education

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

Has my patient been exposed to novichok?

Here's the irresistible *NEJM* guide to the symptoms and signs of chemical weapons poisoning. It is behind a paywall, which should be lifted for doctors in the Salisbury area and Syria. The rest of us will only be reading out of idle curiosity, hopefully.

N Engl J Med doi:10.1056/NEJMra1705224

Tenecteplase *v* alteplase before stroke thrombectomy

Thrombolysis is widely recommended in stroke guidelines, though it remains contentious. John Mandrola's recent piece about stroke thrombolysis in Medscape is a masterly exercise in clear analysis. In many patients, however, the simple procedure has now been superseded by thrombolysis plus clot retrieval: this applies to strokes caused by occlusion of the internal carotid artery, basilar artery, first segment of the middle cerebral artery, or second segment of the middle cerebral artery. In a publicly funded trial from Australia and New Zealand, two tissue plasminogen activators were compared as precursor therapy before thrombectomy. One was alteplase, which requires slow intravenous infusion over an hour, and the other was tenecteplase, a genetically modified variant of alteplase, with greater fibrin specificity and a longer half-life, which permits bolus administration. As well as being simpler to administer, tenecteplase was associated with a higher incidence of reperfusion and better functional outcome than alteplase among patients with ischaemic stroke treated within 4.5 hours.

https://www.medscape.com

N Engl J Med doi:10.1056/NEJMoa1716405

Type 2 diabetes drugs and longevity

Comparing drugs for type 2 diabetes is tiresome work, let me tell you. When I tried it some years ago, it taught me a lot about inadequate surrogate end points, skewed comparators, atypical populations, and publication bias. Things have improved a bit since, and time has allowed data to accumulate about important outcomes for the new drug classes. I really admire the work that has gone into a network meta-analysis of all-cause mortality in trials of three classes of glucose lowering drugs: sodium-glucose cotransporter 2 inhibitors, glucagon-like peptide 1 agonists, and dipeptidyl peptidase 4 (DDP-4) inhibitors. The DDP-4 inhibitors seem to produce the worst outcomes, though there is much devil in the detail.

JAMA doi:10.1001/jama.2018.3024

Getting patients with peripheral artery disease walking

This trial aimed to improve walking distance in people with peripheral arterial disease. The exercise intervention group (n=99) received four weekly medical centre visits during the first month, followed by eight months of a wearable activity monitor and telephone coaching. The usual care group (n=101) received no onsite sessions, active exercise, or coaching intervention. The mean change from baseline to nine month follow-up in the six minute walk distance was 5.5 m in one group versus 14.4 m in the other. Have I changed the order round, as Archie Cochrane famously once did in front of an audience of cardiologists? No, I haven't: usual care was a lot more effective than regular badgering. There is a lesson in here somewhere.

JAMA doi:10.1001/jama.2018.3275

Precisely how abnormal are you?

You're not normal: get used to it. The long predicted day when enough tests can be done to ensure universal abnormality has been reached, even without invoking genomics. But John Ioannidis and two colleagues are not as negative about this as you might expect. In a short article they propose a major rethink of diagnostics in the era of big data. This is the opposite of the woolly hype we usually get on the subject, and required reading for anyone interested in the future of medicine.

JAMA doi:10.1001/jama.2018.2009

Sigmoid screening and Norwegian women

"Offering sigmoidoscopy screening in Norway reduced colorectal cancer incidence and mortality in men but had little or no effect in women." I'd like to offer a prize for the person who comes up with the most plausible explanation for this. For the time being, it just serves as another example of the fact that in medicine, few things are predictable. If you want to know what is going to happen, you have to try it out, and then compare it with what happened elsewhere. I'd be intrigued to see if this crazy phenomenon can be confirmed from other sigmoidoscopy screening databases.

Ann Intern Med doi:10.7326/M17-1441

Dressings for venous leg ulcers

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CPD READING
0.5 HOURS

This is one of a series of occasional articles on therapeutics for common or serious conditions, covering new drugs and old drugs with important new indications or concerns. The series advisers are Robin Ferner, honorary professor of clinical pharmacology, University of Birmingham and Birmingham City Hospital, and Patricia McGettigan, clinical senior lecturer in clinical pharmacology, Queen Mary's University, London. To suggest a topic, please email us at practice@bmj.com.

A 65 year old man presents with a two month history of a wound in the gaiter area of his left leg. He has a history of a left leg deep vein thrombosis after a long flight but is otherwise fit and well. He had been self-managing with dressings bought over the counter, but the wound has gradually increased in size. The wound is not painful but is weeping serous fluid, causing irritation of the surrounding skin. Examination shows a 4×3×0.1 cm wound above the left medial malleolus. There is haemosiderin deposition, venous flare, and moderate oedema in the limb. The ankle-brachial pressure index (ABPI) is normal at 1.0. He is diagnosed with a venous leg ulcer, which is managed with dressings and compression bandaging.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

We asked five patients in our outpatient clinic if they had tips for other patients who needed dressings and incorporated these into the "Tips for patients" box where possible. We also asked a patient with longstanding venous leg ulcers to review the article, and he did not suggest any changes.

WHAT YOU NEED TO KNOW

- The cornerstone of treatment for venous leg ulcers is compression therapy, but dressings can aid with symptom control and optimise the local wound environment, promoting healing
- There is no evidence to support the superiority of one dressing type over another when applied under appropriate multilayer compression bandaging
- When selecting a dressing, look at the wound bed, edge and surrounding skin and decide on the goal of the dressing: for example, if there are signs of localised infection consider an antimicrobial dressing, if there is heavy exudate consider an absorbent dressing

EDUCATION INTO PRACTICE

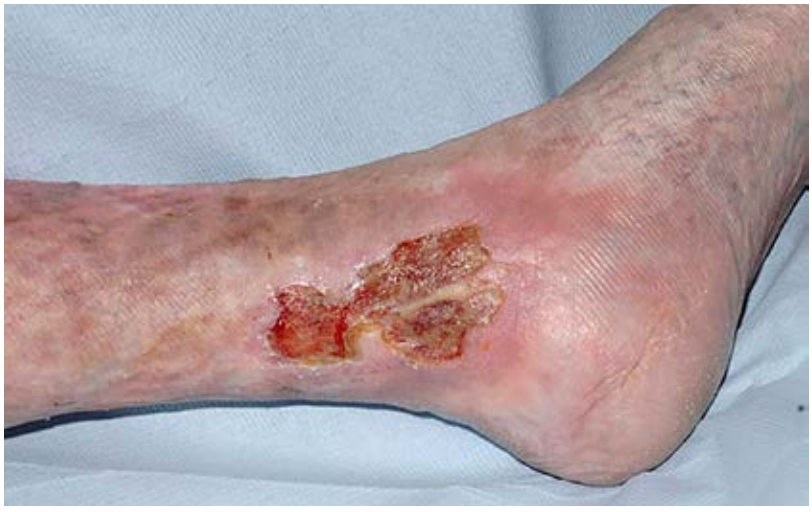
- How do you assess a wound to choose the appropriate dressing? Does this article offer ideas on how to change your practice?
- What did you understand about dressing choice before reading this article? Is there anything you might do differently now?
- How do you involve patients when considering what types of dressings to use? Can you think of ways to offer patients a greater role?

The cornerstone of venous leg ulcer treatment is compression therapy, which increases venous return and reduces venous hypertension.[1] However, dressings are important because they can provide symptom control and optimise the local wound environment to promote healing. This article provides an overview of the dressings that may be used in venous leg ulcers and guidance on selection.

About 1% of the adult population in westernised countries are affected by venous ulcers on the leg or foot.[2] The prevalence increases with age to 1.7% in people over 65.[3] Between 26% and 69% of those affected will have recurrent ulcers.[4] Ulcers have a marked impact on quality of life, and can cause chronic pain, impaired mobility, social isolation, and restricted activities.[5] The annual cost of managing venous leg ulcers has been estimated to be between £500m and £900m in the UK, with most of the spend in the community.[6]

What types of dressing are available and how do they work?

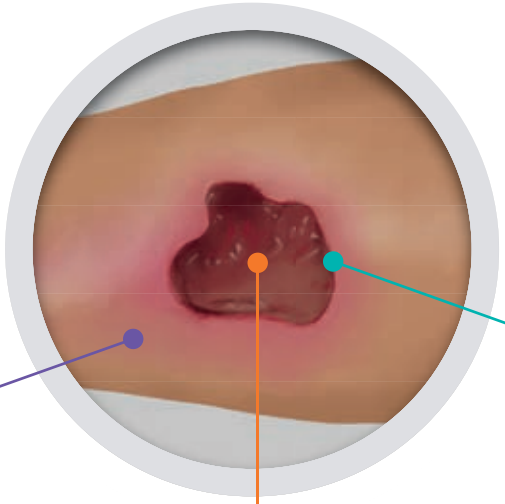
The infographic and table summarise the different types of dressings that may be used. These are usually classified by dressing material, and each class has different properties and mechanisms of action. Availability may depend on the local formulary.



thebmj Visual summary

Wound assessment and dressing choice for venous ulcers

Dressings should be selected based on the properties of the wound and surrounding skin. Consider the wound location, size, depth, exudate level, and presence of infections. Dressings can help symptom control and promote healing. However, compression therapy remains the cornerstone of treatment.



Debridement methods

- Surgical or sharp
- Autolytic with hydrocolloid, hydrogels or honey dressings
- Larvae

Surrounding skin

Dry or flaky

Rehydrate, using exfoliants and emollients. Consider a moisture-donating or moisture-retaining dressing

Macerated or oedematous

Choose a dressing capable of managing exudate and change frequently

Callus or hyperkeratotic skin

Debridement is required to remove non-viable or unhealthy tissue

Evidence of cellulitis

Treat with systemic antibiotics

Active eczema

Topical steroids and emollients as required

Consider whether the dressing could be causing irritation or allergy

Wound bed

Dry or flaky

Rehydrate, using exfoliants and emollients. Consider a moisture-donating or moisture-retaining dressing

Macerated or oedematous

Choose a dressing capable of managing exudate and change frequently

Non-viable, necrotic tissue or slough

Debridement is required to remove non-viable or unhealthy tissue

Local infection or biofilm suspected

Treat with antimicrobial dressing or topical antiseptic preparation

Abnormal inflammation

Consider debridement or protease modulating matrix dressings

Wound edge

Dry or flaky

Rehydrate, using exfoliants and emollients. Consider a moisture-donating or moisture-retaining dressing

Macerated or oedematous

Choose a dressing capable of managing exudate and change frequently

Excessive necrotic skin or slough

Debridement is required to remove non-viable or unhealthy tissue

Raised or rolled edge

Biopsy recommended

Epidermal margin not advancing

Reassess underlying diagnosis

Choice of dressing

Exudate level — Dry · Low · Moderate · High

Flat wounds

- Low-adherent dressings (Dry)
- Semipermeable films (Dry)
- Hydrocolloid sheets (Dry – Low–Moderate)
- Foam dressings (Dry – Low–High)

Shallow wounds

- Hydrogel sheets (Dry – Low)
- Soft polymer dressings (Dry – Low–Moderate)
- Hydrocolloid fibrous (Low–Moderate – Low–High)
- Alginates (Dry – Low–High)
- Low-adherent dressings (Dry)
- Semipermeable films (Dry)
- Hydrocolloid sheets (Dry – Low–Moderate)
- Foam dressings (Dry – Low–High)

Deep wounds

- Hydrogel sheets (Dry – Low)
- Soft polymer dressings (Dry – Low–Moderate)
- Hydrocolloid fibrous (Low–Moderate – Low–High)
- Alginates (Dry – Low–High)

Chronic wound with prolonged inflammatory phase

Protease modulating matrix dressings

Locally infected wounds

Many kinds of dressing are available impermeated with antimicrobial agents, such as:

- Iodine
- Chlorhexidine
- Silver
- Honey
- Dialkylcarbamoyl chloride
- Polyhexamethylene biguanide (PHMB)

How well do dressings work?

We searched the *Cochrane Database of Systematic Reviews* for relevant publications (see bmj.com for a summary). A further Cochrane review of dressings and topical agents for treating venous leg ulcers is in progress.[15]

There is no evidence to support the superiority of one dressing type over another when applied under appropriate multilayer compression bandaging. Overall, high quality evidence of effectiveness from well conducted, large, randomised controlled trials is lacking.[16] This may in part be due to dressings being classed as medical devices, which require less evidence for approval than medicines.[17] Problems with previously conducted trials on dressings have included small sample sizes, small ulcer sizes, and uncomplicated patients (that is, no comorbidities, no concurrent wound infection).[16] Furthermore, using "healed wounds" as the primary outcome measure may be an unrealistic target in the context of a time-limited study for the range of venous leg ulcers seen in clinical practice. The effects of dressings on patients' quality of life and symptom control have not been adequately studied.

How safe are dressings?

Cautions for specific dressing types are listed the table opposite. Patients with venous leg ulcers are at risk of developing allergic contact dermatitis to allergens found in dressings,[18] such as preservatives, emulsifiers, latex, and lanolin. Refer patients with persistent dermatitis or eczema of the skin surrounding the wound (which does not respond to topical corticosteroid treatment) to dermatology for patch testing.[19]

How cost effective are dressings?

Assessing the cost effectiveness of a dressing is complex. The unit cost is important, but there are also many other variable costs such as ancillary supplies required, adjunctive treatments such as analgesia, and caregiver time. Data from a regional audit of wound care practice in the UK[20] estimated that only 17-22% of the costs could be attributed to the dressings. The greatest cost was hospital admissions as a result of wound complications, with nursing time for dressing changes the next most important factor. The authors concluded that selecting the most effective treatment, to heal the wound quickly and prevent complications, had the greatest potential to save money. A health economics study that used linked routine data for 78 090 patients with chronic wounds to estimate the total cost of chronic wounds in Wales also found that the cost of dressings was far outweighed by the cost of nursing time, GP visits, and inpatient episodes.[21] Therefore a dressing's unit cost must be balanced against other factors such as how often it requires changing and how it affects symptoms.

RELEVANT GUIDELINES

- NICE. Clinical Knowledge Summaries. Leg ulcer - venous. 2015. https://cks.nice.org.uk/leg-ulcer-venous.[25]
- *Scottish Intercollegiate Guidelines Network*
  - Management of chronic venous leg ulcers. 2010. www.sign.ac.uk/sign-120-management-of-chronic-venous-leg-ulcers.html.[19]
- *Wounds International Consensus Documents*
  - Harding K, Expert Working Group. Simplifying venous leg ulcer management: consensus recommendations. *Wounds International* 2015. www.woundsinternational.com/consensus-documents/view/simplifying-venous-leg-ulcer-management.[28]
  - Swanson T, Angel D, Sussman G, et al. IWII: Wound infection in clinical practice. *Wounds International* 2016. www.woundsinternational.com/consensus-documents/view/iwii-wound-infection-in-clinical-practice.[29]
- *European Wound Management Association*
  - Franks PJ, Barker J, Collier M, et al. Management of patients with venous leg ulcer: challenges and current best practice. *J Wound Care* 2016;25 (Suppl 6):S1-67.[16]

How do I choose a dressing?

Select a dressing based on the properties of the wound (location, size, depth, exudate level, presence of infection) and of the surrounding skin. Patient factors such as allergies and concurrent medical conditions also need to be considered. Localised assessment and management of a venous leg ulcer is described in the infographic (adapted from Dowsett et al[22] and incorporating the authors' own practice and advice from NICE[17-25] and Scottish Intercollegiate Guidelines Network (SIGN)[19] guidelines).

Given the lack of evidence on superiority of any one dressing type, the SIGN[19] and NICE[17] guidelines recommend low adherent dressings. The ideal condition for wound healing (in the absence of gangrene) is a moist environment, and wounds that are too dry or too wet have impaired epithelialisation.[17-27] Dressings can be used to promote the moist wound environment (infographic). The effects of different dressings on the wound are described in the table opposite.

The frequency of dressing changes should be tailored so that the dressing is neither oversaturated nor dry and adherent to the wound when it is removed. Some wounds require daily dressing changes, whereas others may only need new dressings once or twice a week. It is our practice to use dressings continually until the wound has healed, and occasionally they may be used after healing to protect fragile scar tissue.

It is not possible to say how long an ulcer takes to heal. Arrange regular reassessment to ensure that the treatment is appropriate. At each review, check the wound bed, surrounding skin, and patient factors and adjust the dressing type as necessary. Serial measurements of a wound surface area should be used as an objective measure of healing in clinical practice.[19] There are different methods for this, and using one consistent method is most important.

When the dressing is changed, wash the wound gently with warm, clean tap water or saline and then dry it to remove loose slough and necrotic tissue.[17] Offer oral analgesia as required. There is no evidence to support the routine use of antibiotics, and they should be reserved for infected wounds.[11]

Most venous leg ulcers can be managed successfully in the community with appropriate expertise, but referral to secondary care may be needed if, for example, the diagnosis is unclear or the ulcer is not responding to treatment.

Competing interests: See bmj.com.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.k1604

Available dressings for the management of venous leg ulcers[7 8]

Dressing type	Mechanism	Applications and cautions	Effects on wound environment
Hydrocolloid sheets	The hydrocolloid layer absorbs water and forms a gel in the presence of exudate.	Shallow cavities or flat wounds	Will maintain a moist wound environment in lightly to moderately exuding wounds, and promote autolytic debridement in dry, sloughy, or necrotic wounds. Also promote granulation
Hydrocolloid fibrous	Hydrocolloid dressings made from modified carmellose fibres, enabling greater water absorption	Flat wounds, cavities, and sinuses, safe under compression	Highly absorbent, so can control moderate to high exudate
Hydrogel sheets	Made from a matrix of insoluble polymers with a high water content, enabling them to donate fluid to the wound	Dry to minimally exudative sloughy wounds. Not recommended in infected or gangrenous wounds	Promote autolytic debridement of dry slough
Alginates	Non-woven or fibrous dressings made from calcium alginate or calcium sodium alginate, which is derived from brown seaweed. They form a soft gel in contact with wound exudate	Cavities and sinuses. Secondary dressing required. Can be used if haemostasis required (such as after biopsy or debridement)	Highly absorbent, so suitable for all highly exudative wounds. Promote autolytic debridement. Some types are haemostatic
Low adherent dressings	Dressings are either tulle or textiles, usually made of cotton or viscose fibres, and impregnated with white or yellow soft paraffin to prevent adherence	Flat or shallow wounds with minimal to low exudate. Usually used as an interface dressing under an absorbent dressing	Low adherence minimises trauma on dressing changes
Soft polymer dressings	Made of a soft polymer, often silicone. The silicone makes them gently adherent. Some have an absorbent polyurethane foam pad backing	Can be used on delicate skin. The plain sheet dressings can be used in combination with an absorbent secondary dressing.	Generally suitable for light to moderately exudative wounds; foam-backed polymer dressings have more intrinsic absorbency
Protease modulating matrix dressings	Dressings reduce the activity of proteinases in the wound exudate by absorbing exudate, removing enzyme cofactors, or releasing inhibitors	Chronic wounds with evidence of prolonged inflammatory phase	Different forms with varying levels of absorbency available
Semipermeable films	Flexible sterile sheets of polyurethane coated with a hypoallergenic adhesive. They are impermeable to liquids and bacteria, but variably permeable to air and water vapour	Flat or shallow wounds	No intrinsic absorbency and enclose the local wound environment, so only suitable for wounds with minimal to low exudate
Foam dressings	Hydrophilic polyurethane foam dressings with or without adhesive	Flat or shallow wounds	Some foams are absorbent, so can control exudate. Provide a degree of cushioning
Antimicrobial dressings for locally infected wounds:			
Polyhexamethylene biguanide (PHMB)	PHMB is an antimicrobial agent which works by disrupting cell membrane integrity	Available in impregnated dressings but also as a gel and cleanser form	
Silver	Silver ions have an antimicrobial effect in the presence of exudate	Numerous silver dressings with different properties. Silver sulfadiazine is contraindicated in pregnancy and in patients with significant renal or hepatic impairment, sensitivity to sulfonamides, or G6PD deficiency	All silver dressings have an antimicrobial effect. Other effects on the wound environment are determined by the type of dressing
Iodine	Cadexomer-iodine and povidone-iodine release free iodine when exposed to wound exudate, which has a wide spectrum of antimicrobial activity	Iodoflex and iodosorb are contraindicated in patients receiving lithium or with thyroid disorders, and during pregnancy and breast feeding. Inadine is contraindicated in pregnancy, breast feeding, and renal failure, and caution should be used in patients with thyroid disease	Little or no absorbency, so for use on wounds with low exudate
Dialkylcarbamoyl chloride	Physical hydrophobic reaction between the dressing coating and any bacteria or fungi on the wound surface	Does not use any antimicrobial or antiseptic so often tolerated by patients with sensitivities to other antimicrobials	Comes in different forms with varying levels of absorbency
Honey	Medical grade honey has antimicrobial and anti-inflammatory properties. It is osmotic so promotes autolytic debridement	Dry, sloughy wounds. Contraindicated in patients allergic to bee stings or honey. Blood sugar levels should be monitored in diabetic patients applying honey dressings	Osmotic properties increase moisture levels in the wound environment, so suitable for dry wounds or those with low-moderate levels of exudate
Chlorhexidine	Gauze-based dressing impregnated with soft paraffin and chlorhexidine antiseptic	Do not use on more than 10% of body surface area. Some patients are allergic to chlorhexidine	Low adherent dressing. Little or no absorbency, so for use on wounds with low exudate or with an absorbent secondary dressing

UNCERTAINTIES

Do men with lower urinary tract symptoms have an increased risk of advanced prostate cancer?

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CPD READING
0.5 HOURS

A 72 year old man complains of increased frequency of urination, particularly at night. He also describes a sense of incomplete voiding and a poor stream. He is concerned about whether he might have prostate cancer, and wants to be reassured that this is not the case.

More than half of all men over 50 report problems with urinating.[1]

Grouped as lower urinary tract symptoms (LUTS), these signify problems with the storage and/or voiding of urine, and are often caused by benign prostatic enlargement.[1] LUTS are habitually considered a possible symptom of prostate cancer,[2] and qualitative studies show that men with LUTS are worried about having prostate cancer and consult a doctor to seek reassurance.[3-5] Prostate cancer is one of the most diagnosed cancers in men worldwide. During the previous two to three decades, prostate cancer incidence has greatly increased in high income countries; however, at the same time the mortality of prostate cancer has stayed stable or decreased slightly. Advanced prostate cancer is potentially fatal. In contrast, indolent prostate cancer is per definition harmless and does not cause morbidity or mortality. Moreover, indolent prostate cancer is the most frequent form of prostate cancer, eg, autopsy studies estimate the mean prevalence of indolent prostate cancer to be 59% in men >79 years.[6] Collated with the high prevalence of LUTS in older men, a connection between LUTS and indolent prostate cancer is nearly unavoidable. Most general practice clinical guidelines (table 1) recommend doctors to consider the prostate specific antigen (PSA) test in men with LUTS for prostate cancer detection.[7-11] However, it is uncertain if men with LUTS have increased risk of advanced or potentially fatal prostate cancer and therefore, if they should be offered the PSA test.

The controversy of PSA screening is much discussed, and now a consensus on not screening asymptomatic men is emerging (appendix 1, see bmj.com).[12 13] Data from the five Nordic countries suggest that, despite a rise in the diagnosis of prostate cancer, particularly since the introduction of PSA testing, there has been little change in death from the disease (fig 1).[14] Patterns such as these suggest overdiagnosis. Given the lack of benefits in early prostate cancer detection,[12 15] PSA testing in men with LUTS places them at risk of being diagnosed with indolent prostate cancer and being treated for a condition that would not result in either morbidity or mortality.

SEARCH STRATEGY AND STUDY SELECTION

We searched PubMed in September 2016 with the free-text and MESH-terms: "lower urinary tract symptoms" OR "LUTS" AND "prostatic neoplasm" OR "prostate cancer" OR "prostatic cancer" OR "cancer of the prostate." We identified four[16-19] observational studies that examine whether LUTS is predictive of advanced and potentially fatal prostate cancer. We included studies conducted in a general practice population or screening population, with transparent identification of people with and without LUTS and a specified PSA level as indication for biopsy. We excluded studies conducted in a selected population, eg, referred patients, studies where the differentiation of people with and without LUTS was not clear, and studies that had other indications for biopsy, eg, abnormal digital rectal examination.

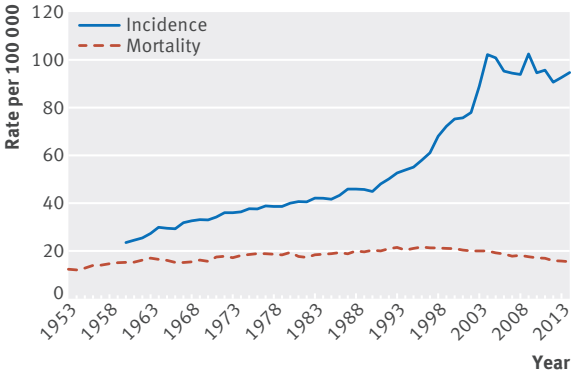
HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

A man who had a PSA test as part of medical examination kindly agreed to review this article. He shared his concern regarding the high rate of indolent prostate cancer in older men, but was also concerned about overdiagnosis and said a diagnostic label could cause fear in patients. He suggested that doctors consider the personal context of the patient in the diagnostic process and stressed the need for patient information tools, especially information on potential harms. We have summarised the current evidence and ways in which doctors might provide this crucial information to patients.

WHAT YOU NEED TO KNOW

- It is uncertain if lower urinary tract symptoms are associated with an increased risk of advanced prostate cancer
- Do not routinely offer prostate specific antigen (PSA) testing in men with only lower urinary tract symptoms and no risk factors for prostate cancer
- Explain the limitations and harms of a PSA test to the patient in terms of downstream procedures, and the possibility of being diagnosed with prostate cancer that might not cause him symptoms or shorten his life

Table 1 | Guidelines for PSA testing in men with LUTS	
Country/guideline	**Recommendations regarding PSA testing**
UK/National Institute for Health and Care Excellence[7]	Men with LUTS should be offered information, advice, and time to decide if they wish to have PSA testing if: – their symptoms are suggestive of bladder outlet obstruction secondary to benign prostate enlargement, or – the prostate feels abnormal on digital rectal examination, or – they are concerned about prostate cancer
USA/American Urological Association[8]	At initial evaluation for benign prostatic enlargement/LUTS, PSA is recommended in selected patients with at least a 10 year life expectancy for whom knowledge of the presence of prostate cancer would change management, or patients for whom the PSA measurement might change the management of voiding symptoms
Denmark/Danish College of General Practitioners[9]	All men with urinary problems should be tested for PSA
Canada/The College of Family Physicians of Canada[10]	For a man presenting with lower urinary tract symptoms, perform a digital rectal examination, and discuss the benefits and harms of PSA testing
New Zealand/Ministry of Health[11]	In men aged 50-70 (or over 40 if they have a family history of prostate cancer) who have prostate related concerns, discuss the benefits and harms of PSA testing and obtain an informed consent before testing



Prostate cancer incidence and mortality in Nordic countries 1953-2013[14]

What is the evidence of uncertainty?

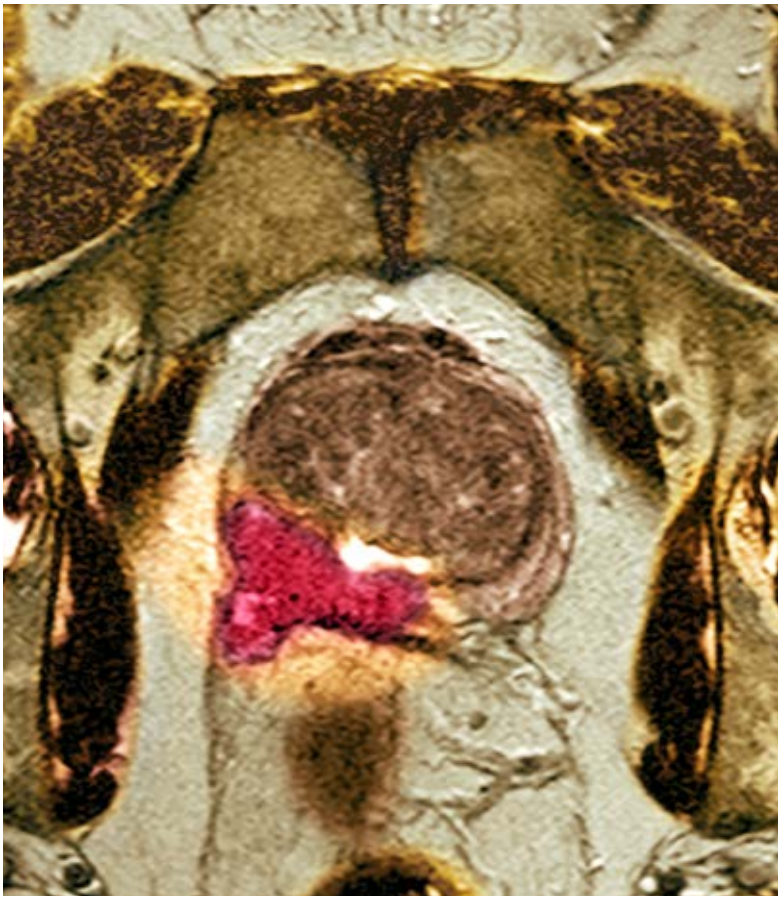
The current evidence is limited to observational studies primarily conducted in PSA screening populations and suggests that men with self-reported LUTS are not at increased risk of having advanced or potentially fatal prostate cancer compared with men without LUTS (see table 2 and appendix 1 on bmj.com).

These studies are large and population based but they vary in design. Three[16-18] of four studies were conducted in PSA screening populations. The Norwegian[19] and Swedish[17] studies used longitudinal follow-up, and the other two studies[16 18] used a cross-sectional design, although they were based on PSA screened cohorts. The tools used to record symptoms are different and there is a potential for bias. Three[16-19] of the four studies used a validated self-reported questionnaire to measure LUTS. In two studies,[18 19] asymptomatic men were asked to complete a questionnaire on lower urinary tract symptoms, and in the other two studies[16 17] men with raised PSA levels were asked about symptoms. The outcomes varied in terms of severity of prostate cancer and the time period. Only one study[19] recorded prostate cancer incidence and mortality nine years later.

Three[16-18] of four studies offered biopsy when PSA was ≥3 ng/ml.[9] Hence, the true association between LUTS and prostate cancer now or in the future remains unknown, and the discovered association can only be applied for men with a raised PSA level. An American population based cohort study has shown that increased diagnostic intensity among men who present with LUTS is possible for the association between LUTS and prostate cancer observed in some studies.[20]

Is ongoing research likely to provide relevant evidence?

We searched clinical trial registers (clinicaltrials.gov, controlled-trials.com, who.int/trialsearch) in September 2017 for observational studies of associations between LUTS and current or future prostate cancer diagnosis. We did not identify any relevant studies examining whether LUTS are predictive of advanced or potentially fatal prostate cancer or studies offering PSA testing in men with LUTS for cancer detection.



SIMON FRASER/SPL

Colour magnetic resonance image showing cancer (red) of the prostate gland (brown, centre)

WHAT PATIENTS NEED TO KNOW

- There is no evidence that problems with urinating suggest advanced prostate cancer
- Your doctor will perform a digital rectal examination and might discuss prostate specific antigen (PSA) testing if you have a family history of prostate cancer in addition to lower urinary tract symptoms (LUTS)
- Be aware of the risk of overdiagnosis and overtreatment of an indolent prostate cancer if you have a PSA test with LUTS as a single symptom with no other risk factors

What should we do in light of the uncertainty?

There is no consensus regarding PSA testing in men with LUTS, and most guidelines recommend shared decision making (table 1).[7-11] In addition to cancer detection, urologists request the PSA test in men with LUTS to assess the prostate volume and predict prostate growth and clinical progression.[21] Some guidelines support the use of clinical nomograms in selected patients to determine the risk of high grade prostate cancer.[10] Otherwise, current guidelines recommend a PSA test if the patient's LUTS are suggestive of bladder outlet obstruction,[7] if the man is over 40 with unexplained symptoms such as lower back pain, bone pain, or weight loss suggestive of metastatic prostate cancer,[10] or there is a family history of prostate cancer.[11] We have not identified evidence that these recommendations improve the prognosis in men with LUTS.

There is insufficient evidence to recommend PSA testing in men with only LUTS and no other known risk factors for prostate cancer.

Explore why your patient is concerned about prostate cancer, and assist him in making an informed choice regarding PSA testing. Ask for age, family history of prostate cancer, and ethnicity to assess risk for prostate cancer.

Offer to perform a physical examination including a digital rectal examination that can help detect prostate enlargement or cancer. Offer a urine dipstick test to detect blood, glucose, protein, leucocytes, and nitrites. You might ask the patient to complete a urinary frequency volume chart to assess the severity and perhaps help pinpoint the type of the problem and furthermore aiding the decision making regarding medical treatment.[7]

Discuss with your patient the lack of direct evidence that LUTS symptoms in isolation suggest prostate cancer. Explain the possible limitations and harms of a PSA test such as downstream procedures, and the possibility of being overdiagnosed with prostate cancer and related treatment. When communicating the uncertainty about testing, using terms like "abnormal indolent cells in the prostate gland" rather than "localised prostate cancer" might reassure the patient and reduce patient preferences for aggressive management responses to a low risk condition.[22]

Competing interests: None declared.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.k1202

EDUCATION INTO PRACTICE

- How do you discuss lower urinary tract symptoms with a patient who is concerned about the risk for prostate cancer?
- To whom do you consider offering a PSA test for prostate cancer? Does this article offer you ideas for change?
- How do you explain the benefits and harms of testing for prostate cancer? Are there ways you could alter this?
- If you were to make a leaflet at your practice for men with LUTS, what information about prostate cancer testing would you include?

RECOMMENDATIONS FOR FURTHER RESEARCH

- A prognostic intervention study to evaluate if men with LUTS are overdiagnosed with prostate cancer if they have a PSA test, and how the PSA test affects their prognosis. Men with LUTS in general practice would be randomly selected to receive PSA testing or not. Both groups would be offered usual care including a digital rectal examination, urinary frequency volume chart, urine flow rate examination, and pharmacological or surgical treatment for their LUTS in discussion with their healthcare provider. Primary outcomes include prostate cancer: localised or disseminated, prostate cancer mortality and all-cause mortality. Secondary outcomes include quality of life, morbidity, and treatment.
- A large prognostic observational cohort study including men in general practice with baseline assessment of LUTS and other factors potentially predictive of prostate cancer. The cohort should be prospectively followed and prostate cancer related outcomes measured. This study might reveal predictors of advanced prostate cancer and potentially help develop a clinical nomogram to aid decision making in men with LUTS.
- Research for new biomarkers capable of distinguishing between low grade and high grade prostate cancer

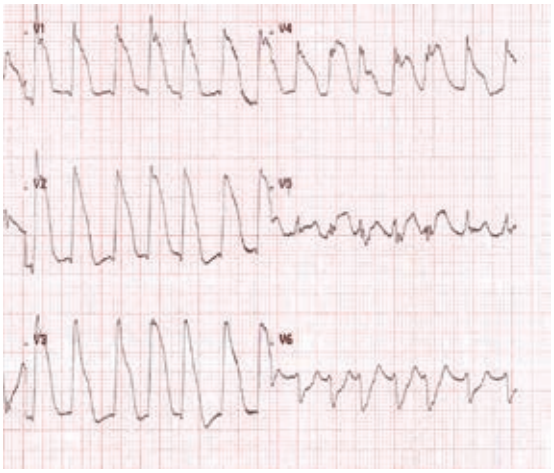

Fig 1

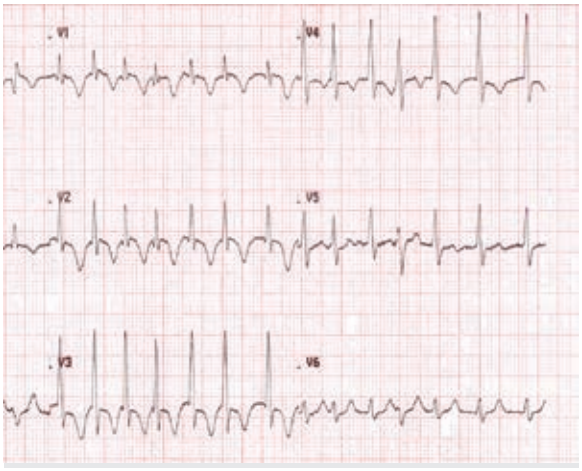

Fig 2

CASE REVIEW **A man with chest pain and a broad QRS complex tachycardia**

A 50 year old man with "heavy" chest pain was referred urgently from a local district hospital to the cardiothoracic centre because a broad QRS complex tachycardia had been noticed on electrocardiogram (ECG). The chest pain was intermittent and had started two hours before presentation. He was a cigarette smoker and his medical history included asthma and a myocardial infarction eight years earlier, for which no invasive treatment was carried out. In the past year he had experienced frequent episodes of chest pain in the early morning, but did not report exertional angina. On examination, the patient was tachycardic with a heart rate of 160 beats/min but with a normal blood pressure of 125/75 mm Hg. Physical examination was otherwise unremarkable. ECGs were recorded after referral. Figure 1 shows an ECG recorded while the patient had chest pain, and figure 2 when he was free of pain.

1 What do the ECGs show?

2 What are the two main differential diagnoses?

3 How would you manage this patient?

Submitted by Ever D Grech and Bastiaan Zwart

Parental consent obtained.

Cite this as: *BMJ* 2018;361:k1191

If you would like to write a Case Review for Endgames, please see our author guidelines at http://bit.ly/29HCBAL and submit online at http://bit.ly/29yyGSx

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answers

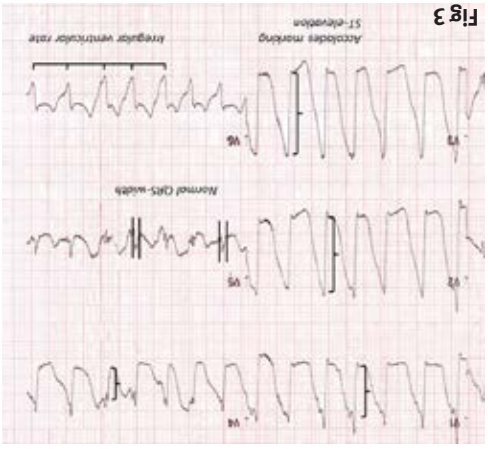

Fig 3

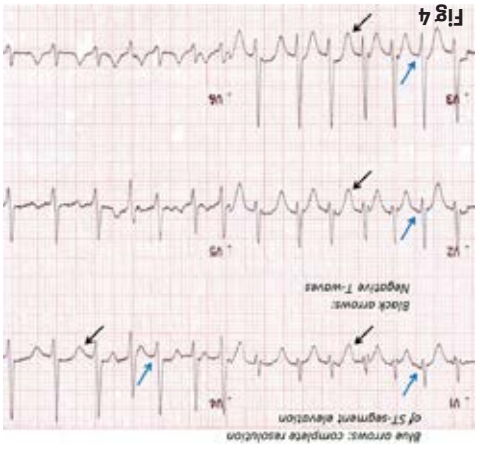

Fig 4

CASE REVIEW **A man with chest pain and a broad QRS complex tachycardia**

1 The first ECG looks suspicious for broad QRS complex tachycardia, but closer inspection shows atrial fibrillation with an irregular ventricular rate, normal QRS width, and marked ST segment elevation in leads V1-V4 (fig 3). The second ECG shows deep T wave inversion with normalisation of the ST segments (fig 4).

2 The main differential diagnoses are acute ST segment elevation myocardial infarction and vasospastic angina (also known as Prinzmetal angina or variant angina).

3 Urgent coronary angiography should be performed to distinguish coronary spasm from acute thrombotic occlusion. Emergency (primary) percutaneous coronary intervention is indicated in ST elevation myocardial infarction, whereas vasospastic angina is normally treated medically with nitrates, calcium channel blockers, and/or β blockers.

Xanthogranulomatous pyelonephritis causing subcutaneous collections in the thigh

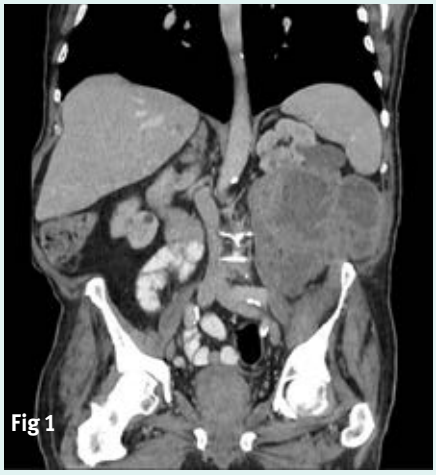
Fig 1

A 77 year old man presented with a four month history of weight loss and night sweats and one month of abdominal distension. There was a palpable mass in the left lower quadrant. Computed tomography (fig 1) and positron emission tomography/computed tomography showed a fluorodeoxyglucose avid cystic mass inseparable from the left psoas and kidney. A mass then developed in the left thigh, and imaging showed extension of the retroperitoneal mass into the thigh (fig 2). Histopathology of the retroperitoneal mass showed xanthogranulomatous inflammation. *Enterococcus faecalis* was isolated from urine and aspirated fluid from the retroperitoneal mass and thigh. The patient improved on intravenous antibiotics.

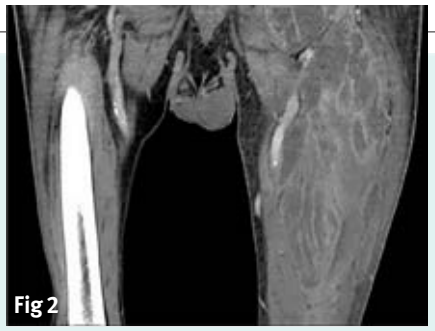
Fig 2

Xanthogranulomatous pyelonephritis is a destructive granulomatous inflammation of the kidney, typically associated with renal infection and obstruction.

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Patient consent obtained.

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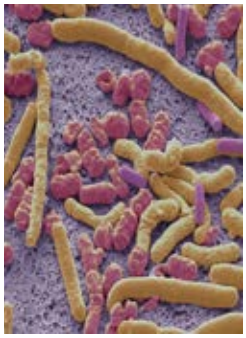
Probiotics



Dietary supplements containing live bacteria are widely advertised as improving health and wellbeing. Nonetheless, a systematic review finds little to suggest that elderly people derive any benefit from them, at least as far as infectious illness is concerned (*Age Ageing*). In 15 trials involving nearly 6000 people, mean age 75 years, there were no statistically significant differences in the occurrence or duration of infections between those taking probiotics and those taking placebo.

White matter hyperintensities

Small areas of hyperintensity in the white matter are common on T2 weighted brain magnetic resonance imaging, especially in older people. Although their pathogenesis isn't fully understood, several studies have shown that they're associated with high levels of vascular risk factors and an increased risk of stroke. A seven year longitudinal study of adults from New York, mean age 65 years at baseline, now shows that those with a higher volume of white matter hyperintensity experience a steeper decline in functional status as measured by the Barthel index of activities of daily living (*PLoS Med*).

Pulmonary function tests

Vast numbers of pulmonary function tests are performed every day so it's good to know that the associated risks are extremely low. An audit of 20 years' worth of data from a single hospital reports that adverse events occurred less often than one in a thousand tests (*Thorax*). And even among these, only a tenth were severe enough to require hospital admission. Syncope was the commonest adverse event, followed by breathing difficulties such as hyperventilation.

Treating hypertension in elderly people

General practitioners are unwilling to make changes in their elderly patients' antihypertensive medication according to a qualitative study from the Netherlands (*BMJ Open*). When interviewed, they gave a number of reasons, including lack of clarity in guidelines, doubts about the benefit of intensive treatment, fear of precipitating a stroke, and reluctance to upset an established routine. Minerva feels entirely sympathetic to their conservative approach. After all, it's much easier to make asymptomatic patients feel worse than to make them feel better.

Pyoderma gangrenosum

Pyoderma gangrenosum is a rare neutrophilic dermatosis characterised by painful ulcer formation, usually on the legs, and often at the site of a minor injury. A large series of cases collected from hospitals in North America finds that the condition affects white women more frequently than other population groups (*JAMA*). About two thirds of these patients with pyoderma gangrenosum had comorbidities. In people under 65, inflammatory bowel disease was the commonest associated condition. In older people, rheumatoid arthritis, ankylosing spondylitis, and neoplasia were more frequent.

The postman knocks

In a blog in the *London Review of Books*, a postman longs to do something more useful than deliver junk mail. He envies his colleagues on the Channel Island of Jersey where, for the price of a special delivery letter, they will knock on the door, have a brief chat, and make sure the occupant is all right. He thinks that Jersey's Call and Check scheme could be adapted for other communities and points out that posties are well placed to keep a benevolent eye on elderly people who are isolated or immobile.

Cite this as: *BMJ* 2018;361:k1835