education

FROM THE JOURNALS Edited highlights of weekly research reviews

How long are your telomeres?

Leucocyte telomere length (LTL) is a biomarker for cell damage and can be seen as a mitotic clock, ticking away as we age. A cohort study using UK Biobank data from more than 450 000 people, and with a follow-up of over five million person-years, found that shorter baseline LTL was associated with a small increased mortality rate overall and an increase in some disease-specific mortalities such as deaths from cardiovascular and respiratory disease.

However, shorter LTL wasn't associated with an increase in total cancer-related deaths, although some cancers such as myeloid and oesophageal cancers were more prevalent. This important study confirms the impression that LTL on its own is unlikely to become a meaningful marker for overall mortality.

JAMA Intern Med doi:10.1001/jamainternmed.2021.7804

Warning: screening can damage your health

Screening can damage your health if poorly targeted and ill conceived. This huge population-based ecological study of 12 million Taiwanese women, 95% of whom didn't smoke, found that promoting lung cancer screening was associated with marked overdiagnosis and an apparent rise of 40% in five-year survival rates, which the authors say is spuriously high. There was a sixfold increase in the incidence of early stage lung cancer (stages 0-I), but no change in the incidence of late stage (II-IV) or deaths from lung cancer.

The inference is that lots more early lung cancers were picked up on screening—with all the attendant increase in testing, follow-up, cost, and anxiety for patients—but without any impact on mortality. Diagnosing cancers that are never going to cause death makes the five-year survival rate look good but has no real meaning.

JAMA Intern Med doi:10.1001/jamainternmed.2021.7769

Artificial pancreas for young children

The artificial pancreas is a game changer for people with type 1 diabetes, but is it safe for young children? An artificial pancreas is a hybrid closed loop system in which an algorithm automatically adjusts insulin delivery via a pump in response to a continuous glucose monitoring sensor that samples blood glucose levels. Closed loop systems improve management of diabetes for adults and older children: this small but well designed trial looked at whether 16 weeks of using a closed loop algorithm would be practical, safe, and effective in children aged 1-7 years. The time spent within the target glucose range was 8.7 percentage points higher using the closed loop rather than standard care, with no difference in time spent in hypoglycaemia and one case of severe hypoglycaemia with the closed loop. The positive results will be good news for young children who will have to live with diabetes for the rest of their lives.

N Engl J Med doi:10.1056/NEJMoa2111673

Peanut allergy: avoid or treat?

Can children be cured of their peanut allergy? A randomised US study found that initiating peanut oral immunotherapy before the age of 4 years was associated with increased desensitisation (a rise in the threshold of peanuts that can be tolerated, risk difference 69%) and remission (remaining able to tolerate peanut protein after stopping therapy, risk difference 19%) compared with those treated with placebo. Of those treated, 71% could safely eat 5000 mg peanut protein, equivalent to about 17 peanuts, after 2.5 years of immunotherapy.

The younger the child was started on immunotherapy, the more likely they were to achieve remission, but, for most, full remission didn't last. Six months after stopping maintenance treatment, only one in five was still able to tolerate 5000 mg peanut protein, although three in five could safely manage small amounts (600 mg or about two peanuts). Nearly a fifth of those given immunotherapy needed at least one dose of adrenaline.

Lancet doi:10.1016/S0140-6736(21)02390-4

Boost for boosters

As the national booster programme continues, this study asks a pertinent question: do three doses of an mRNA vaccine (Pfizer or Moderna) protect against symptomatic covid-19 with omicron and delta variants compared with not being vaccinated? This test-negative case-control study (a design which recruits people at a clinic who test positive for covid and compares them with controls who attend the same clinic but who test negative) found that, among more than 70 000 symptomatic people who attended US pharmacies for covid tests, there were far more unvaccinated than vaccinated people who tested positive (odds ratio 0.33 for omicron and 0.065 for delta) compared with controls. Two doses were less effective than three (adjusted odds ratio 0.34 for omicron, 0.16 for delta). Even being triple jabbed gives less protection against omicron than delta, but it's still a lot better than nothing (or two doses).

JAMA doi:10.1001/jama.2021.23619

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Managing neuropsychiatric symptoms in patients with dementia

CPD READING
0.5 HOURS

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Neuropsychiatric symptoms such as depression and agitation are reported in 11% to 90% of community dwelling patients with dementia, as per a systematic review published in 2015.[1] These symptoms are associated with earlier admission to nursing homes and earlier functional decline in people with dementia, and cause distress for carers.[2-4]

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

A person living with dementia who advocates for improving the lives of people with dementia and their carers was involved in the conception, writing, and revision of this article. In addition, a carer kindly reviewed this paper for *The BMJ* and emphasised the need to consider access, costs, severity of disease, communicative abilities, and patients' and carers' goals and preferences in tailoring the management. The reviewer also suggested considering the patient's contribution to goal setting. We have modified our example accordingly.

We gratefully acknowledge their inputs.

WHAT YOU NEED TO KNOW

- Non-medical interventions such as psychological treatments and psychosocial and environmental modifications are recommended for people with dementia who experience neuropsychiatric symptoms such as agitation, aggression, and depression
- Evidence of low to moderate quality shows that multidisciplinary care and non-medication interventions are as effective, or more so, than medications (eg, antipsychotics) for reducing neuropsychiatric symptoms
- Avoid prescribing medications in lieu of antipsychotics (eg, antidepressants and anticonvulsants) because they are associated with potential harms in people with dementia (eg, risk of fall or fracture)
- Develop person centred and measurable treatment goals and re-evaluate these at regular intervals
- Support change at an organisational level by establishing an interprofessional team responsible for psychotropic medication stewardship, and agree on criteria for appropriateness of psychotropic medication, educate care staff, inform and involve family and friend carers, and establish a process for regular review of medications

Neuropsychiatric symptoms can be challenging to treat in people with dementia. Access to multidisciplinary care teams that can identify and treat underlying causes is often limited. Little evidence is available on interventions to lessen the severity and burden of symptoms. Guidelines from the National Institute for Health and Care Excellence (NICE) recommend offering non-medication interventions as initial management for these symptoms.[5] In many countries, Choosing Wisely campaigns emphasise non-medication interventions and recommend against use of antipsychotics as a first choice to treat these symptoms because of limited benefit and potential to cause harm, including premature death.[6]

In this article we discuss how healthcare professionals can support people with dementia who are experiencing neuropsychiatric symptoms. We examine evidence for non-medication interventions, and describe how to set patient centred goals, offer a social prescription, and deprescribe antipsychotics.

How to assess patients with dementia who have neuropsychiatric symptoms

Patients may exhibit a range of behaviours that suggest neuropsychiatric symptoms (table 1). These can be transient if the precipitant is acute, or may persist for longer. Often carers notice changes in the patient's behaviour and bring these to the attention of care providers.

Evaluate the patient for signs of delirium, which include acute changes in awareness of their environment, or changes in ability to concentrate, and in cognition (eg, disorientation to time or place).[7 8] If the suspicion for delirium is low, attempt to identify factors in the patient's environment or situation that may be contributing to occurrence of these symptoms (table 2). Ask carers about consequences of symptoms to better understand if inappropriate responses to symptoms are leading to further escalation (figure).[9]

Use language that helps everyone understand contributing factors, the nature of the patient's behaviour, and what happened (some refer to these behaviours as "responsive behaviours"—that is, behaviours that are in response to external stimuli or unmet needs). Try to avoid labelling behaviours as "agitation" or "aggression." For example, instead of saying someone was "agitated," a carer could describe what happened: a person with dementia was pacing in the kitchen and repetitively asking for snack foods. On further questioning, a clinician discovers that these behaviours are manifestations of anxiety because the person with dementia is worried that they cannot prepare their own food anymore; this happens every day.

Table 1 | Neuropsychiatric symptoms in people with dementia[7]

Symptom	Examples of how symptoms manifest in people with dementia
Agitation/aggression	Hitting, kicking, restlessness, screaming
Depression/dysphoria	Sadness, slowed movements or speech, early morning awakenings, mood congruent delusions
Delusions	False beliefs that someone is trying to harm or steal from them
Hallucinations	Hearing, feeling, or seeing people or things that are not real
Anxiety	Physical manifestations such as shortness of breath, separation anxiety, excessive worry, excessive fear that something bad is going to happen
Elation/euphoria	Excessive happiness
Apathy/indifference	Less interest in participating in activities of daily living or other activities
Disinhibition	Impulsiveness, saying or doing inappropriate things
Irritability/lability	Impatience, easily made angry or sad
Motor disturbances	Pacing, restlessness, performing the same activities repetitively, wandering
Night time behaviours	Frequent night time awakenings, early morning awakenings, excessive daytime napping
Changes in appetite/eating	Weight loss or weight gain, changes in food preferences

Table 2 | Factors to consider when assessing neuropsychiatric symptoms of dementia

Factor	Examples of contributors to neuropsychiatric symptoms of dementia
Protective	Presence of a familiar carer
	Being in a familiar environment
	Carer knowledge of dementia
	Availability of support for carers
	Use of glasses and hearing aids
	Creation of a tailored dementia care plan that alerts carers to important predisposing, precipitating, and perpetuating factors for the person with dementia
	Carer knowledge of person with dementia's preferred non-medication interventions for reducing neuropsychiatric symptoms
Predisposing	Over- or under-stimulating environment
	Vision or hearing impairment
	Co-morbid psychiatric diagnoses
	Worsening dementia severity
	Carer burden or distress
Precipitating	Pain
	Hunger
	Thirst
	Medication changes
	Feeling too hot or cold
	Sleep disturbances
Perpetuating	Poor communication strategies between carers and people with dementia
	Inadequate identification and treatment of precipitating factor[s]
	Inadequate implementation of the tailored dementia care plan
	Lack of support for carers

Multidisciplinary care and interventions such as massage and touch therapy lead to clinically meaningful reductions in symptoms

How to manage neuropsychiatric symptoms in people with dementia

NICE guidelines support non-medication interventions including psychological therapies and psychosocial and environmental modifications as first line therapy in people with dementia who experience distressing neuropsychiatric symptoms.[5] Medications are reserved only for certain situations associated with distress or danger.

Multidisciplinary care and interventions such as massage and touch therapy lead to clinically meaningful reductions in symptoms (ie, the threshold above which clinicians, patients, and researchers perceive a change on an outcome scale) of agitation and aggression, as per a systematic review (189 studies, 25 736 patients, 17.5% of studies conducted in a clinic/community setting) published in 2019.[11] Another systematic review published in 2021 (256 studies, 28 483 patients, 41% of studies conducted in a clinic/community setting) found that multidisciplinary care, occupational therapy, and non-medication interventions (eg, animal therapy and exercise, fig 2, bmj.com) resulted in clinically meaningful reductions in symptoms of depression in people with dementia (without a major depressive disorder).[12]

Medications alone were not more efficacious than usual care in both of these reviews.[6 8] The level of confidence in review findings was low to moderate for most treatment comparisons. Missing outcome data and a lack of participant blinding limit validity of findings (table 4, bmj.com).[11 12] Studies included in these systematic reviews ranged from less than one week to two years in duration and were conducted across different care settings (eg, community, nursing home) in predominantly high income countries.[11 12] The comparative cost effectiveness of efficacious interventions identified in these systematic reviews is unknown.

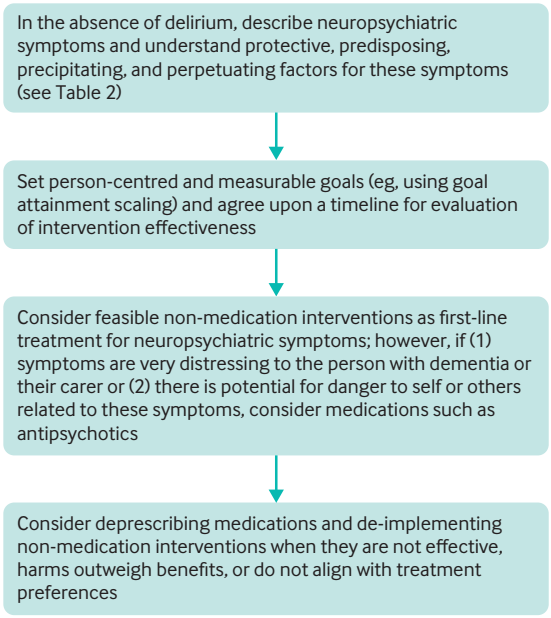
How to offer non-medication interventions

Goal attainment scaling is a tool that can be person centred and specific in measuring treatment response.[14] In goal attainment scaling, people with dementia and carers describe a problem in their own words, select a follow-up time for re-evaluation, define one or more clinically meaningful treatment goals, and define clinically meaningful improvement (table 3, bmj.com).[14] Match them with resources and decide on an appropriate follow-up time to ascertain intervention effectiveness and measure progress.[14]

Check in with carers of people living with dementia to understand how you can best support them in coping with their care giving role. Tailor interventions based on care setting, dementia severity, contributing factors, and the preferences and context of patient and carers (table 2) (box 1, bmj.com).

What is the role of social prescribing?

Social prescribing programmes link patients and carers with community resources that support their social care needs.[15] Prescribed non-medication interventions



Key steps in evaluating neuropsychiatric symptoms of dementia and developing a treatment plan

in dementia can include exercise, socialisation, and recreation programmes.[11-15] A systematic review in 2017 identified limited evidence that social prescribing improves patient wellbeing and did not identify any studies specifically targeted at patients with dementia. More research is needed to support the implementation of social prescribing (box 3, bmj.com).[15 16]

Identify community resources or connect patients with community coordinators who have this knowledge. Share paper based and online resources about locally available non-medication and multidisciplinary care interventions for patients, to facilitate shared decision making.

What is the role of medications?

Reserve medications (eg, antipsychotics) for specific circumstances when symptoms are distressing to patients, or the patient poses an imminent danger to themselves or others.[5-18] Antipsychotics are associated with potential harms in people with dementia, including an increased risk of stroke, falling, fracture, and death.[17-21]

Use of antipsychotics in people with dementia is stabilising or decreasing over time in Canada, the UK, and the US following targeted regulations and quality improvement initiatives. But use of alternative psychotropic medications such as antidepressants and anticonvulsants has been rising in people with dementia.[22-24] Observational studies have reported harms associated with antipsychotic substitutes.[25-28] For example, trazodone (an antidepressant) was associated with a similar risk of falling compared with benzodiazepines or atypical antipsychotics in people with dementia, but trazodone was associated with a decreased risk of death compared with atypical antipsychotics.[25 26] Anticonvulsants were associated with an increased risk of death compared with placebo in a subgroup of randomised trials included in a systematic review enrolling people with dementia, in which the mean population age was at least 80 years.[29]

How to deprescribe antipsychotic medications

At the time of prescribing, discuss treatment goals and establish a timeline for review of symptoms. Define criteria for when medications should be discontinued and discuss alternative interventions. A Cochrane review (10 trials, 632 participants) found low quality evidence that discontinuation of antipsychotics for treating neuropsychiatric symptoms in older adults with dementia after at least three months has little or no effect on symptoms. A subgroup analysis suggested potential worsening of neuropsychiatric symptoms in those with more severe baseline symptoms.[30]

If you see a person with dementia who is taking psychotropic medication in which the harms outweigh the benefits or when the medication is not necessary or consistent with treatment preferences, consider deprescribing and discussion of alternative non-medication interventions.[5] However, do not initiate deprescribing in people with dementia and a concurrent chronic psychotic illness (eg, schizophrenia) without speaking with a clinician who has expertise in older patients' mental health.[31]

No validated tools are available to support psychotropic medication deprescribing in patients with dementia.[32 33] In people with neuropsychiatric symptoms of dementia when symptoms have stabilised or no response is seen to an adequate trial of antipsychotics, guidelines recommend slowly tapering antipsychotics (eg, 25% to 50% dose reduction every one to two weeks until discontinued) in collaboration with the patient and carer, who can monitor for symptom recurrence.[31] If neuropsychiatric symptoms recur, discuss potential treatment strategies:

- Initiate non-medication interventions
- Restart the antipsychotic with a goal to attempt deprescribing again in three months. Make at least two attempts at antipsychotic deprescribing, or
- Initiate an alternative psychotropic medication.[11 31]

Support for providing non-medication interventions

Practices that support organisational level change include:

- Establishing an inter-professional team responsible for psychotropic medication stewardship
- Agreeing on psychotropic medication appropriateness criteria
- Educating care staff
- Informing and involving family and friend carers
- Establishing a regular medication review process, discontinuing potentially inappropriate medications, and implementing non-medication strategies.[6]

Competing interests: See bmj.com.
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EDUCATION INTO PRACTICE

- Think about the last time you spoke with a person living with dementia and their carer about how neuropsychiatric symptoms associated with dementia were affecting their lives. To what extent did you use person centred language (eg, describing examples of behaviours as opposed to using medical jargon) that would help patients and carers feel comfortable disclosing their concerns and describing their values and goals?
- What would you do differently based on reading this article?
- How would you discuss non-medication interventions for neuropsychiatric symptoms of dementia?

Which antihypertensive treatment is better for mild to moderate hypertension in pregnancy?

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CPD READING
0.5 HOURS

Around 18 million women have pregnancy hypertension each year, with approximately 27 800 maternal deaths as per 2019 Global Burden of Disease estimates. In the UK, approximately 8-10% of pregnant women (around 70 000 each year) have high blood pressure in pregnancy (also known as pregnancy hypertension).[1] This includes chronic hypertension, gestational hypertension, and pre-eclampsia (see figure). Age standardised incidence rates are highest in sub-Saharan African countries.[2]

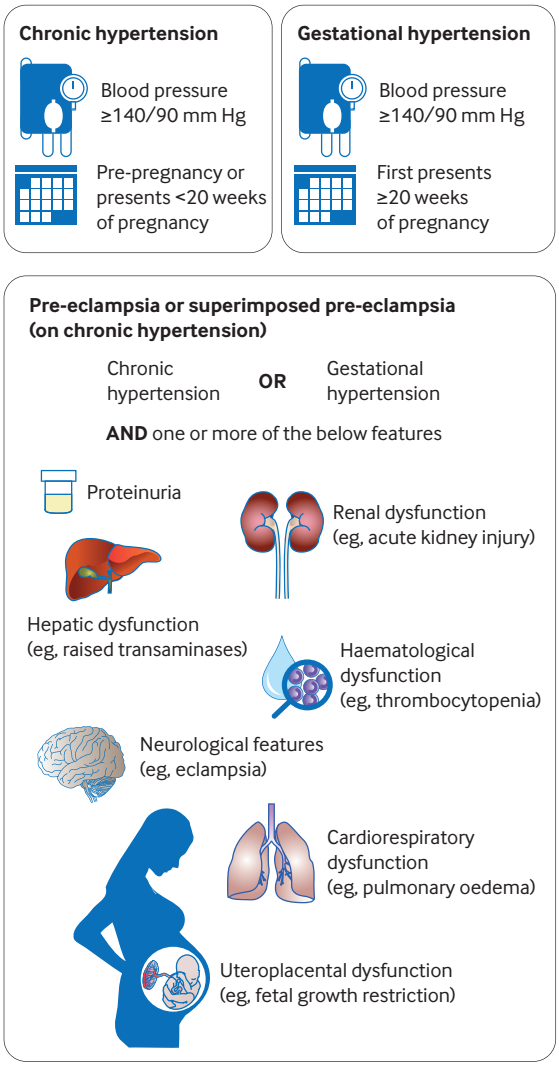
Pregnancy hypertension is associated with adverse maternal and perinatal outcomes.[3 4] These may be related to direct complications such as maternal stroke, pregnancy specific disorders such as pre-eclampsia, and fetal growth restriction, often mediated through impaired placental function. These conditions may affect the infant through iatrogenic preterm delivery or perinatal death.

International guidelines recommend pharmacological treatment for pregnancy hypertension. Blood pressure thresholds for initiating treatment differ (see table 1 on bmj.com). The most widely recommended antihypertensive drugs in pregnancy are:

- Labetalol—a mixed α and β blocker administered orally or intravenously
- Nifedipine—an oral calcium channel blocker
- Methyldopa—an oral antiadrenergic agent.

Antihypertensive therapies are applied similarly across chronic hypertension, gestational hypertension, and pre-eclampsia in most settings. These antihypertensives are not commonly used outside of pregnancy, because there are more effective drug classes (such as renin-angiotensin system blockers) that are contraindicated in pregnancy, or due to side effects (methyldopa), or because other drugs within the same class (such as other calcium channel blockers) have better pharmacodynamic profiles but less safety data in pregnancy.

It is uncertain which antihypertensive treatment in pregnancy is associated with optimal maternal and perinatal outcomes. We focus on ongoing antenatal management of mild to moderate pregnancy hypertension (defined as systolic blood pressure 140-169 mm Hg and/or diastolic 90-109 mm Hg[11]).



Types of hypertension in pregnancy

It is uncertain which antihypertensive treatment in pregnancy is associated with optimal maternal and perinatal outcomes

WHAT YOU NEED TO KNOW

- Pregnancy hypertension (encompassing chronic hypertension, gestational hypertension, and pre-eclampsia) affects around 10% of women
- Labetalol and nifedipine are recommended by national guidelines and commonly used in clinical practice to reduce the risk of developing severe hypertension in these women
- There is little evidence from head-to-head comparisons of effectiveness and tolerability to guide choice of antihypertensive treatment in pregnancy, and uncertainty about impact on clinical outcomes such as stroke, pre-eclampsia, perinatal death, fetal growth restriction, or preterm birth

What is the evidence of uncertainty?

A Cochrane systematic review published in 2018 found moderate certainty evidence that antihypertensive treatment for mild to moderate hypertension in pregnancy halves the risk of developing severe hypertension compared with placebo or no treatment (risk ratio 0.49 (95% CI 0.40 to 0.60), 20 trials, 2558 women).[11] The effect on other clinical outcomes such as stroke, pre-eclampsia, perinatal death, fetal growth restriction, or preterm birth is not clear. β blockers and calcium channel blockers were found to be more effective than methyldopa in avoiding severe hypertension (risk ratio 0.70 (0.56 to 0.88), 11 trials, 638 women).[11] Two trials (274 women) directly compared labetalol and nifedipine.[12 13] The sample sizes are too small to provide definitive evidence on clinical outcomes. An updated search did not identify any additional trials comparing these drugs.

Population based cohort studies have reported that babies born to women taking β blockers (including labetalol) are at increased risk of being small for gestational age[14] and/or hypoglycaemia at delivery (compared with other drug classes), and UK national guidelines require regular postnatal blood sugar monitoring of infants exposed to maternal β blockers around the time of birth.[15]

A 2018 network meta-analysis (46 studies) of short term treatment of acute, severe hypertension in pregnancy (typically within a 6 hour period) showed similar efficacy and safety profiles for three drugs (oral nifedipine, intravenous labetalol, and intravenous hydralazine).[16] These findings cannot be extrapolated to longer term management of pregnancy hypertension beyond the acute phase.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Two authors of this article have had direct personal or family experience of pre-eclampsia and contributed their unique insight. Our research study has also been informed by Patient and Public Involvement and Engagement (PPIE) workshops and surveys, including 147 women and partners/family members with experience of pregnancy hypertension.

EDUCATION INTO PRACTICE

How might you discuss pregnancy hypertension with a woman you are looking after, including the following:

- Their choices around antihypertensive medication in pregnancy?
- The benefits and risks of treatment with antihypertensive medication?
- Their rationale for choosing the antihypertensive medication offered?
- The clinical uncertainty that exists in this field?

Treating a pregnant woman who has high blood pressure with antihypertensive medication halves the risk of developing very high blood pressure

WHAT PREGNANT WOMEN NEED TO KNOW

- Around 1 in 10 women have high blood pressure in pregnancy. Without treatment, high blood pressure can cause damage to a woman's heart, kidneys, and brain, and be harmful to her baby
- Treating a pregnant woman who has high blood pressure with antihypertensive medication halves the risk of developing very high blood pressure
- Doctors are unsure of which antihypertensive medication works best, and they may offer one of the two medicines most commonly used, labetalol or nifedipine. There is ongoing research to answer this uncertainty
- Pregnant women can use a decision aid to help choose, available at www.nice.org.uk/guidance/ng133/resources/endorsed-resource-high-blood-pressure-in-pregnancy-decision-aid-and-infographic-6958842157

Is ongoing research likely to provide relevant evidence?

We searched the World Health Organization trial registry, ISRCTN, and ClinicalTrials.gov databases using the search terms "(labetalol) AND (nifedipine) AND (pregnancy)" with no other restrictions. Of the 23 identified studies, only one study will assess ongoing treatment of pregnancy hypertension (beyond acute management) in the antenatal period. The Giant PANDA study is a prospective, open label, randomised controlled trial of treating women with pregnancy hypertension with labetalol versus nifedipine. The primary outcome is reduction in severe maternal hypertension without increasing fetal or neonatal death, or neonatal unit admission. This study started recruiting in 2021 in approximately 50 UK maternity units aiming to randomise 2300 women. Results will be stratified by ethnicity to understand if tailoring blood pressure medication by ethnicity could improve outcomes for pregnant women and their babies, given the disproportionate burden and increased risk of adverse outcomes in women from ethnic minority backgrounds.[17]

What should we do in the light of the uncertainty?

We recommend following national guidelines on treatment of hypertension in pregnancy, most of which endorse use of either labetalol or nifedipine, where drug availability and cost permit. Explain to pregnant women that there is evidence in favour of offering treatment for hypertension (compared with no treatment) to reduce the risk of severe hypertension, but the effect on other pregnancy outcomes and the optimal choice of drug remains uncertain. It would be reasonable to prescribe either labetalol (if the woman is not asthmatic) or nifedipine (if no contraindications to the drug). Consider switching to the alternative if there is suboptimal blood pressure control or if side effects preclude adequate treatment.

Competing interests: See bmj.com.

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Even low doses of steroids increase the risk of cardiovascular disease in people with inflammatory diseases

The study

Dose-dependent oral glucocorticoid cardiovascular risks in people with immune-mediated inflammatory diseases: a population-based cohort study

Pujades-Rodríguez M, Morgan AW, Cubbon RM, Wu J

PLoS Med 2020;17:e1003432

Why was this study needed?

Glucocorticoids are commonly prescribed to treat a range of long term inflammatory diseases, such as rheumatoid arthritis and inflammatory bowel disease. About one in 100 people take this medication to reduce inflammation and other symptoms. For some of these diseases, alternative treatment options are limited.

One known risk of glucocorticoids is that long term use in high doses may increase a person's chance of developing cardiovascular disease, including heart disease and stroke. Until recently, the impact of low to moderate doses was less clear.

What did this study do?

This study aimed to assess cardiovascular disease risk in people with six inflammatory diseases taking lower doses of glucocorticoids. Most glucocorticoid prescriptions (96%) were for prednisolone.

Researchers analysed the medical records of 87 794 patients treated in 389 primary care practices in the UK between 1998 and 2017. They were aged 56 on average and had all been diagnosed with one or more of six inflammatory diseases.

The six diseases are

- Rheumatoid arthritis
- Inflammatory bowel disease
- Giant cell arteritis
- Polymyalgia rheumatica
- Lupus
- Vasculitis.

None of the people in the study had cardiovascular disease when they were first treated for their inflammatory disease.

The researchers assessed their risk of six common cardiovascular diseases. They considered

- Atrial fibrillation
- Heart failure
- Myocardial infarction
- Stroke and other diseases affecting blood vessels supplying the brain
- Peripheral arterial disease
- Abdominal aortic aneurysm.

What did it find?

The study found that the risk of developing all six cardiovascular diseases increased with higher daily dose and duration of prednisolone. This increased risk was present even at a low dose of 5 mg a day.

After a year of treatment:

- People taking a daily dose of less than 5 mg prednisolone had twice their original risk of developing cardiovascular disease
- People taking daily doses of 25 mg or more had six times their original risk of developing cardiovascular disease (increased from 1.4% to 8.9%).

Why is this important?

A low daily dose of prednisolone (5 mg or less) was previously believed to be safe long term. This study suggests that prednisolone increases the risk of a range of fatal and non-fatal cardiovascular diseases. It concludes that this risk increases with the dose and duration of steroid treatment. People on high doses develop a risk similar to those with diabetes.

What's next?

Tools for scoring cardiovascular risk do not take into account glucocorticoid dose. Refining methods of risk prediction may help doctors identify which patients would benefit from taking steps to reduce their risk.

This study highlights the need for new treatment approaches for long term inflammatory diseases. These should avoid or minimise long term glucocorticoid treatment and have less effect on the risk of developing cardiovascular disease. When new potential therapies are identified, their benefits and risks need to be compared with those resulting from glucocorticoid treatment.

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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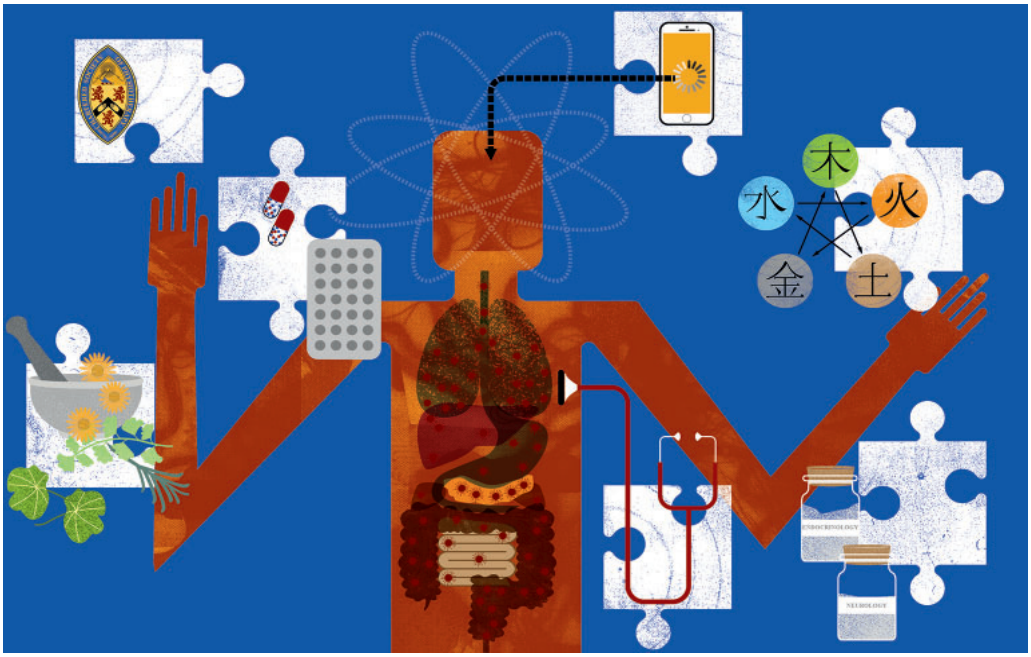
How can you help me integrate my long covid care?

CPD READING
0.5 HOURS

Carl Jreidini discusses his search for answers on his road to recovery



ROSE LLOYD

EDUCATION INTO PRACTICE

- How could you work more collaboratively with your patients who are experiencing long covid?
- How could you improve your knowledge of the evidence base for non-medical treatments for people managing long covid symptoms?
- What could you do to help patients centralise their care and plans when they are being seen by multiple specialties?

WHAT YOU NEED TO KNOW

- Develop a collaborative relationship with your patients and respect their suggestions
- Support patients if they explore alternative therapies to treat long covid
- Do what you can to centralise the patient's recovery plan

When I contracted covid-19 my symptoms were mild and my initial recovery rapid. Then, overnight, everything changed: fatigue, brain fog, and neurological disturbances followed. I was experiencing long covid. More than 18 months later I have improved, but my recovery is still a work in progress.

As I searched for ways to understand and manage my symptoms, it seemed conventional treatments and medication alone would not be sufficient given the multi-faceted nature of long covid.

Trying to collect the pieces

From the start, an integrated approach seemed the most effective. I do not dispute the capabilities of conventional medicine; however, it can be quite specialised. I preferred to take an approach that considered the whole body, and which combined functional medicine and alternative therapies, such as traditional Chinese medicine.

This became my starting point for an exercise in information gathering and sharing that continues still. I have spent hours searching for answers to my questions about long covid in medical research, covid support groups, forums, and seminars. I would then share my findings with the people treating me.

I zigzagged between specialists, who included neurologists, an endocrinologist, a doctor of internal medicine, integrative doctors, functional medicine practitioners, a specialist physiotherapist, a fatigue clinic, and my supportive general practitioner.

Like a puzzle, pieces of information had to be arranged one by one in the right place to get some answers to my questions. No one had all the pieces, but at least between us—and with relentless trial and error—some ideas were emerging. Eventually, I discovered a combination of approaches that helped improve my symptoms and through it all I found comfort and strength in my faith.

> Pieces of information had to be arranged one by one in the right place

Finding a collaborative balance

No strict rules apply to managing long covid. Different practices suit different people, but the end goal is essentially the same. For me, individual approaches or treatments had merit, but the power came in combining them, and the aim was to find the right blend and balance.

Long covid clinics in the UK can be a useful way to offer an organised medical response. But, in the UK, truly integrated clinics that comprise multiple disciplines are not readily available to all. Patients have to do much of the coordinating themselves. By taking the lead on my care, I have developed new insights into wellbeing and healthcare, and I see value in a collaborative approach where patients have more involvement. I hope that this cooperation will yield better results for people with long covid but also for those with other chronic conditions.

Fortunately, some encouraging initiatives are now taking place to understand and treat long covid. In time, I am hopeful we will find a comprehensive solution for this condition and others like it. In the meantime, we have an opportunity to learn more about ourselves, to develop more collaborative, open minded relationships with healthcare professionals, and to become—at least in small part—our own integrated physicians. I hope we can look back on this concept positively, despite the challenges that so many have faced.

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CASE REVIEW Teenage girl with asymmetrical shoulder height

A girl in her early teens presented to her general practitioner with six months of progressively worsening right scapula prominence, left shoulder tilting, and left hip prominence. She did not report pain or dysfunction.

The patient had no relevant family or medical history. Over the past year her height had increased rapidly. Menarche occurred six months earlier.

The patient was concerned that she felt "slightly lopsided," and her clothes no longer fitted properly over her shoulders and hips.

No café au lait spots, axillary freckles, hairy patches, or skin dimpling were seen on inspection of her trunk and lower back.

When standing, her right scapula and posterior ribs were prominent and her right shoulder was higher than the left (fig 1a). On forward bending, her right thoracic prominence was accentuated (fig 1b). Neurological examination of the upper and lower limbs was normal.

Whole spine posteroanterior (fig 2) and lateral plain radiography with measurement of the Cobb angle was requested for suspected scoliosis.

1 **What is the most likely diagnosis?**
2 **What are the potential differential diagnoses?**
3 **When would you refer a patient with scoliosis for specialist assessment?**

Submitted by Kelechi C Eseonu, Uche Oduoza, and J D Lucas

Parental consent obtained.
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Fig 1a | Patient standing

Fig 1b | Patient bending forwards

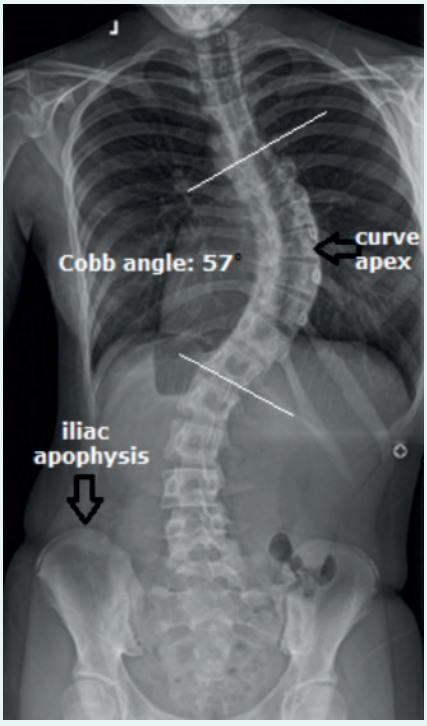


Fig 2 | Posteroanterior radiograph of whole spine with Cobb angle 57°. On a posteroanterior view of the spine, tangents (white solid lines) are drawn along the superior endplate of the superior end vertebra and the inferior endplate of the inferior end vertebra. The Cobb angle is formed by the intersection of these two lines

answers

CASE REVIEW Teenage girl with asymmetrical shoulder height

1 What is the most likely diagnosis?

Adolescent idiopathic scoliosis—the most common form of juvenile scoliosis in patients with no other developmental delay or abnormal neurological findings. In this condition the spine has a lateral curvature, or Cobb angle, of >10°. Radiography showed a thoracic scoliosis with the right sided curve apex at T7. The Cobb angle measured 57° (fig 2).

2 What are the potential differential diagnoses?

Other causes of scoliosis include congenital vertebral malformation, neuromuscular disorders, and syndromes resulting in developmental delay.

Chest wall abnormalities, hairy patches, café au lait spots, axillary freckles, and skin dimpling over the lower back are possible signs of a neuromuscular cause. Definitive exclusion of underlying structural abnormalities requires whole spine magnetic resonance imaging.

3 When would you refer a patient with scoliosis for specialist assessment?

- Patients younger than 13 years with a Cobb angle >10°
- Patients aged 13-17 years with a Cobb angle >20°
- Cobb angle >10° in a patient younger than 18 years with an underlying condition (eg, neuromuscular condition, chromosomal or genetic abnormality).

PATIENT OUTCOME

The paediatric spinal orthopaedics team confirmed the diagnosis after whole spine magnetic resonance imaging.

The patient underwent posterior spinal instrumented correction and fusion. She had an excellent outcome at two year follow-up.

LEARNING POINTS

- Cobb angles <10° are normal variants of the spine.
- Indication for referral depends on curvature, age, and skeletal maturity.
- Patients' resources include www.sauk.org.uk.

CPD READING
0.5 HOURS

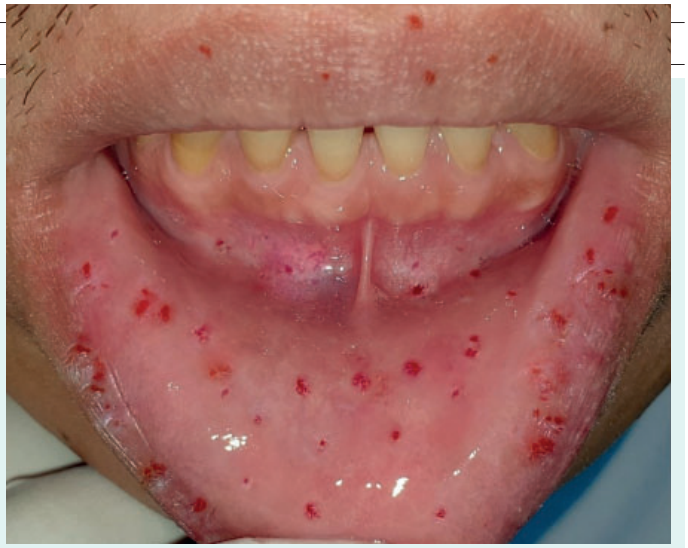
You can record CPD points for reading any article. We suggest half an hour to read and reflect on each.

LEARNING MODULE

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

MINERVA

Hereditary haemorrhagic telangiectasia



This is the lower lip of a man in his 50s with hereditary haemorrhagic telangiectasia (HHT), or Osler-Weber-Rendu disease.

At the patient's routine dental check-up, telangiectasias were observed on his lips, tongue, palate, and hands. He had a history of occasional epistaxis. The family history included similar lesions but no formal diagnosis of HHT.

HHT, an autosomal dominant disease affecting 1-2 per 10 000 population, is characterised by fragile vascular dilations of terminal vessels in the skin and mucous membranes as well as arteriovenous malformations of internal organs, particularly the lungs, brain, and liver. A clinical diagnosis is made in the presence of any three of recurrent epistaxis, mucocutaneous telangiectasias (this might not occur until the fourth decade), visceral arteriovenous lesions, or first degree relatives with HHT. Afro-Caribbean residents of Curaçao and Bonaire have a higher prevalence of HHT.

Clinical sequelae of HHT can result in blood loss with varying degrees of severity. Clinicians examining the oral cavity should be familiar with HHT because telangiectasias on oral mucosa are the most easily identifiable sign.

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Patient consent obtained.

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If you would like to write a Minerva picture case, please see our author guidelines at http://bit.ly/29HCBAL and submit online at http://bit.ly/29yyGSx

Origins of antibiotic resistance

The emergence of antibiotic resistant strains of microorganisms is usually blamed on the over-prescription of antibiotics in clinical practice and the use of antibiotics in livestock farming. But a survey of European hedgehogs (yes, hedgehogs) shows that antibiotic resistance has been widespread in the natural world for years (*Nature* doi:10.1038/s41586-021-04265-w). Most of these spiny creatures carried a strain of methicillin resistant *Staphylococcus aureus* that had evolved long before antibiotics had been used therapeutically or in agriculture.

Benefits of breastfeeding

It's already known that breastfeeding is linked to a reduced risk of breast cancer, ovarian cancer, and type 2 diabetes in mothers. Now a meta-analysis of data from more than a million women shows that it's also associated with a lower risk of coronary heart disease and stroke. Women who had ever breastfed were about 10% less likely to get cardiovascular disease than those who had never breastfed (*JAHA* doi:10.1161/JAHA.121.022746).

A survey of European hedgehogs shows antibiotic resistance has been widespread in the natural world for years

Ophthalmic complications of microgravity

Spaceflight associated neuro-ocular syndrome, characterised by a persistent reduction in visual acuity, focal retinal ischaemia, and swelling of the optic disk, is common in people who have spent time in space. Magnetic resonance imaging in 12 astronauts before and after a spaceflight finds that it's related to an increase in intracranial dural venous volume. It's thought that loss of hydrostatic pressure in conditions of microgravity leads to a rostral shift of fluids from the lower body, resulting in venous congestion in the head and neck and raised intracranial pressure (*JAMA Surg* doi:10.1001/jamanetworkopen.2021.31465).

Antibiotic failure in acute appendicitis

Several trials have shown that uncomplicated acute appendicitis can often be treated safely and effectively with antibiotics alone. A secondary analysis of data from one of these trials identifies an appendiceal diameter of ≥15 mm or fever >38°C as risk factors for antibiotic failure and subsequent need for surgery. Optimal treatment of appendicitis might include early appendectomy if these features are present (*JAMA Surg* doi:10.1001/jamasurg.2021.5003).

Diabetes after bariatric surgery

Long term follow-up of 6000 people whose obesity was treated surgically finds, as one would expect, that weight loss is strongly associated with remission of type 2 diabetes. Likelihood of remission improved with increasing weight loss until there had been a 20% reduction in pre-surgical weight. At this point, remission of diabetes was two to three times commoner than in those whose weight loss was less than 5% of pre-surgical weight, even if they had been using insulin at the time of surgery (*Diabetes Care* doi:10.2337/dc21-0714).

Olive oil and lower all-cause mortality

Among 90 000 people taking part in the Nurses' Health study or the Health Professionals follow-up study, those with a higher dietary intake of olive oil experienced substantially lower mortality from all causes, cardiovascular disease, cancer, and neurodegenerative diseases. Mediterranean diets have long been linked to lower cardiovascular disease risk and, as olive oil is a prominent feature of such diets, this isn't a very surprising result. An unanswered question is whether olive oil has directly protective effects or if it's just a marker for a healthy way of life (*J Am Coll Cardiol* doi: 10.1016/j.jacc.2021.10.041).

Cite this as: *BMJ* 2022;376:o148