

education

FROM THE JOURNALS Edited highlights of weekly research reviews on <https://bit.ly/2PLtl8>

MMR vaccine safety

Yet another study fails to find any excess risk of autism in children vaccinated with MMR. Investigators used Danish population registries to link information on vaccination, diagnosis of autism, sibling history of autism, and risk factors for autism in children born between 1999 and 2010.

During more than 5 million person-years of follow-up, 6517 children were diagnosed with autism, but the risk was no higher in MMR vaccinated children than it was in unvaccinated children. Indeed, the hazard ratio of 0.93 (95% confidence interval 0.85 to 1.02) shows that, if anything, MMR vaccine protects against autism. This is one of the largest studies published and, apart from adding statistical power, it refutes ideas about susceptible subgroups and clustering of cases. Whether it will change anyone's mind is another matter.

• *Ann Intern Med* doi:10.7326/M18-2101

Sequelae of Ebola virus infection

No one will be surprised to learn that people who have survived Ebola virus disease complain of multiple health problems. A longitudinal study from Liberia followed nearly 1000 antibody positive survivors, comparing them with twice that number of antibody negative close contacts.

Symptoms of urinary frequency, headache, fatigue, muscle pain, and memory loss were commoner in survivors, who were also more likely to have abnormal findings when examined, particularly uveitis. With the exception of uveitis, the prevalence of these conditions declined during 12 months of follow-up. Ebola virus RNA persisted in semen samples from around a third of the male survivors.

• *N Engl J Med* doi:10.1056/NEJMoa1805435



Christopher Martyn is an associate editor, *The BMJ*



Fluorouracil for actinic keratosis

Actinic keratoses, also known as solar keratoses, are rough patches of skin caused by damage from years of sun exposure. They're most commonly found on the scalp, face, and forearms and hands. Although the NHS website is reassuring, actinic keratosis is the most common premalignant skin disease in white populations.

Left untreated, actinic keratoses may develop into squamous cell carcinoma. A trial at four hospitals in the Netherlands compared four established treatments head to head (fluorouracil cream, imiquimod cream, methyl aminolevulinate photodynamic therapy, and ingenol mebutate gel). Judged by the primary outcome of a reduction of $\geq 75\%$ in the number of lesions 12 months after the end of treatment, fluorouracil cream was the most effective. Patient satisfaction and health related quality of life were also highest in the fluorouracil group.

• *N Engl J Med* doi:10.1056/NEJMoa1811850

Glyceryl trinitrate after stroke

Raised blood pressure is common after stroke and predicts a poor outcome. However, it's not clear whether treatments to lower blood pressure are helpful. A few years ago, a large trial showed no benefit from transdermal glyceryl trinitrate given within 48 hours of stroke. But 48 hours might be too late: given in the hyper-acute phase of stroke, blood pressure lowering treatment might be more effective.

This idea has been tested in a remarkable trial in which trained paramedics recruited and treated people with presumed stroke within four hours of onset of symptoms with transdermal glyceryl trinitrate. Over a third of patients received treatment within an hour of the onset of the stroke. The intervention successfully lowered blood pressure (by around 6 mm Hg), but there were no differences between groups in functional outcome at 90 days.

• *Lancet* doi:10.1016/S0140-6736(19)30194-1

Evacuation of intracerebral haematoma

Surgical evacuation of the haematoma after spontaneous intracerebral haemorrhage might lessen compression and distortion in the surrounding brain tissue and reduce ischaemia, but trials have failed to show benefit in terms of mortality or functional outcome. Unfortunately, the results are no better when craniotomy is replaced by a minimally invasive approach.

The MISTIE trial used image guided catheters to aspirate the haematoma and then irrigate it with alteplase, randomising 506 patients either to this intervention or to standard medical care. At a year's follow-up, there were no differences between groups in the proportion of patients who had achieved a good functional outcome.

• *Lancet* doi:10.1016/S0140-6736(19)30195-3

Health anxiety

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A 46 year old man visits his general practitioner worried about episodes of chest pain and tightness. A recent CT coronary angiogram was normal. He has had numerous appointments with different GPs over the past year for a variety of symptoms that seem to settle down after reassurance or further investigation.

Normal concern about our health can sometimes turn into a persistent and excessive fear of being seriously ill. This is often referred to as health anxiety. In this article we offer practical tips to help clinicians identify and help people with persistent and disabling health anxiety, based on available evidence and our own clinical experience.

Box 1 | Screening for health anxiety with the Bodily Preoccupation Scale of the Illness Attitude Scales^{7,8}

Ask the patient to respond to the questions below using options “No,” “Rarely,” “Sometimes,” “Often,” or “Most of the time”

1. When you read or hear about an illness, do you get symptoms similar to those of the illness?
2. When you notice a sensation in your body, do you find it difficult to think of something else?
3. When you feel a sensation in your body do you worry about it?

Scoring and interpretation

No = 0, Rarely = 1, Sometimes = 2, Often = 3, Most of the time = 4 (total scale range 0-12).

A score of ≥6 discriminates severe health anxiety from the general population with 92% sensitivity and 90% specificity

Box 2 | Differential diagnosis of health anxiety

Health anxiety—Excessive worry about health that leads to functional impairment

Generalised anxiety disorder—Worry in several domains (such as financial or job related worry)

Obsessive-compulsive disorder—Rituals in response to intrusive thoughts dominate the clinical picture

Panic disorder—Recurrent acute panic attacks

Medically unexplained symptoms—Symptoms (such as pain or tremor) are the main problem, whereas in health anxiety it is the fear of serious disease

HOW PATIENTS WERE INVOLVED IN THIS ARTICLE

A patient who is receiving care from PT and HT after six years of incapacitating health anxiety was an adviser for this article. He has noted in particular that the comment “There is nothing wrong with you,” is remarkably unhelpful and that persistent reassurance only makes him attend more frequently.

What you should cover

When to consider health anxiety

Health anxiety is common, with prevalence estimated at up to 20% in medical settings.¹ Somatic symptom disorder and illness anxiety disorder replaced the term hypochondriasis in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*,¹ but the less pejorative term health anxiety is typically favoured in practice. Whichever term is used, the central questions for the clinician to answer are whether the patient’s worry is excessive in relation to the actual risk and what impact is this having on their life. These patients undergo more tests and examinations and use more health service resources than those without health anxiety.² Although children can experience health anxiety,³ it typically begins in adulthood and follows a chronic but fluctuating course. Having a medical disease or diagnosis does not exclude health anxiety¹—many people have both.

Clues that may prompt further inquiry about health anxiety include:

- Worry about health that quickly and repeatedly resurfaces after reassurance. This was demonstrated in a study of 60 adults reassured that there was nothing seriously wrong after attending an endoscopy clinic.⁴ In those with high levels of health anxiety, worry about their health and illness belief resurfaced 24 hours after their endoscopy and was sustained at one year follow-up; those with low health anxiety had immediately reduced levels of worry and illness belief that was maintained at one year
- Frequent attendance
- Spending excessive time online searching for health related information, sometimes described as cyberchondria. This may lead to increased anxiety and distress as it can increase the risk that normal bodily sensations are interpreted as signs of serious somatic disease^{5,6}
- Health worries that lead to substantial functional impairment.

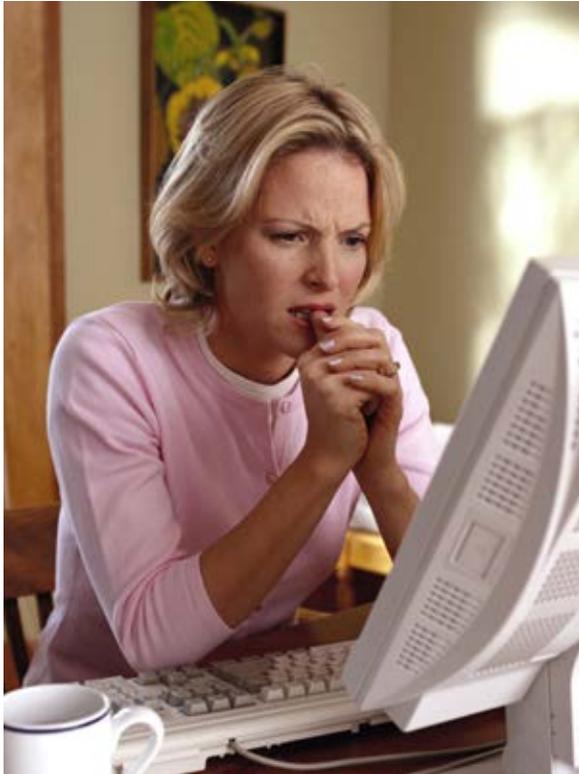
How to discuss health anxiety in the consultation

Allow the patient to express their symptoms in full without interruption—this helps them to feel that they have been listened to and taken seriously. Use the following questions to establish whether the patient has health anxiety.

- *Have you been worrying a lot about this? Do you tend to worry about your health in general? Do you think that you have not been taken seriously by doctors in the*

WHAT YOU NEED TO KNOW

- Consider health anxiety if the patient reports excessive worry about health that causes suffering and impairment
- Avoid routinely reassuring the patient that all is well. Instead, acknowledge that that patient is worried and suggest seeking ways to address this
- Cognitive behaviour therapy focused on health anxiety is an effective treatment



GETTYIMAGES

past? Someone with health anxiety is likely to answer yes to at least one of these.

- *What is the worst thing you fear could happen?* This can help you to understand what is driving the fear.
- *When did you start to worry more about your health?* Triggers might be a serious disease they or a family member were diagnosed with, the death of a loved one, or other external stresses.
- *How has this worry about your health affected your work, social, and family life?* A hallmark of pathological health anxiety is that it leads to excessive checking and health monitoring, and creates great suffering through intolerable anxiety.

People with health anxiety tend to be very attentive not only to bodily sensations but also to medical information, which is easily misinterpreted. Hours can be spent looking at skin blemishes, measuring pulse rate and blood pressure, asking relatives for reassurance, and searching online. These preoccupations typically fail to provide an explanation for their symptoms and make anxiety worse. Many start avoiding certain places or activities that trigger bodily sensations (such as hospitals, cemeteries, or physical exercise). These avoidance behaviours can reduce quality of life and maintain health anxiety in the long run.

A brief screening tool for health anxiety, such as the Bodily Preoccupation Scale of the Illness Attitude Scales (box 1), can help to identify those with severe health anxiety.⁸

Explore comorbid symptoms

Many people with health anxiety have a comorbid mental health problem, summarised in box 2. If you identify an additional mental health problem, discuss which is causing most distress and which the patient would like to address first.

What you should do

Someone with persistent and disabling health anxiety can be helped through developing a shared understanding of the problem with the clinician, psychological therapies, and, in some circumstances, medication.

Avoid reassurance

Reassurance to patients with health anxiety is like an addictive drug—it provides immediate relief but wears off quickly,^{4,9} sometimes even by the end of the consultation. Instead, the clinician might say, “It is clear that you are worried about your health; we have ways of helping this, and this will not affect any other treatment you are receiving.” The final clause is important as patients sometimes feel that if they admit to health anxiety their other medical problems will be ignored or minimised.

Validate symptoms

Acknowledge that you believe that their symptoms are real and genuinely experienced. By concentrating on worry as the most important symptom and recognising how unpleasant serious worry can be, you can validate the patient’s feelings and increase motivation for treatment.

Provide an alternative explanation

An important task for the clinician is to explain to the health anxious patient that a range of sensations—in the present case palpitations, chest pain, and tightness in the chest—can be symptoms of anxiety rather than disease. We often explain to patients that health anxiety is like a false alarm: fear is our body’s alarm that helps us to survive when there’s a threat; in the case of health anxiety, the body’s alarm system goes off even when there is no actual threat. Another tool we use is to recognise that our bodies are naturally “noisy” and most sensations are not symptoms of severe disease. Follow this up with written information that includes an explanation of health anxiety and initial self care advice.¹⁰

Discuss treatment options

The first choice of treatment should be cognitive behaviour therapy.^{11,12} In England health anxiety treatment should be available through Improving Access to Psychological Therapies (IAPT) services.¹³ GPs may have a role in advising non-medical therapists that health anxiety is the issue to be treated and that further physical investigations should not delay this.

Antidepressants may be considered for patients with debilitating health anxiety who are interested in treatment but who decline talking therapies.^{14,15} Fluoxetine and paroxetine have been shown to be more effective than placebo in reducing health anxiety, but there are few randomised trials, generally with small sample sizes and high drop-out rates.¹⁶

Check understanding and arrange follow-up

Misinterpretation is a core feature of health anxiety, both of bodily sensations and health information. To minimise the risk of this in the consultation, ask the patient to summarise what you’ve discussed.

One or more follow-up appointments is likely to be helpful, to address questions that arise after the consultation and monitor progress.

Competing interests: EH-L and HT have authored books about cognitive behaviour therapy for health anxiety.

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UNCERTAINTIES

Can environmental assessment and modification prevent falls in community dwelling older people?

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One third of people over the age of 65 experience a fall.¹ The health and social care costs of falls are increasing with longevity.^{2,3} Falls are one of the leading causes of morbidity and death caused by injury in people over 75. Nearly a quarter of older people who fall are concerned about further falls, and some restrict activity. This can result in physical deconditioning, increased risk of future falls, institutionalisation, and reduced quality of life.⁴

Box 1 lists features that predispose older people to falls.⁵

Risk factors for falls can be categorised as

- Intrinsic (personal risk factors such as age and gender)
- Extrinsic (environmental risk factors/environmental hazards)
- Behavioural (activity related risk factors).^{6,7}

Environmental hazards, such as trailing cables and poor lighting, are linked to 30-50% of falls in observational studies.^{1,8} Guidelines

WHAT YOU NEED TO KNOW

- Evidence suggests that environmental interventions can prevent falls in older people at high risk of falls, but they have little or no benefit in people at low risk
- Offer environmental assessment and modification led by an occupational therapist to people over 65 who have had a fall in the past year, use a mobility aid, need assistance with any activities of daily living, take psychoactive medications, or are concerned about falling
- Environmental assessment and modification encompasses a comprehensive, validated functional assessment of the individual in their home environment, a joint problem solving approach, and follow-up as required

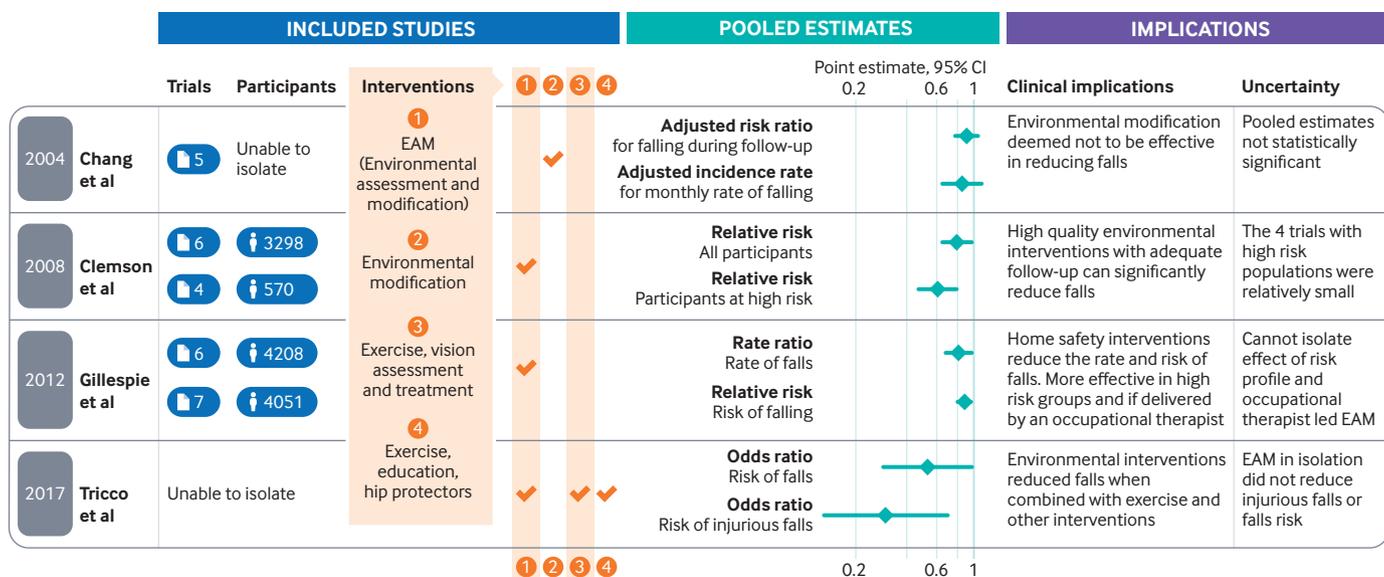
in Australia,⁹ the US,¹⁰ and Britain^{6,11} recommend interventions to reduce environmental hazards for older people at risk of falling. However, it remains uncertain whether environmental assessment and modification reduces falls in high risk older people, and which healthcare workers most effectively provide this intervention.

Box 2 gives examples of environmental interventions. Such interventions are typically provided by occupational therapists who specialise in environmental assessment and modification. However, in research studies, environmental interventions have been provided by healthcare support workers and healthcare professionals such as nurses and physiotherapists. The intensity of environmental assessment and modification ranges from hazard screening checklists, administered without the older person necessarily being present, to high intensity intervention comprising a comprehensive functional assessment of the older person in their home environment. Thus, the level of expertise of the healthcare worker and the intensity of the environmental intervention are likely to influence the outcome.

Box 1 | Risk factors for falls in community dwelling older people

Age (≥ 65)
History of falls in the past year
Use of mobility device, such as a walking aid
Requiring assistance for any activities of daily living
Use of psychoactive medications
Fear of falling

We categorise falls risk as
High falls risk— ≥65 years, have a history of falls, and also possess one or more of the other risk factors for falls
Moderate risk of falls— ≥65 years and possess one of the above additional risk factors
Low falls risk— Possess only one falls risk factor



Summary of systematic reviews of environmental management for falls prevention

Box 2 | Types of environmental intervention to reduce risk of falls

- Assessment and modification of the environment and tasks performed, including raising awareness of risks of falls and problem solving with the older person to find solutions
- Home modifications to improve task performance, independence and/or safety (eg, modifying a shower to improve access)
- Assistive technology to maintain or improve independence (eg, provision of mobility aids, grab rails, and personal alarms)

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

A member of the OTIS Consumer Reference Group reviewed the manuscript and provided feedback. We thank her for her input. As a result, we changed the article in the following ways:

- We clarified the term “community dwelling”
- We specified that only some, not all, of those who are fearful of falling subsequently restrict their activity
- We provided more information on factors causing escalation in the cost of falls

WHAT PATIENTS NEED TO KNOW

- If you are 65 or over and live in the community, your risk of falls in the future is higher if you have had a fall in the past year, use a mobility aid, need assistance with any activities of daily living, take psychoactive medications, or are concerned about falling
- It is likely that environmental assessment and modification, provided by an occupational therapist, would reduce your risk of future falls
- An occupational therapist visits your home to assess and recommend modifications to the environment and tasks that you perform. This may reduce falls hazards and improve your independence and/or safety. The therapist would also consider whether assistive technology might help to maintain or improve your independence
- Occupational therapists typically ask you to identify what you think puts you at risk of falling and you jointly problem solve and agree on solutions.

What is the evidence of uncertainty?

We found four systematic reviews of trials on environmental assessment and modification in community dwelling older people, including a Cochrane Review which included eight randomised controlled trials isolating the clinical effectiveness of environmental assessment and modification, and four clinical guidelines.

Best evidence suggests a possible benefit of high intensity occupational therapist led environmental assessment and modification in reducing falls in high risk populations.¹²⁻¹⁵ These led to a reduction in falls of 19-21% in all risk categories and around a 38-39% reduction in high risk groups.^{12,13} Specialism in environmental assessment (eg, by occupational therapists) and participant risk profile are likely to influence effectiveness of the intervention. Falls prevention interventions have less effect when delivered by health workers other than occupational therapists or to low risk populations.¹² The figure presents a summary of the systematic reviews (all data are in the supplementary files on bmj.com). Of the trials that isolate environmental assessment and modification, five studies showed a statistically significant reduction in falls in high risk participants through high intensity, occupational therapist led environmental assessment and modification.³⁻¹⁹ The remaining three trials found no effect on falls when low intensity interventions were provided by other professionals²⁰ or trained support workers to both high and low risk populations.^{21,22}

Methodological weaknesses and the small sample sizes in studies mean that it is difficult to ascertain which interventions are effective. Most studies include people at low risk of falls and there is considerable variation in the expertise of the healthcare worker delivering the intervention and in the intensity of the intervention. Some studies incorporated a checklist/screen as opposed to a functional environmental assessment.



PHOTOFUSION/GETTYIMAGES

EDUCATION INTO PRACTICE

- How would you assess whether an older person is at high risk of falls?
- What would you include in a comprehensive environmental assessment, who would provide it, and which patients would you offer it to?
- Of the frail older patients that you treated in the last year following a fall, how many received an environmental assessment and functional assessment in their home with follow-up?

RECOMMENDATIONS FOR FUTURE RESEARCH

Large trials in community dwelling older people ≥ 65 at high risk of falls to evaluate whether

- Occupational therapist led environmental assessment and modification is clinically effective compared with usual care controls
- High intensity environmental assessment and modification is as clinically effective in reducing falls if delivered by other trained professionals as compared with occupational therapists
- Intensive follow-up to implement recommendations, immediately after occupational therapist led environmental assessment and modification, produces a greater reduction in falls than no follow-up or a single follow-up visit. A nested project to identify the most effective level of follow-up would enable resources to be deployed efficiently
- Qualitative studies to understand what occupational therapists consider in their clinical reasoning when carrying out environmental assessment and modification. This would help determine what the important elements are and inform future staff training

Is ongoing research likely to provide relevant evidence?

We searched the Cochrane Database of Systematic Reviews, ClinicalTrials.gov, the World Health Organization, and Australian New Zealand Clinical Trials Registry for research protocols on environmental assessment and modification; environmental interventions; occupational therapy; falls prevention; and community dwelling older people.

Ongoing research is likely to add to the evidence on the clinical effectiveness of environmental interventions delivered by occupational therapists for falls prevention. The question of whether trained home care support workers and other professionals can deliver environmental assessment and modification still needs to be addressed.

We found two ongoing studies: a small study (15 participants) in Chicago investigating an occupational therapist led falls prevention intervention to reduce fear of falling, and the Occupational Therapy Intervention Study (OTIS) which we are conducting. The OTIS trial aims to evaluate effectiveness of occupational therapist led environmental assessment and modification delivered to older people at moderate to high risk of falls.²³ To date, 1331 older people have been randomised to high intensity environmental assessment and modification or usual care control. The trial is in the follow-up phase, in which fall events are being recorded over one year. Follow-up is scheduled to be completed in late 2019. This trial will add to the evidence base on whether occupational therapist led environmental assessment and modification delivered to people at moderate to high risk is clinically effective in preventing falls.

What should we do in the light of the uncertainty?

We recommend that occupational therapist led environmental assessment and modification is only offered to older people at high risk of falls (box 1).⁵⁻¹³ This appears pragmatic given the lack of evidence on benefit in moderate or low risk people, and considering the cost and resource implications of occupational therapists intervening with people in all risk categories.

In the United Kingdom, guidelines from the National Institute for Health and Care Excellence (NICE) and the College of Occupational Therapists recommend that occupational therapist led environmental assessment and modification is routinely provided for older people at risk of falling or who are admitted to hospital following a fall.^{6,11} This has not routinely happened, however, as indicated by recent qualitative and implementation research.^{24,25} This could be due to a perceived lack of robust evidence, limited awareness of clinical guidelines, complexity of the intervention, and a perceived lack of practitioner skill and time to carry out the assessment.²⁴

When referring older people at high risk of falls for occupational therapy intervention, explain to your patient that the occupational therapist will support them to identify hazards in the home and those activities which might increase the risk of falling, and that the therapist and patient will jointly consider solutions.¹³ Active engagement of older people in environmental interventions is vital. The context, environment, use of environment, and a person's capacity are key features of environmental assessment and modification to reduce falls risk. Occupational therapy practice aims to enhance, restore, or create a balance between these elements. Interventions encompassing functional assessment of the individual will be more effective, rather than a checklist style hazard removal.

Competing interests: None declared.

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Assuming the worst

Daksha Trivedi discusses how a family history of cancer affected her during her diagnosis, and how best to support patients from different cultural backgrounds

The last thing my family had expected to find out and when my mother came to spend Christmas with us was that I had cancer of the lower oesophagus. We were especially in shock as only six months earlier my twin brother had died of advanced stomach cancer.

It felt like lightning had struck twice, and I was taken back to the journey with my brother, which made me fearful of going through the same procedures as he did and enduring the same pain. I worried that his fate would also be mine. Knowing what might be to come was hard to deal with emotionally, but having this knowledge allowed me to focus on the things I knew I could control and let go of the things I couldn't.

Cultural background matters

Many South Asian families have preconceived ideas about cancer from stories within their communities—for example, if one person has had a poor prognosis, it is assumed that any other person diagnosed with cancer will follow the same path.

These assumptions are often made without adequate knowledge or information about treatment options and prognosis. The word cancer often carries a stigma, and some people have their own beliefs about why the cancer has occurred—for example, lifestyle and “karmic consequences” are considered contributing factors.

During my treatment, I believed that everyone would assume the worst about my diagnosis, giving me little hope to focus on. Finding ways of engaging with people from different cultures, who may process information in different ways, is important. Healthcare professionals can better support South Asian families by being mindful that they might assume the worst when faced

with a cancer diagnosis because of stories from within their community.

Communicating facts about the treatment and diagnosis sensitively can help demystify false ideas. For me, the most productive consultation was before surgery and I would have welcomed those discussions sooner. Being open about the uncertainties will also help patients and families to better understand the diagnosis.

What carers need to know

My husband had no choice but to find out more from various sources, which increased his stress. He searched online for information on the management and treatment of my cancer, particularly what might be expected of him after surgery. He needed someone to talk to about what to expect after my surgery and information on what was expected of family carers. One source he found helpful was the Oesophageal Patients Association (www.opa.org.uk), where he was able to read about other patients who had gone through what I was about to experience.

My mother was given information by my husband. She was looking for guidance on how to care for me after surgery, in understanding my symptoms, and my complex needs, particularly around food and drink. Up until then, denial of my diagnosis was her coping mechanism.

After an eight hour operation and several weeks in hospital, we were told that although no further treatment would be required at this stage, regular monitoring would be needed. I hope our community will now see that the worst should not always be assumed.

Competing interests: None declared.

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ROSELLOYD

WHAT YOU NEED TO KNOW

- It is important to consider the cultural background of patients and their families, particularly older people, who may not understand and feel alone
- Family history of a condition may increase the worry and anxiety after a diagnosis
- The communication of facts and evidence around a diagnosis may provide patients with something positive to focus on

EDUCATION INTO PRACTICE

- What variation in understanding and information needs do you notice in people from different cultural backgrounds who are facing a cancer diagnosis? Are there ways you could explore concerns or give information differently?
- How could you better ensure family members are included?
- How might you discuss a new diagnosis and management plan when the family has already had another member affected by cancer?

Adrenaline can restart the heart, but is no good for the brain

The study

A randomised trial of epinephrine in out-of-hospital cardiac arrest

Perkins GD, Ji C, Deakin CD, Quinn T, Nolan JP, Scomparin C, Regan S, Long J, Slowther A, Pocock H, Black JMM, Moore F, Fothergill RT, Rees N, O'Shea L, Docherty M, Gunson I, Han K, Charlton K, Finn J, Petrou S, Stallard N, Gates S, Lall R for the PARAMEDIC2 Collaborators

Published on 18 July 2018 *N Engl J Med* 2018;379:711-21. This project was funded by the National Institute for Health Research HTA Programme (project number 12/127/126).

Why was this study needed?

Adrenaline (epinephrine) injections have been commonly used during cardiopulmonary resuscitation (CPR) for cardiac arrest for more than 60 years, without clear evidence if they are helpful or harmful. Adrenaline can increase the likelihood that the heart will regain a normal rhythm as it directs blood flow to the heart. However, it also causes constriction of small blood vessels, which can reduce blood flow to other organs—

including the brain—and may lead to neurological damage.

Use of adrenaline has been linked to better short term survival in observational studies, so it has remained in the cardiac arrest guidelines. Randomised controlled trials have been needed to determine if the benefits outweigh the potential harms. This study assessed routine adrenaline use in cardiac arrests occurring outside hospital.

What did this study do?

The PARAMEDIC2 randomised controlled trial allocated 8014 people with cardiac arrest (average age 70) to receive either 1 mg adrenaline or placebo saline injections as part of advanced CPR treatment by paramedics at the scene. On average, people in the adrenaline group received a total dose of 4.9 mg.

In 59% of each group, bystanders performed CPR. Ambulances took just over six minutes to arrive and

paramedics gave the injections on average 21 minutes after emergency services were first called. Major outcomes were adjusted for variations in these factors.

More than one third of patients had unwitnessed cardiac arrest, more than half had no heart electrical activity (asystole), and only 19% had a shockable rhythm. This may have contributed to the low survival rates.

What did it find?

- People who received adrenaline had a slightly higher rate of survival at 30 days, 130/4105 (3.2%) compared with 94/3999 (2.4%) who received the saline placebo (adjusted odds ratio 1.47, 95% confidence interval 1.09 to 1.97).
- Return of spontaneous circulation was much more likely with adrenaline, occurring in 1457 (36.3%) people in the adrenaline group versus 468 (11.7%) people in the placebo group. A substantially higher number of people given adrenaline survived until hospital admission, 947 (23.8%) compared with 319 (8%) of the placebo group.

- Although the overall rate of survival at 30 days was slightly better with adrenaline, 39/126 (31%) people had severe neurological disability in the adrenaline group, compared with 16/90 (17.8%) in the placebo group.
- Only 27 people in total had no neurological symptoms at discharge. There were similar numbers of people in each group when combining those with no symptoms, mild or moderate neurological disability, modified Rankin scale 0 to 3 (odds ratio 1.19, 95% confidence interval 0.85 to 1.68).

What does current guidance say on this issue?

The 2015 Resuscitation Council UK guideline recommends giving adrenaline every three to five minutes during CPR if a normal heart rhythm is absent. Guidance on the early management of people who have had a cardiac arrest by the

Faculty of Pre-Hospital Care at the Royal College of Surgeons of Edinburgh (2017) emphasises the importance of recognising that the person is having a cardiac arrest and beginning CPR as soon as possible.

Competing interests: *The BMJ* has judged that there are no disqualifying financial ties to commercial companies. Further details of other interests, disclaimers, and permissions can be found on bmj.com

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To read the full NIHR Signal, go to: <https://bit.ly/2NPTnxQ>



0.5 HOURS

What are the implications?

Adrenaline improved the return of spontaneous circulation and likelihood of survival to reach hospital, but only slightly increased survival rates at 30 days. More of those survivors had severe neurological problems.

It remains unclear if out-of-hospital protocols should change as a result of this trial. The findings are also not able to inform hospital cardiac arrest protocols, as use of adrenaline typically occurs within three minutes of cardiac arrest.

Strategies to increase public training in CPR and make more defibrillators available may increase the number of people surviving out-of-hospital cardiac arrest.

It remains unclear if out-of-hospital protocols should change



ENDGAMES

SPOT DIAGNOSIS

A white ring around a naevus

A 23 year old man presented with a white ring around a congenital melanocytic naevus. The white ring had been present for three months. The naevus, present at birth, had grown relatively proportionally with the patient and became hairy when he reached 14. Examination revealed a dark brown, smooth, regular, well demarcated hairy naevus measuring

1.2 cm×0.8 cm in diameter, surrounded by a 0.3-0.8 cm white ring of depigmented skin below the left ear (figure). Some of the hairs had become white.

What is the most likely diagnosis?

Submitted by Fei Han and Fei Wang
Patient consent obtained.

Cite this as: *BMJ* 2019;364:1997



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

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Minerva pictures are cases which offer an educational message, and are of interest to a general medical audience. Please submit as "Minerva" via our online editorial office (see bmj.com) and follow our advice on submitting images. Please provide two or three sentences (no more than 100 words) explaining the picture, and send us the signed consent to publication from the patient. We require written consent from every patient, parent, or next of kin, regardless of whether the patient can be identified or not from the picture.

For more information see <http://www.bmj.com/about-bmj/resources-authors/article-types>

CORRECTION

In an article on prescribing loop diuretics published 21 February (<https://www.bmj.com/content/364/bmj.l359>), Box 3 "Equivalent doses of loop diuretics" contained an error in the equivalent dose of torsemide.

The correct equivalent doses are as follows:

80 mg PO furosemide ≈ 40 mg IV furosemide ≈ 20 mg PO or IV torsemide ≈ 1 mg PO or IV bumetanide ≈ 100 mg PO or IV ethacrynic acid diuretics

The article has been corrected online.



0.5 HOURS

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



Articles with a "learning module" logo have a linked BMJ Learning module at <http://learning.bmj.com>.

A central congenital melanocytic naevus (birthmark) surrounded by a depigmented ring ("halo") is suggestive of halo naevus. Halo naevus occurs in approximately 1% of the population. Melanocytic naevi are often acquired, but may be congenital, and can be blue naevi, Spitz naevi, or melanoma. It is thought that the halo formation involves destruction of melanocytes surrounding the naevus by cytotoxic T lymphocytes, and the condition has been associated with vitiligo. Approximately half of halo naevi regress over months to years (2-9-14-5 years) leaving a depigmented macule, which may persist for an average of 7-8 years. Congenital melanocytic naevi are present at birth in 0.6-1.6% of newborns. The halo phenomenon is more common in acquired melanocytic naevus than congenital. Multiple lesions may be present, typically on the trunk and mostly in adolescents or young adults. For naevi with a benign clinical appearance (well defined borders, homogeneous colour, symmetric halo), no treatment is needed. Consider a biopsy if melanoma is suspected (where there are atypical central lesions, irregular halo, and new onset in older adults).

LEARNING POINTS

- 1 Halo naevus occurs with increased frequency in patients with vitiligo; examine patients with halo naevus for vitiligo.
- 2 Red flags include asymmetry, border irregularities, colour variability, irregular halo, and new onset halo naevus in older adults.

A white ring around a naevus

SPOT DIAGNOSIS

For extra material, including patient outcome, go to bmj.com/endgames

answers

Lymphoedema of lower limbs in systemic lupus erythematosus

A 36 year old woman presented with two weeks of bilateral widespread swelling, weakness, numbness, and redness of the legs, three months of knee joint pain, and a malar rash (figure).

On examination, both legs were warm and tender and she had reduced motor function and sensation. Her temperature was 37.5°C.

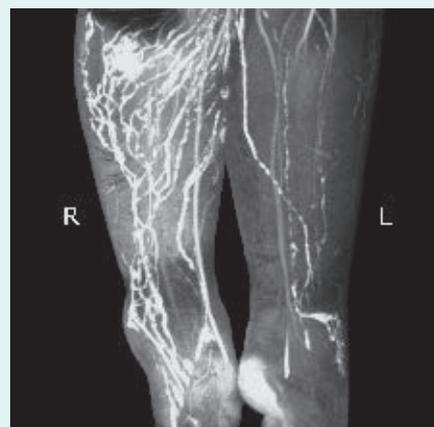
Antinuclear and anti-double stranded DNA antibodies were positive, suggesting systemic lupus erythematosus (SLE).

Normal albumin levels and liver, renal, and thyroid function tests ruled out hypoalbuminaemia, liver, and renal impairment related oedema, and thyroid disease related pretibial myxoedema.

Magnetic resonance lymphangiography showed skin and muscle swelling, knee joint fluid, and hyperplasia and dilatation of leg lymph vessels—suggestive of lymphoedema. Symptoms improved with prednisone and cyclophosphamide.

Lymphoedema in SLE is rare. Causes include pre-existing lymphatic abnormalities, lymphangitis secondary to joint inflammation, or vasculitis leading to lymphatic vessel obstruction.

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Patient consent obtained

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Peripherally inserted central catheters

Peripherally inserted central catheters are convenient for delivering long term antibiotic treatment or chemotherapy.



Complications, of which venous thromboembolism and bloodstream infection are the most serious, are well documented but thought to be uncommon. However, a prospective study finds that, if you ask patients directly, you get a different story (*BMJ Qual Saf*). Among more than 400 patients, 60% reported signs or symptoms of at least one complication. Some, such as redness around the insertion site, were minor. Others, such as fever and chills, pain, and swelling of calves and chest pain, were potentially serious.

Small renal tumours

More and more small renal tumours are turning up as incidental findings and nobody knows what to do about them. Is it better to keep them under observation and wait to see if they enlarge? Or does it make better sense to remove them completely while they're still small? The answer of course requires a randomised controlled trial. In the meantime, follow-up of a series of cases suggests that radio frequency ablation is a

safe and effective option for tumour removal (*J Urol*). Of just over a hundred patients treated in this way, 89% were alive and free of disease six years after the intervention.

Central retinal artery occlusion

The central retinal artery is the first branch of the ophthalmic artery, which is itself the first branch of the internal carotid artery. Knowing the anatomy makes it easy to understand why a review of the records of 300 patients with a diagnosis of central retinal artery occlusion shows that there is a high risk of stroke or transient ischaemic attack occurring within a few days of the retinal artery event—particularly when the cause of the occlusion was embolic. The corollary is that central retinal artery occlusion should stimulate urgent investigation for upstream sources of emboli (*Mayo Clin Proc*).

Bleeding peptic ulcer

The long term outlook is poor when endoscopic interventions fail to stop a bleeding peptic ulcer. Follow-up of 282 patients treated surgically or by transcatheter arterial embolisation between 2000 and 2014 in hospitals in Stockholm, Sweden, finds a 5 year cumulative mortality of close to 50% (*Ann Surg*). Transcatheter arterial embolisation carried a slightly lower mortality than open surgery, although it was

associated with a higher risk of rebleeding. However, treatments weren't allocated at random and these results are vulnerable to confounding by indication.

Detecting arrhythmias

A smart phone linked wirelessly to a miniature electrocardiogram (ECG) recorder (AliveCor) can be used to store and transmit an ECG rhythm strip by email. The device was evaluated by the National Institute for Health and Care Excellence a few years ago and it has now been trialled in people presenting to emergency departments with palpitations or syncopal symptoms in whom an underlying cardiac arrhythmia was suspected but not confirmed (NICE summary at bit.ly/2VlrCuM). More than half of the people given the device to carry with them after discharge were able to record a diagnostic ECG when symptoms recurred (*E Clin Med*).

Cite this as: *BMJ* 2019;364:l1045

