women try several methods sequentially or in combination.^{4–8} The figure presents a common



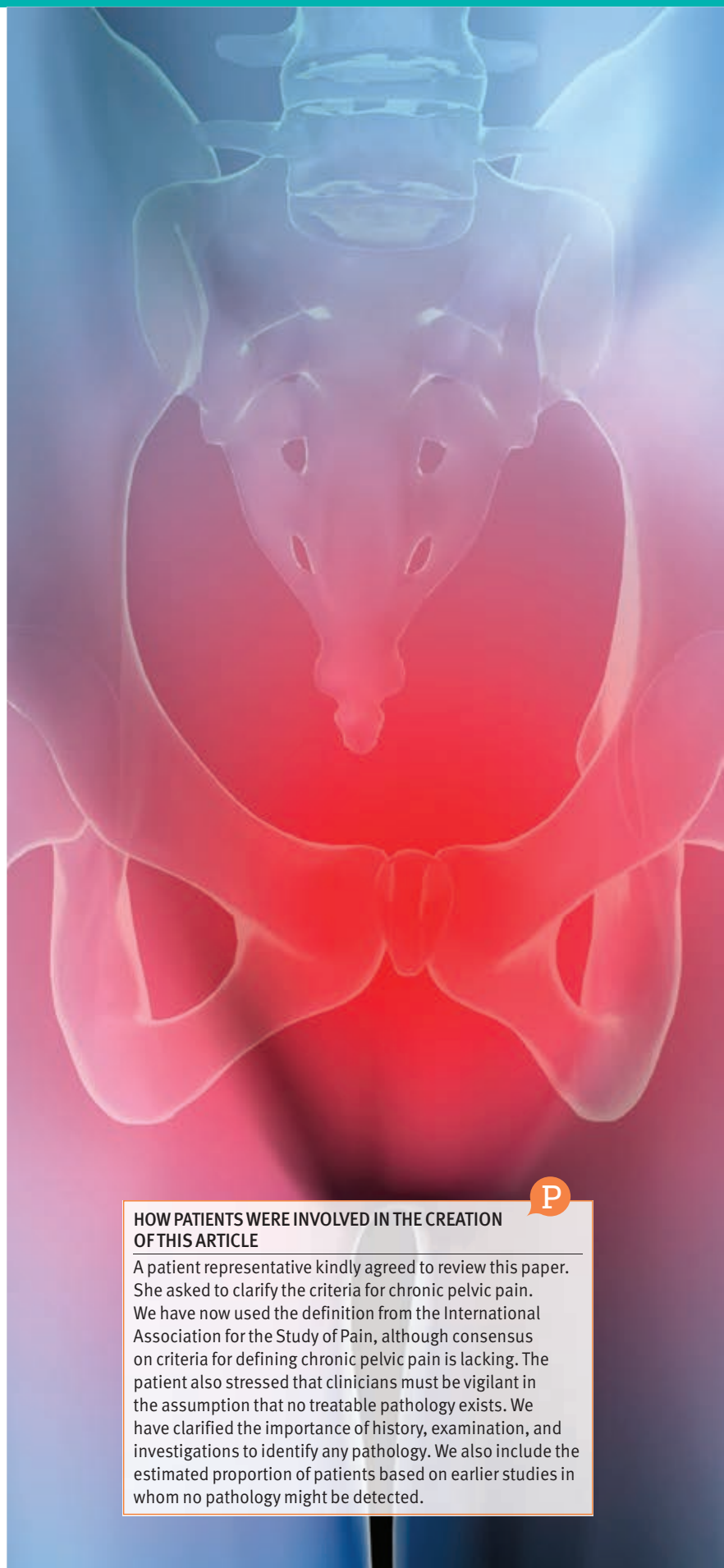
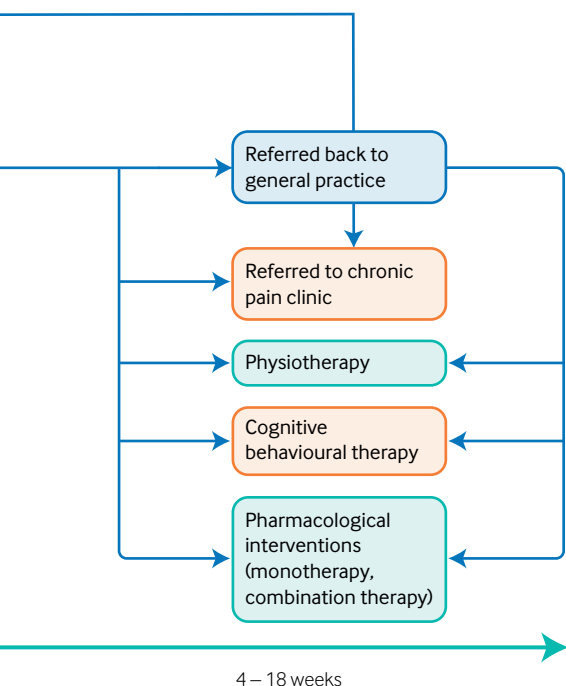
Flow diagram showing the possible “treatment journey” (and timelines) for a woman who presents to primary care with chronic pelvic pain (adapted from guidance from the Royal College of Obstetricians and Gynaecologists)

SEARCH STRATEGY

We searched PubMed, Embase, the Centre for Reviews and Dissemination database, and the Cochrane Library from their inception to 20 December 2016 for published studies on effectiveness of gabapentin for treatment of women with chronic pelvic pain.

diagnostic and treatment approach that women with chronic pelvic pain might be offered.

One option is the prescription of neuromodulators, including gabapentin, which can help address some of the potential pain generating/maintaining mechanisms that could be responsible. Neuromodulators primarily affect modulation of pain by the central nervous system, in contrast with non-steroidal anti-inflammatory drugs, for example, which act on peripheral mediators of inflammation. Neuroimaging studies have shown gabapentinoids to affect brain function in models of central sensitisation and in patients with chronic pain.^{9 10} Like most neuromodulators, gabapentin and pregabalin are only licensed for peripheral neuropathic pain¹¹ and their use in chronic pelvic pain is off licence. There is uncertainty around the effectiveness and safety of gabapentin in women with chronic pelvic pain.



HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

A patient representative kindly agreed to review this paper. She asked to clarify the criteria for chronic pelvic pain. We have now used the definition from the International Association for the Study of Pain, although consensus on criteria for defining chronic pelvic pain is lacking. The patient also stressed that clinicians must be vigilant in the assumption that no treatable pathology exists. We have clarified the importance of history, examination, and investigations to identify any pathology. We also include the estimated proportion of patients based on earlier studies in whom no pathology might be detected.

What is the evidence of uncertainty?

There are very sparse data from trials of the use of gabapentin in women with chronic pelvic pain. We found one randomised controlled trial comparing gabapentin and amitriptyline for chronic pelvic pain in women with a range of pelvic pathologies,¹² and our own recently published pilot trial (GaPP1) comparing gabapentin with placebo in women with chronic pelvic pain and no identifiable pelvic pathology.¹³ In both studies, gabapentin was shown to improve pain scores compared with the control arm; however, neither study has sufficient power to guide practice.

Data on harms from trials in women with chronic pelvic pain are lacking, although side effects such as drowsiness have been reported.

Is ongoing research likely to provide relevant evidence?

We searched the World Health Organization trials portal, ClinicalTrials.gov, and the ISRCTN registry, for ongoing randomised controlled trials in women with chronic pelvic pain comparing gabapentin with no treatment or a control treatment or placebo to alleviate pain. Our search identified our own trial, GaPP2.

Although this study will likely provide evidence on whether gabapentin (monotherapy) is beneficial in the management of women with unexplained chronic pelvic pain, further research is required to determine the effectiveness of gabapentin in women with chronic pelvic pain with endometriosis,¹⁵ or other pain conditions, and how it compares with other treatments.

Competing interests: We have read and understood the BMJ policy on declaration of interests and declare the following interests: AWH reports collaborating with Roche on a project to identify a biomarker for endometriosis. KV reports advising Grunenthal on a set of documents regarding conditions associated with chronic pelvic pain and receiving a grant from Bayer Healthcare to investigate pain mechanisms in endometriosis. KV also received payment from Bayer Pharmaceuticals on chronic pelvic pain. RC consulted Allergan on the mechanism of botox to treat chronic pelvic pain.

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CORRECTION

An image accompanying an article on penicillin allergy that appeared in the 5 August print edition of *The BMJ* p246 showed dropper containers with the label 'penicillum.' The picture should have shown instead containers with the label 'penicillin.'

COMMENTARY

What should we do in light of the uncertainty?

Treatment of women with chronic pelvic pain is directed towards achievement of higher function with some pain rather than a cure.⁴ At the initial consultation, explore and document the severity of pain, and its effect on lifestyle, daily activities, including sleep disturbance, and participation.⁵ Reassure the patient that no treatable pathology has been identified on investigation. Explain that this is not unusual and some approaches might be tried to relieve the pain.

Guidelines from the Royal College of Obstetricians and Gynaecologists recommend initial pain management with non-steroidal anti-inflammatory drugs with or without paracetamol.^{6,7} Compound analgesics such as co-dydramol can also be considered.⁷ Encourage the woman to monitor and record pain, its impact on daily activities, and treatment side effects. Ask her to report if the pain worsens or she develops other symptoms, which might warrant repeat investigations for a suspected pathology.

If pain relief is insufficient, consider referral to a pain management team or a specialist pelvic pain clinic. These can deliver a multidisciplinary care model, including components of physical treatment, cognitive behavioural therapy, complementary therapies, transcutaneous nerve stimulation, and other medical disciplines, such as anaesthesia and gynaecology.⁴⁻⁸

Gabapentin is currently recommended only in a specialist setting for women with suspected neuropathic pain. Explain the uncertainty in evidence of benefit and potential side effects of gabapentin within the context of chronic pelvic pain. Warn about common side effects, including dizziness, fatigue, drowsiness, and peripheral oedema.^{9,10}



Treatment is directed towards achievement of higher function with some pain rather than a cure

These can limit compliance but are often tolerated.⁸ An increased risk of suicidal thoughts and behaviour has been observed with use of gabapentin. Ask patients or carers to report any changes in moods or behaviour. Gabapentin is not recommended in pregnant women. Caution is advised in patients with renal impairment as it is exclusively excreted by the kidneys.¹⁰

Arrange a follow-up

visit to assess dosage titration, tolerability, adverse effects, and continued need for treatment.⁵ If the overall benefit is limited by side effects, the lowest effective dose should be found by downtitration. If side effects are not tolerated or if there is no benefit, gabapentin should be withdrawn.

A treatment approach embedded within a multidisciplinary care model, which takes into account the individual needs and preferences of women with chronic pelvic pain, can reduce the disruption to the woman's life and avoid an endless succession of referrals, investigations, and operations.⁷

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Competing interests: None declared.

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EDUCATION INTO PRACTICE

- Recollect a woman you have seen at your practice with unexplained chronic pelvic pain.
- How did you manage her pain?
- What would you do differently in explaining about her pain and the treatment options?
- Do you routinely document the severity of pain and impact on functioning and quality of life?



CASE REVIEW An older woman with spontaneous bruising

An 85 year old woman attended the emergency department with large bruises on her right forearm and left leg, which had appeared four days earlier. She had not sustained any injuries to account for the bruising. There was no bleeding from any other site. Her only medical history was hypertension. Her medications included amlodipine. On examination there were extensive subcutaneous haematomas on the right forearm extending up to the upper arm and on the left leg extending up to the thigh. Initial investigations showed low haemoglobin of 95 g/L with a normal platelet count ($369 \times 10^9/L$). Coagulation assays showed markedly elevated activated partial thromboplastin time of 74 seconds (reference range 25 to 35 seconds).

Prothrombin time was normal, however, and fibrinogen assay was within normal limits (3.8 g/L, reference range 1.5 to 4.0 g/L). Mixing studies with 1 part of patient's plasma and 1 part of pooled normal plasma showed no correction of elevated activated partial thromboplastin time. Factor assays revealed very low level of factor VIII (<1 IU/dL, reference range 50-150 IU/dL), and factors IX, XI, and XII were within normal ranges.

- 1 What is the most likely diagnosis?
- 2 How is this condition diagnosed?
- 3 What is the management for this condition?

Submitted by Muhajir Mohamed and Ajay Prakash

Patient consent obtained.

[Cite this as: BMJ 2017;358:j3863](#)

CASE REVIEW

Sudden onset headache in a 50 year old woman

A 50 year old woman presented to the emergency department several hours after the sudden onset of a severe headache with associated neck stiffness, photophobia, and vomiting. She reported having a dental abscess, and was taking norethisterone regularly for persistent vaginal bleeding. She had

a 50 pack year smoking history. She was afebrile, alert (Glasgow coma scale 15), and had no focal neurological signs. Blood tests were unremarkable, in particular her white blood cell and neutrophil counts were within the normal range. A non-contrast computed tomography (CT) scan of the head was obtained in the emergency

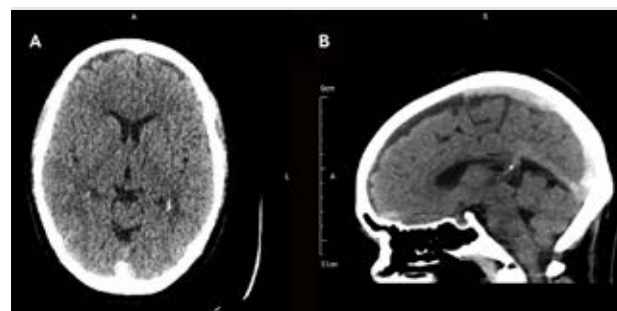
department (below).

- 1 What is the diagnosis based on the history and CT scan?
- 2 What are the risk factors for this condition?
- 3 What is the treatment for this condition?

Submitted by Divyansh Gulati, Michael William Shea, and James Ray

Patient consent obtained.

[Cite this as: BMJ 2017;358:j4016](#)



answers

CASE REVIEW

An older woman with spontaneous bruising

1 Acquired haemophilia A.

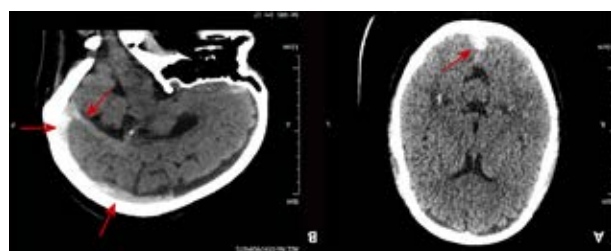
2 A prolonged activated partial thromboplastin time value that is

not corrected by mixing with normal plasma (1:1) provides a clue about the presence of factor VIII inhibitor. Low factor VIII values associated with the identification of factor VIII inhibitor confirms the diagnosis. Treatment of acquired haemophilia A consists of controlling the bleeding, inhibitor eradication, and supportive measures.

1 Cerebral venous thrombosis, seen by the "dense triangle sign," a hyperdensity at the posterior part of the superior sagittal sinus (fig 2a), and the "cord sign" (fig 2b), a homogeneous hyperdensity that fills a sinus. Diagnosis is usually made from magnetic resonance (MR) or CT venography.

Prothrombin G20210A mutation, antiphospholipid syndrome), oral contraceptive pill, pregnancy/puerperium, cancer, infectious/inflammatory conditions,

3 Anti-coagulation with heparin (unfractionated or low molecular weight heparin) in the short term, followed by warfarin.



CASE REVIEW Sudden onset headache in a 50 year old woman



0.5 HOURS

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



An unusual palmar eruption

A 21 year old woman presented with episodic palmar itching, stinging, and skin peeling after brief exposure to water. Palmar water immersion in the dermatology clinic resulted in multiple whitish papules and exaggerated wrinkling after seven minutes, consistent with aquagenic palmar wrinkling (right). Aquagenic palmar wrinkling is a clinical diagnosis demonstrated by reproducible signs on water immersion. Its pathogenesis has been attributed to sweat electrolyte dysfunction. It is common in cystic fibrosis (especially homozygous

DF508) but also occurs in cystic fibrosis carriers; referral to specialist genetics services for testing is therefore essential. Aquagenic palmar wrinkling can be induced by medication or, as in our patient, can be idiopathic. Treatments include topical antiperspirants and iontophoresis.

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Patient consent obtained.

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Statins in the elderly

In the UK in the early 2000s, the prevalence of statin use in people over 80 was around 10%. By 2015, it had risen to almost 50%, largely because people who had started taking statins in their 60s and 70s had got older (*Age Ageing* doi:10.1093/ageing/afx100). Cardiovascular risk increases with age, of course, so this level of use might be appropriate. However, in the absence of clinical trial evidence showing that cholesterol lowering treatment reduces mortality in elderly people, no one can be sure that it's a sensible idea.



Syncope and postural hypotension

A longitudinal study from Sweden finds that middle aged people admitted to hospital after an episode of loss of consciousness, and discharged with a diagnosis of syncope or postural hypotension, are subsequently at increased risk of cardiovascular diseases (*Heart* doi:10.1136/heartjnl-2017-311857). A diagnosis of unexplained syncope was associated with coronary events, cardiovascular death, and aortic stenosis. Orthostatic hypotension, by contrast, was more strongly associated with stroke and heart failure.

Mortality among children with type 1 diabetes

Paediatricians in Wales have been tracking new cases of type 1 diabetes in children under 15 since 1995 (*Arch Dis Child* doi:10.1136/archdischild-2016-312581). What they've found is rather disappointing: mortality rates are about three times higher than in the general population and, despite developments in clinical care, showed no signs of decreasing over time. Ketoacidosis remains the most common cause of death before age 30. Chronic complications of diabetes were not a cause of mortality in this age group.

Using pen and paper to diagnose the cause of tremor

Tremor is a presenting feature of several neurological diseases, and an article in *Practical Neurology* explains how simple tests with pen and paper can be used to tell them apart (*Pract Neurol* doi:10.1136/practneurol-2017-001719). Watching a patient's upper limb as they write a short sentence can reveal bradykinesia and dystonic posturing. Asking them to draw a spiral and a straight line records the frequency, amplitude, and consistency of the tremor.

Survival after heart transplant

A systematic review of observational studies of recipients of heart transplants identifies several variables associated with higher mortality at one year (*Heart* doi:10.1136/heartjnl-2017-311435). They include increasing age, congenital aetiology of heart disease, age of the donor heart, and donation from a female to a male recipient. These findings raise questions about optimum selection of donors and recipients. Perhaps the current

practice of matching older donors to older recipients isn't in the best interests of older candidates for transplants?

Bone marrow biopsies

The likelihood of getting a reliable diagnosis from a bone marrow biopsy depends on the length of the biopsy core available for examination. As is so often the case with routine investigations, there's not much research into the best way to get an adequate specimen. The traditional approach is to bore the needle straight down from the posterior superior iliac spine, in a direction perpendicular to the back. A trial in the *Journal of Clinical Pathology* finds that substantially longer biopsies can be obtained by aiming the needle in the direction of the anterior superior iliac spine (*Clin Pathol* doi:10.1136/jclinpath-2017-204686).

Alcohol, health education, and the public in 1970s Britain

Articles in *Social History of Medicine* tend to be long and thoughtful, and they rarely come to anything as vulgar as a conclusion. Although it's impossible to distil its message into a short paragraph, Minerva recommends an essay on attempts at alcohol health education in Britain in the 1970s (*Soc Hist Med* doi:10.1093/shm/hkw094). It's critical of a clumsy advertising campaign that targeted problem drinkers, and the failure to engage with the social and environmental factors that encouraged drinking.

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