education

RESEARCH REVIEWS Fortnightly round up from the leading medical journals

Ondansetron for gastroenteritis in children

Ondansetron is often given to vomiting children in emergency departments. But does giving parents or caregivers a supply of the anti-emetic at discharge from hospital help their children recover sooner?

A trial enrolled children aged between six months and 18 years who had presented to the emergency department with acute gastroenteritis after vomiting at least three times. After receiving an initial dose of ondansetron in the emergency department they were randomised to go home with either up to six doses of oral ondansetron (one dose up to three times a day) or placebo. Those given ondansetron were less likely to have moderate-severe gastroenteritis over the next seven days (5.1% v 12.5%, adjusted odds ratio 0.50, 95% confidence interval 0.40 to 0.60). Vomiting stopped slightly sooner in the children randomised to ondansetron, but there was no difference between the groups in some of the other secondary outcomes, including ongoing vomiting after enrollment and subsequent need for intravenous fluids.

N Engl J Med doi:10.1056/NEJMoa2503596

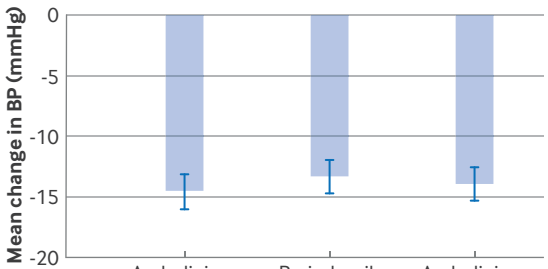
Retrospectoscopes and cancer diagnosis

The term "retrospectoscope" is often used cringingly in debriefs looking back at missed opportunities to diagnose or treat a serious illness. The retrospectoscope may be going digital—and getting larger—if a new cohort study in *JAMA Internal Medicine* is anything to go by. Researchers developed digital quality measures for advanced colorectal and lung cancers and found that around two thirds of patients had missed opportunities for diagnosis. The retrospectoscope found frequent opportunities to act on abnormal chest imaging findings in those with advanced lung cancer,

Dual anti-hypertensive therapy in India

Prescribing a single antihypertensive tablet containing two drugs seems to be a common approach in many countries, but still hasn't really caught on in the United Kingdom. A randomised control trial sought to determine which combination is most effective for patients of South Asian origin. The study randomised 1981 participants across multiple sites in India, where 300 million people are estimated to have hypertension. The three drug combinations studied were amlodipine–perindopril, perindopril–indapamide, and amlodipine–indapamide. Doses were titrated upwards if participants weren't meeting target blood pressures at two and four months. All three combinations lowered ambulatory blood pressure by around ~14/8 mm Hg (see fig 1), with similar side effect profiles.

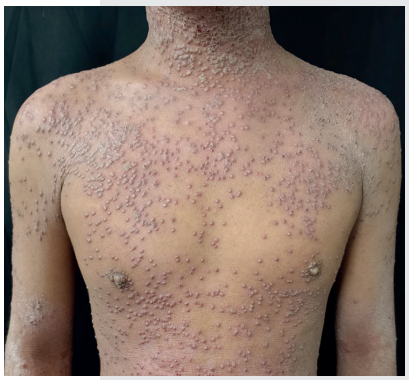
Nature Med doi:10.1038/s41591-025-03854-w



	Amlodipine-perindopril	Perindopril-indapamide	Amlodipine-indapamide
Baseline	135.9 (661)	135.4 (662)	135.3 (658)
6 months	121.4 (661)	122.1 (662)	121.4 (658)

Unadjusted mean change in ambulatory systolic blood pressure after six months

CAVALCANTI, DM, DE OLIVEIRA FERREIRA DE SALES, L, FERREIRA DA SILVA, A, ET AL. LANCET 2025; DOI:10.1016/S0140-6736(25)01186-9



CLINICAL PICTURE

Widespread cutaneous eruption in a patient with atopic dermatitis

This patient in his late teens presented with a one week history of a widespread painful rash, accompanied by fever and fatigue. Two weeks previously he had started oral upadacitinib—a Janus kinase inhibitor—at 15 mg once daily for severe, widespread atopic dermatitis. Physical examination showed numerous vesicles, some with central umbilication, distributed over the neck, anterior trunk, and both upper limbs (figure), with no lymphadenopathy. Herpes simplex virus type 1 (HSV-1) infection was detected by polymerase chain reaction (PCR) testing of a swab specimen, confirming the diagnosis of eczema herpeticum. Treatment with upadacitinib was stopped temporarily. The patient was treated with intravenous aciclovir (5 mg/kg three times daily) for seven days because of the severity of symptoms and his intolerance to oral therapy. He also received topical fusidic acid for localised bacterial superinfection. The

and multiple patients with iron deficiency anaemia and presenting with blood in the stool in those with advanced colorectal cancer.

JAMA Intern Med doi:10.1001/jamainternmed.2025.2875

Metformin for covid-19

A lot of interest has been shown in metformin as a treatment for acute covid-19, both to treat initial symptoms and to prevent long covid. A new randomised control trial finds little evidence for either. People with symptomatic mild-moderate covid-19 were recruited from outpatient settings in the United States, with 3214 participants randomised to receive either metformin or placebo. There was no significant difference in the number of days from beginning treatment to sustained recovery between the two groups, or the likelihood of recovery after 7, 14, or 28 days.

JAMA Intern Med doi:10.1001/jamainternmed.2025.2570

CBT for chronic pain

Cognitive behaviour therapy (CBT) delivered by telehealth (telephone or video calls) or self-directed online modules are more scalable than in-person sessions, and can improve access for people in rural settings or who can't travel. Both telehealth and online methods were more effective than a control intervention for people with chronic pain in a new study set in the United States. The telehealth course of CBT was slightly more likely to lead to a meaningful reduction in pain than online CBT modules. When suggesting cognitive CBT, patients often seem more reluctant to try self-directed online CBT: this seemed to be the case in this trial too, with 48% of those allocated to the online tool completing 6-8 sessions, versus 70% allocated to the telehealth group.

JAMA doi:10.1001/jama.2025.11178

Tom Nolan, clinical editor, *The BMJ*, London; sessional GP, Surrey

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blisters and fever resolved after one week, leaving post-inflammatory hyperpigmentation.

Patients with atopic dermatitis are at an increased risk of developing eczema herpeticum owing to impaired epidermal barrier function and immune dysregulation. Upadacitinib, although effective in managing atopic dermatitis, has been associated with a higher risk of infections, including HSV-1.

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Patient consent obtained.

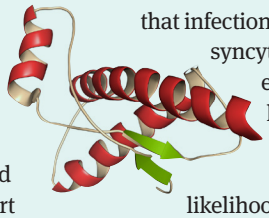
Cite this as: *BMJ* 2025;390:e083871

MINERVA From the wider world of research

Severe neonatal morbidity

Babies who survived serious illness soon after birth continue to have a high mortality risk into adolescence, according to a longitudinal study from Sweden (*JAMA Pediatr* doi:10.1001/jamapediatrics.2025.1873). Among two million children born from 2002 to 2021, around 2% had experienced severe neonatal morbidity. Followed until 2023, their mortality was six times higher than children who hadn't had neonatal problems. Neonatal neurological conditions carried the highest risk.

Misfolded proteins



For decades, Alzheimer's research has focused on two misfolded proteins, amyloid-beta and tau. These may only be part of the story. Using mass spectrometry, more than 200 other misfolded proteins were identified in samples taken from the hippocampi of ageing brains. Although these brains came from a rat model of cognitive ageing, the finding suggests new targets for research (*Sci Adv* doi:10.1126/sciadv.adt3778).

Physical activity and mortality

A systematic review combines data from 85 studies to link higher levels of physical activity to lower mortality from all causes, cardiovascular disease and, to a lesser extent, cancer (*Br J Sports Med* doi:10.1136/bjsports-2024-109122). The effects are large. People who are active throughout life reduce their mortality risk by 30–40%. One weakness is that most studies relied on self-report of how much exercise was taken. Another is doubt about the direction of cause and effect. Does exercise improve health? Or do healthy people take more exercise?

Zoster vaccination and cardiovascular events

Vaccination against herpes zoster is highly effective in preventing shingles and postherpetic neuralgia in older people. A database study from South Korea suggests that it might have wider benefits (*Eur Heart J* doi:10.1093/eurheartj/ehaf230). Among a million people who had received live zoster vaccination, major adverse cardiovascular events were reduced by a third. The protective association persisted for eight years after vaccination.

RSV and cardiovascular events

A retrospective analysis of 500 cases from Rochester, New York, reports that infection with respiratory syncytial virus (RSV) severe enough to require hospitalisation in adults over the age of 18 years greatly increases the likelihood of cardiovascular events (*Clin Infect Dis* doi:10.1093/cid/ciaf310). More than a third of patients experienced such events within 28 days of admission, with heart failure, atrial fibrillation, and myocardial infarction being the most common. Half of these events occurred in individuals with no history of cardiovascular disease.

RSV vaccination in pregnancy

Respiratory syncytial virus (RSV) is the most common cause of acute lower respiratory tract illness in infants. Two years ago, an international trial demonstrated that vaccinating pregnant women against RSV reduced the number of newborns admitted to hospital with lung infections (N Engl J Med 2023 doi:10.1056/NEJMoa2216480). A case control study from the United Kingdom confirms the benefits (*Lancet Child Adolesc Health* doi:10.1016/S2352-4642(25)00155-5). It estimates that RSV vaccine, which was introduced across the UK in late summer 2024, led to a 72 per cent reduction in babies hospitalised with the virus if mothers had been vaccinated.

Cite this as: *BMJ* 2025;390:r1583

CLINICAL UPDATE

CPD READING
0.5 HOURS

Skin cancer prevention and sunscreens

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Skin cancer is the most commonly diagnosed cancer worldwide.[1] The Global Burden of Disease study shows rates of skin cancer continue to rise, largely owing to an ageing population.[1 2] The most common skin cancers include keratinocyte cancers, basal cell cancer and cutaneous squamous cell cancer, and melanoma.

Deaths due to melanoma are projected to increase by about 68% from 2020 to 2040.[1] Although improvements in treatments for advanced melanoma have reduced mortality rates globally, these therapies are expensive and contribute to the high economic burden of skin cancer.[3 4] Access to healthcare and the financial costs of skin cancer diagnoses and treatments are barriers to early detection and survival in low and middle income countries,[2 5] emphasising the importance and cost effectiveness of prevention.[6 7]

Here, we discuss the current evidence regarding skin cancer prevention and sunscreens, including the role of the clinician and how to provide evidence based, tailored behavioural counselling for skin cancer prevention.

WHAT YOU NEED TO KNOW

- The global burden of disease from melanoma is high and increasing; it occurs predominantly as a result of exposure to ultraviolet (UV) radiation (from sunlight or sunbeds) most commonly in people with fair, sun sensitive skin
- The World Health Organization recommends sun protection measures when the UV index is forecast to reach 3 and above
- Regular use of sunscreen can prevent melanoma and squamous cell carcinoma; however, the effectiveness of sunscreen is dependent on the amount applied, coverage of exposed skin, and reapplication
- Opportunistic behavioural counselling from healthcare professionals can increase sun protection behaviours and is recommended for parents of young children, adolescents, and groups at high risk
- Tailor sun protection recommendations to individual risk factors, considering skin pigmentation, concurrent risk of vitamin D deficiency, immune system status, and UV radiation exposure

EDUCATION INTO PRACTICE

- How do you identify patients at greatest risk of skin cancer, and what behavioural counselling do you provide to them?
- What evidence based recommendations for sun protection are you aware of and how do you tailor these by skin type, UV radiation exposure, and other risk factors?

What is the relation between ultraviolet radiation and skin cancer?

Solar ultraviolet (UV) radiation, which is part of the electromagnetic spectrum, can be divided into three bands based on wavelength: UVA (315-400 nanometres), UVB (280-315 nanometres), and UVC (<280 nanometres). All UVC is absorbed by the atmosphere, and all UVA and 90% of UVB passes through the Earth's atmosphere and is absorbed by human skin.[8 9]

Exposure to UV radiation, either from the sun or artificial sources (sunbeds), is the leading cause of skin cancer.[9] UV radiation can also cause sunburn, skin damage, and eye damage, including cataracts and pterygium.[4 9] WHO identifies children and adolescents as particularly vulnerable to the harmful effects of UV radiation, because of their functionally immature skin and eye structure, which provide less protection from UV radiation.[9 10]

The International Agency for Research on Cancer estimates that 76% of new melanoma cases are attributable to UV radiation exposure.[11]

Who experiences melanoma?

Phenotypic characteristics, including eye colour, hair colour, skin pigmentation, and propensity to develop naevi, are controlled by melanin pigmentation. Melanin (especially eumelanin and pheomelanin) determines individual susceptibility to DNA damage and tumour development.[17]

In general, people who have fair skin, high sun sensitivity, freckles, light eyes, and red or light hair are at increased risk of melanoma[17 18] (table). Other clinical predictors include personal history of melanoma and other skin cancers, family history of melanoma, and immune system deficiency.[18-25] These clinical risk factors, combined with age and patterns of exposure to UV radiation (including sunbed use), determine overall risk of melanoma. Online risk calculators can assist healthcare professionals to consider how multiple risk factors combine to assess an individual's absolute risk of first and subsequent melanoma.[26 27] Polygenic risk scores provide modest gains in risk prediction (ie, above demographic, clinical, and UV exposure risks), which are insufficient to support their use in routine clinical practice.[28]

Solar UV radiation is the predominant cause of melanoma, but genetic risk factors are particularly important for people with a low propensity to develop naevi, and for melanomas that develop in less sun exposed areas.[29 30]

Acral lentiginous melanoma is a rare subtype that accounts for 2-3% of melanomas and affects people with more deeply pigmented skin disproportionately, including black, Hispanic, and Asian populations.[31] The cause of acral lentiginous melanoma remains unknown. However, as acral lentiginous melanoma appears in areas of the body that experience repetitive stress commonly, such as the palms, soles, and nailbeds, it has been suggested that mechanical factors (and not UV radiation) may be an important contributing factor.[31]

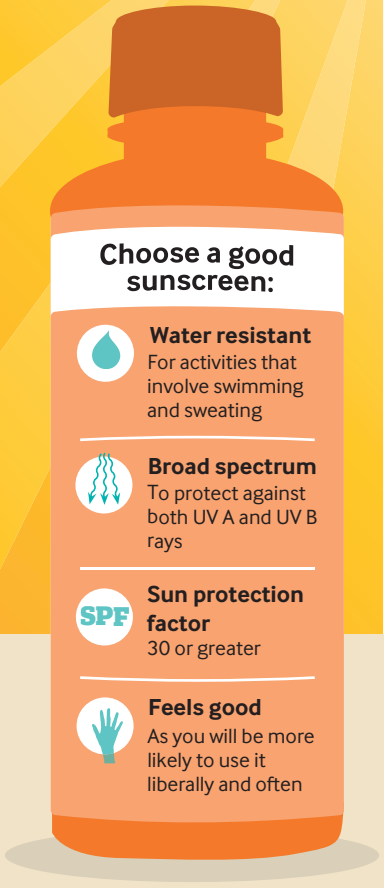
thebmj Visual summary

Sun protection: How to avoid being caught out

Skin cancer is the most commonly diagnosed cancer worldwide. Tailored skin cancer prevention could be implemented by opportunistically counselling high-risk patients during skin lesion checks and full-body examinations. This graphic presents recommendations for using sun protection

Combine sunscreen with other forms of sun protection

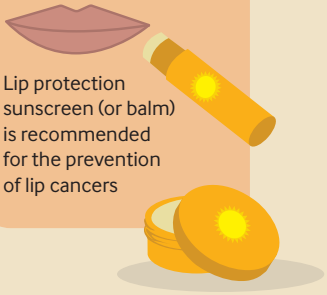
- **For greatest protection, avoid midday sun or seek complete shade cover**
- **Use protective clothing:**
  - Clothes that reach the wrists and ankles
  - Broad brim, bucket, or legionnaire style hat
  - Sunglasses with a UV 400 rating
- **Avoid using sunscreen in isolation, or to extend time in the sun**



Choose a good sunscreen:

- **Water resistant**
  For activities that involve swimming and sweating
- **Broad spectrum**
  To protect against both UV A and UV B rays
- **Sun protection factor**
  30 or greater
- **Feels good**
  As you will be more likely to use it liberally and often

Use lip protection



Lip protection sunscreen (or balm) is recommended for the prevention of lip cancers

Avoid aerosol spray sunscreens

- It can be difficult to judge whether they have been applied evenly and generously
- Up to 1/3 aerosol sunscreens can be lost in even light wind (10 kph)

Make sunscreen part of your daily routine

- Apply sunscreen on days when the UV Index is forecast to reach 3 and above
- Use the SunSmart Global UV app to check the UV index forecast and set notifications

Apply generously on all areas of exposed skin

Use 1 teaspoon for:

- Each limb
- Front and back of torso
- Head and neck

Total: 7 teaspoons (35 mL)

Re-apply when needed

Re-apply after swimming, sweating, and towel drying (including for water resistant sunscreens)

Re-apply every 2 hours during prolonged exposure

Risk factors associated with developing melanoma

Relative risk	Risk factors
Reduced relative risk	Deeply pigmented brown-black skin that never or rarely burns
Increased relative risk	Fair skin that burns or minimally tans, freckling, light eye colour, light or red hair colour Actinic damage indicators, including actinic keratoses (a precursor to cutaneous squamous cell carcinoma) Past history of keratinocyte cancer Medical history of compromised immunity, including immunosuppressive treatments for solid organ transplant, HIV-AIDs co-infection, some lymphoproliferative disorders (eg, chronic lymphocytic leukaemia) Family history of melanoma in first degree relative Social history of high sun exposure and sunburns during childhood, and/or high intermittent, intense UV radiation exposure from suntanning or sunbed use
High-very high relative risk	>5 atypical (dysplastic) naevi >100 common naevi Medical history of previous melanoma

Reduced relative risk= <1.00 (compared with unexposed group); increased relative risk = 1.00-4.99: high to very high relative risk= ≥5.00. Estimates for relative risk synthesised from systematic reviews and meta-analyses.[18-24] There is uncertainty around the increased relative risk among people receiving treatment for immune mediated inflammatory diseases (eg, inflammatory bowel disease, rheumatoid arthritis), owing to a lack of large studies for inclusion in meta-analytic studies[25]

What role do clinicians play in melanoma prevention?

Clinicians and healthcare professionals working in primary care are well placed to identify individuals with risk factors for melanoma and provide tailored advice. A 2018 US Preventive Services Taskforce systematic review recommended that clinicians should provide behavioural counselling for prevention of skin cancer to young adults, adolescents, children, and parents of young children, as well as adults with fair, sun sensitive skin types (table 2, bmj.com).[32] Although the review concluded that behavioural interventions can lead to small to moderate improvements in sun protection behaviours in children and adults, it also reported a paucity of evidence demonstrating effectiveness in reducing sunburn and skin cancer.[33] Notably, no studies included in the review extended beyond three years' follow-up, which limited the evidence available to evaluate reductions in naevi and skin cancers.[33]

Consultation record audits and survey data on skin cancer related medical appointments show that opportunistic counselling for this highly preventable cancer is sporadic.[34-36] In one cross-sectional study of 1506 US medical professionals, awareness of the US Preventative Services Taskforce Recommendations increased the odds of frequently providing behavioural counselling on sun protection (adjusted odds ratio (AOR) 1.56, 95% confidence interval (CI) 1.24 to 1.95) and indoor tanning (AOR 1.89, 95% CI 1.31 to 2.72).[35] However, clinicians from high income countries, where the global burden of skin cancer is concentrated,[1] report significant resource constraints to providing behavioural counselling within standard consultations.[27 35]

Regarding how to counsel people's behaviour, the Taskforce review found no clear or consistent patterns to recommend specific intervention components or characteristics.[33] Similarly, a 2024 narrative review identified 31 mixed methods studies relating to the provision of skin cancer prevention interventions in a primary care setting.[27] The study's findings on effectiveness of behavioural counselling echo those of the Taskforce review; however, it additionally found limited evidence to support the use of risk assessment tools and new technologies, such as smartphone apps, to tailor sun protection advice.[27]

In the absence of dedicated interventions to support behavioural counselling and healthcare resourcing, healthcare professionals are encouraged to consider how tailored skin cancer prevention could be implemented by opportunistically counselling high risk patients during skin lesion checks and physical examinations,[27] or as an add-on to presentations for other reasons. Furthermore, behaviour change theory suggests that health service funding models that incentivise and resource clinicians to provide risk tailored skin cancer prevention counselling may be needed to increase uptake of this intervention.[37]

WHO recommends using sun protection when outdoors on days when the UV index is forecast to reach 3 and above

When is sun protection needed?

WHO recommends using sun protection when outdoors on days when the UV index is forecast to reach 3 and above.[9] Although the UV index is central to determining when to protect the skin, population level use of the UV index to inform sun protection is low across all regions globally.[38 39]

Reflexive responses, whereby sunshine and warm temperatures drive sun protection behaviour, rather than the UV index, leave people vulnerable to UV damage, which can also occur on overcast and cloudy days. Tools like the WHO's SunSmart Global UV app, which is free, non-commercial, and available in multiple languages, can be used to support patients to use the UV index to establish sun protection routines globally.

Sun protection measures recommended by WHO including limiting time in midday sun, seeking shade, wearing protective clothing that reaches the wrists or ankles and a broad brim, bucket, or legionnaire style hat, wearing sunglasses that provide 99% to 100% UVA and UVB protection, and applying broad spectrum, high SPF sunscreen to remaining areas of exposed skin.[9] Use sunscreen in combination with other sun protection measures, as a last line of defence.[40]

How to tailor prevention advice for different population groups

Infants and children under 2

- Recommend that infants and children under 2 are kept out of direct sunlight where possible, as their skin is vulnerable to UV damage, and they are susceptible to overheating and dehydration[50 51]
- When outdoors, encourage complete protection using a combination of shade, light weight, loose, closely woven clothing that covers the skin, wide brim/legionnaire style hats, and sunglasses as appropriate for age
- Infants and young children are at increased risk of systemic drug absorption because of their small body mass to surface area ratio. As such, parents and carers should be advised that sunscreen is not recommended for young babies (<6 months)[42-51]
- For children over 6 months, sunscreen can be used as a last line of defence on small areas of unprotected skin.

Advise parents and carers to:

- Choose a fragrance free, low irritant, or special infant formulation to minimise potential allergens. Formulations that use inorganic UV filters—for example, zinc oxide and titanium dioxide, will reduce potential for irritation, sensitisation, and skin penetration[51-53]
- Avoid aerosol sunscreens. Further to application challenges, they may trigger or exacerbate asthma and allergy symptoms in children[50]

People who work outdoors

- Encourage the use of all available protective measures. This includes good quality shade (from above and the sides) and personal protective equipment (ie, clothes that cover as much of the skin as possible, a wide brimmed hat or hardhat with sun shields, ear and neck guards, lip balm with SPF 15 or more, and a broad spectrum, high SPF sunscreen that is reapplied frequently) whenever outdoors[54 55]
- To protect the eyes, recommend that people who work outdoors routinely wear safety glasses, sunglasses, or prescription eyeglasses with UV protective lenses in combination with headwear[54 55]
- Water and sweat resistant "dry touch" sunscreens may be preferable, but there are no international standards to evaluate sunscreen biostability during activity or in response to environmental challenges such as dust, dirt, and salinity[54]
- Wherever possible, recommend that employers restructure work duties to avoid working in unshaded outdoor areas during peak UV radiation times[54 55]

People who are immunocompromised

- Include patient education on fostering photoprotective behaviours as a vital component of routine care for people who are immunocompromised, especially for those receiving solid organ transplant[56 57]
- Advise patients to be diligent about sun protection and avoid unnecessary UV radiation exposure.[56 58] Phone apps with reminders may help to establish sun protection routines[59]
- Early detection is key: educate patients on skin self-examination and refer to local skin cancer services if indicated
- The evolving role of neoadjuvant strategies, targeted therapy, and immunotherapy requires further exploration[56]

People with deeply pigmented skin

- Photo-exacerbated pigmentary disorders are among the most common dermatology consultations for people with skin of colour[60]
- To protect against photo-ageing, acquired pigmentary disorders, and other adverse skin effects, recommend sun protection if outdoors for an extended period (eg, ≥2 hours) when the UV index is 3 and above, and that sunglasses are routinely used for eye protection[61 62]
- Few articles (5%) on sunscreens consider people with skin of colour.[63] Further, there is a lack of experimental evidence regarding efficacy and potential harm of routine use of high SPF sunscreen among people with deeply pigmented skin.[4] Daily sunscreen application may not be needed for this patient group unless they are out for extended periods in high solar UV radiation environments. Therefore, discuss sun protection recommendations with consideration of vitamin D requirements[61]
- Advise patients with deeply pigmented skin to choose broad spectrum sunscreens that provide protection against long wave UVA (340-400 nm) and visible light,[53-62] such as a tinted sunscreen that contains iron oxides and pigmentary grade titanium dioxide.[64 65] There is a need for research and development of effective and cosmetically appealing sunscreen formulas for people with deeply pigmented skin[60]

People with oculocutaneous albinism

- Undertake patient education on fostering photoprotective behaviours from an early age for people with oculocutaneous albinism, who lack melanin and are highly susceptible to UV radiation damage and skin cancer, especially cutaneous squamous cell carcinoma[66 67]
- Advise people with oculocutaneous albinism to be diligent about sun protection and avoid unnecessary UV exposure.[62 66] Encourage making use of shade (both built and natural) and reducing outdoor activities during maximal UV radiation period
- Recommend that sun protective measures include daily use of protective clothing, hats, sunglasses with a UV 400 rating and broad spectrum, high SPF (50+) sunscreen on the ears, lips, eyelids, and neck as well as all other exposed bodily sites
- To provide adequate protection to the head, neck, and ears, hats should have a broad brim, or legionnaire style neck covering. When worn in conjunction with sunglasses with a UV 400 rating, this will also reduce the amount of UV radiation reaching the eyes[42]
- There are no internationally endorsed standards for sun protection for high risk population groups. As such, most of the recommendations are drawn from topical, narrative style evidence summaries,[4-66] in addition to one systematic review,[67] one scoping review,[57] two Delphi studies,[53 55] and two evidence based position statements.[61 62]

How effective are sunscreens?

The degree to which sunscreens protect against sunburn is indicated by their sun protection factor (SPF). Importantly, sunscreens also reduce the risk of other forms of UV damage. Evidence reviews conclude consistently that regular sunscreen use can reduce the risk of melanoma, cutaneous squamous cell carcinoma and precursor lesions, as well as signs of ageing, including wrinkles, telangiectasia, and UV radiation induced pigmentary alterations.[41-43] However, although there is compelling, consistent evidence that regular sunscreen use prevents DNA damage, conclusions about prevention of skin cancer are drawn from a small number of experimental trials.

An Australian randomised controlled trial that compared daily to discretionary sunscreen use found that, relative to the discretionary use group, a 40% reduction in cutaneous squamous cell carcinoma and no effect on basal cell carcinoma in the daily sunscreen use group at the end of the 4.5 year study.[44] Treatment effects (ie, of daily sunscreen use) were similar at 8 year follow-up.[45] Ten years after trial cessation, there were 11 melanomas in the treatment group and 22 in the control group (hazard ratio (HR) 0.50, P=0.051), and a statistically significant reduction in invasive melanoma in the treatment group (HR 0.27, P=0.048).[46] Two additional randomised controlled trials, conducted with Australian and US adults, found that daily or routine sunscreen use also reduces the risk of new actinic keratoses.[47 48]

Competing interests: See bmj.com.

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Find the full version with references at https://doi.org/10.1136/bmj-2025-085121

EDITORIAL

Improving skin cancer prevention

Achieving behaviour change through tailored recommendations

Skin cancer continues to be a substantial and increasing public health concern in many countries. The global incidence of melanoma and the keratinocyte cancers—basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)—has been steadily rising over the past two decades, particularly in fair skinned populations, partly driven by ageing populations.[1 2]

In their education article (doi:10.1136/bmj-2025-085121), Nicholson and colleagues present a summary of current evidence based recommendations for preventing skin cancer.[7] As is established practice, they recommend seeking shade during peak sun hours, wearing protective clothing, and regularly applying broad spectrum, high sun protection factor (SPF) sunscreen to exposed skin. Avoiding sunbeds and promoting early detection through regular skin self-examinations (and professional skin checks when indicated) are also strongly recommended. Importantly, the authors highlight the vital role of clinicians in prevention efforts.

Behavioural counselling

Growing evidence suggests that tailored advice for people at high risk—such as those with fair skin, a history of sunburn, numerous or atypical moles, a family history of melanoma, or a personal history of skin cancer—may have the greatest effect on sun safe behaviours.[8] Opportunistic behavioural counselling is particularly recommended for people in these high risk groups, as well as for parents of fair skinned young children and adolescents. However, one size does not fit all. Behavioural counselling on sun protection should be adapted for people at increased risk of vitamin D deficiency, such as those with darker skin types, limited sun exposure, or cultural clothing practices that reduce skin exposure to sunlight.

Guidance should be adapted based on risk factors, skin type, and family history

Evidence based tools are being developed to support this approach, offering tailored recommendations that reflect the varying skin cancer risks and vitamin D requirements of diverse populations.[9 10] For example, an updated position statement developed for the Australian population includes advice on how to balance the benefits and harms of sun exposure based on skin type. For people with darker white or olive skin types, the recommendations are further tailored depending on whether they have risk factors for melanoma. Those with deeply pigmented skin are advised that routine sunscreen application is not needed, but that sun protection may be needed if outdoors for two hours or more. The National Institute for Health and Care Excellence has also recommended that clinicians offer sun protection advice tailored to balance skin cancer risk and vitamin D requirements.[9]

Role of sunscreen

Although sunscreen is important in protecting against ultraviolet radiation, it should be considered an adjunct measure, used when shade and protective clothing are impractical. Using any type of sunscreen to prolong time in the sun or to support intentional tanning undermines its purpose.[11] Experimental studies have shown that sunscreen prevents ultraviolet induced DNA damage in human skin cells in vivo,[12] and a randomised controlled trial found a protective effect against melanoma and squamous cell carcinoma.[13 14] However, some observational studies have reported a positive association between sunscreen use and melanoma risk.[15] This probably reflects intractable confounding, particularly confounding by indication, when people at higher risk are more likely to use sunscreen.[16]

One of the biggest challenges is the spread of misinformation through digital media, often amplified by algorithms prioritising emotionally charged content over evidence based information, which has undermined public trust in sunscreens.[18] Nicholson and colleagues provide practical, evidence based guidance for clinicians to address potential patient concerns about sunscreen use, including links to trusted information sources.[7] An effective approach might be to listen respectfully, validate the patient's concerns, and then redirect them towards accurate, evidence based information.

There are also reports of a stabilisation in the incidence of BCC and SCC in younger birth cohorts in Canada,[24] as well as a decline in treatment rates for keratinocyte cancers among people aged under 45 years in Australia.[25] Although this may reflect the success of primary prevention programmes, other factors may be contributing. These include demographic changes caused by migration—for example, a reduction in the proportion of people with high risk European ancestry in Australia[20]—and a trend among younger generations to spend more time indoors.[26] Ongoing monitoring of incidence trends will be important to respond to the long term net effects of prevention efforts and shifting population behaviours.

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STATE OF THE ART REVIEW

Cognitive and mental health outcomes in long covid

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CPD READING

0.5 HOURS

Long covid refers to a range of chronic, systemic, and often disabling health conditions associated with SARS-CoV-2 infection.[1 2] By September 2024, 5.3% of the US general population reported symptoms lasting three or more months after acute SARS-CoV-2 infection,[3] whereas the World Health Organization (WHO) estimates that 10–20% of people infected by SARS-CoV-2 worldwide go on to develop long covid.[4]

The reported prevalence of long covid varies widely by study, time, and data source. Even among high quality studies, data range from conservative estimates of 6.2% of adults who ever had covid-19 to 45% across prospective epidemiological studies, cross-sectional health surveys, electronic health records (EHR), and systematic reviews and meta-analyses.[23-26]

Among the range of symptoms experienced by those with long covid, cognitive and mental health concerns (commonly referred to as neuropsychiatric symptoms), such as "brain fog," concentration and memory difficulties, depression, and anxiety are especially common,[7-9] affecting approximately 20.4% of long covid patients.[10] Neuropsychiatric symptoms often persist longer than other long covid symptoms,[8 11-14] are associated with functional limitations[7 11 15 16] and ultimately pose considerable burden on individuals, health systems, and the economy.[17]

WHAT YOU NEED TO KNOW

- Roughly one in five adults who meet criteria for long covid present with objective or subjective cognitive dysfunction or elevated symptoms of depression or anxiety lasting ≥12 weeks from an acute covid illness
- Neuropsychiatric long covid symptoms are thought to be causally diverse, and a range of risk factors as well as biological, psychological, and environmental mechanisms have been suggested as contributors
- When present, objective cognitive deficits tend to be modest, with some evidence suggesting increased risk of dysfunction and decline specifically for older adults with a history of severe acute illness. Delayed emergence of psychiatric symptoms may occur in the weeks and months after acute covid
- Emerging research points to the early recovery period as a potential window for intervention, but evidence based treatment remains lacking

Definition of long covid

A reliable diagnostic marker for long covid is currently lacking, as is a consensus definition or generally agreed set of diagnostic criteria. Hence, a range of terms exist to characterise long covid, including post-covid-19 condition or syndrome (PCC or PCS), post-acute sequelae of SARS-CoV-2 infection (PASC), long haul covid-19, or chronic covid-19.[32] Definitions from national and international organisations differ on clinical criteria, particularly regarding the initial diagnosis of covid-19, timing since symptom onset, and duration of symptoms required for long covid diagnosis (see table1 online).

Mechanisms

The mechanistic pathways of long covid neuropsychiatric symptoms are complex and multifactorial. While many studies have explored pathways related to acute neurological complications, fewer have examined the mechanisms behind persistent cognitive dysfunction and mental health symptoms.

Direct neuroinvasion by SARS-CoV-2, peripheral inflammation and related immune responses, endothelial disruption, and vascular processes such as thrombosis, ischaemia, and hypoxia have been reported as potential mechanisms of long covid (see fig 1).[49-52] Some studies indicate that long covid neuropsychiatric dysfunction may result from an overproduction of cytokines, with the related hyperinflammatory response allowing viral particles, cytokines, and immune cells to enter the central nervous system, potentially altering brain function.[54 55] Increased permeability of the blood-brain barrier has been observed during acute SARS-CoV-2 infection and thereafter, including among those with persistent cognitive complaints.[56 57]

Proinflammatory and hypercoagulable states associated with covid-19 can increase the risk of serious vascular complications such as ischaemic stroke and related cognitive dysfunction.[58-60] Microvascular injury in the absence of stroke has been observed in the brains of individuals who died of covid-19.[61] Hypoxia and hypoxaemia may further contribute to brain dysfunction via a pathway of metabolic alterations, cell apoptosis, and neural systems dysfunction.

Higher aggregate systemic inflammation during acute covid-19 has predicted both depressive symptoms and cognitive performance following hospital discharge.[72-74] Several studies point to specific immune profiles related to long covid neuropsychiatric outcomes. Inflammatory proteins, including those associated with endothelial repair, neural growth regulation, and cell turnover, have also been significantly elevated in those with severe covid-19 and persistent long covid cognitive and mental health symptoms.[76]

Although these remain promising areas for future investigation, the mechanisms underlying long covid related neuropsychiatric dysfunction remain speculative.

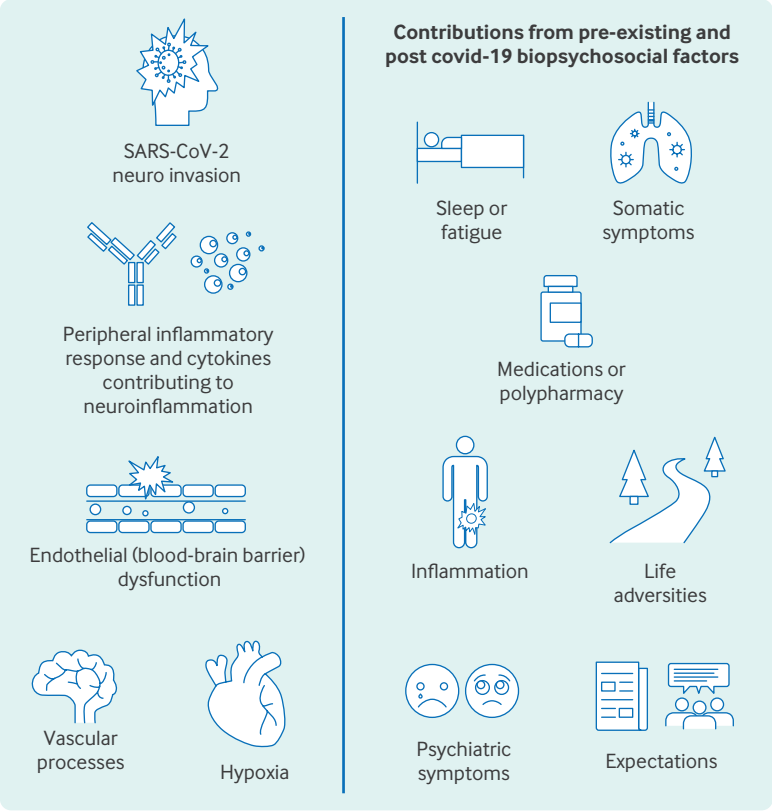

Fig 1 | Potential mechanisms of long covid

Limited data suggest that, in a proportion of individuals with long covid, symptoms may reflect a somatic symptom disorder.[88 89] Long covid and somatic symptom disorder share several predisposing, precipitating, and perpetuating factors including demographic characteristics, psychiatric comorbidities, and adverse childhood experiences.[88-91] Clinical data from adults presenting with cognitive concerns after non-severe acute covid-19 illness demonstrate elevated rates of heightened somatic preoccupation often paired with clinically significant symptoms of depression and anxiety.[94 95] Notably, the presence of a somatic symptom disorder does not preclude the existence of demonstrable physical dysfunction.

Neuropsychiatric symptoms in long covid

Risk factors

A greater proportion of women than men report cognitive dysfunction and psychiatric symptoms following covid-19 and meet criteria for long covid.[45-102] Age has been found to modify the relation between covid-19 and later outcomes, though findings are conflicting.

The association between severity of acute illness and neuropsychiatric symptoms after SARS-CoV-2 infection is complex. Data from patient registries, large epidemiological studies, and meta-analyses indicate that greater severity of acute illness, typically indexed by the need for hospitalisation, is associated with poorer cognitive and mental health outcomes.[45 107-110] However, findings are not uniform, and neuropsychiatric symptoms are also reported at high rates among individuals who experienced less severe acute illness, particularly in treatment-seeking cohorts.[95 105 111-113] There are also data indicating that rates of neurocognitive symptoms and new onset mental health disorders after hospitalisation for covid-19 are similar among those hospitalised for non-covid illness of matched severity, suggesting that factors related to severe illnesses and hospitalisation may drive such outcomes.[83 114]

A series of studies demonstrated that vaccination is associated with lower risk for long covid, including cognitive dysfunction[45 115 116] and mental health symptoms.[117] Data on the risk of neuropsychiatric outcomes by covid-19 variant is mixed. While persistent or increased rates of psychiatric and cognitive diagnoses were reported with the emergence of the later delta and omicron variants,[58] evidence suggests more recent SARS-CoV-2 variants confer lower risk of long covid[118] and are linked to smaller cognitive deficits.[44 115]

A range of pre-existing physical health comorbidities (such as cardiovascular disease, obesity, hypertension, sleep apnoea) are related to poorer neuropsychiatric outcomes following an acute covid-19 illness.[45 119 120] Many of these serve as independent of covid-19 risk factors for cognitive dysfunction. Pre-existing mental health conditions and subjective cognitive dysfunction have also emerged as risk factors for more severe acute covid-19 as well as for the development and persistence of long covid neuropsychiatric and somatic symptoms[121 122] in hospitalised and non-hospitalised patient groups.[113 121-125] Several studies with pre-existing and early neuropsychiatric data reveal a dose dependent relation between early neuropsychiatric symptoms and the risk of developing persistent symptoms following covid-19.[122 126]

Cognitive outcomes

Electronic health records (EHR) data suggest that SARS-CoV-2 infection increases the risk of cognitive disorder diagnosis. For example, a study of >1.5 million US veterans with covid-19 (compared with >5.8 million contemporaneous no-covid-19 controls) found heightened risk for diagnoses of memory dysfunction (hazard ratio 1.77 (95% CI 1.68 to 1.85)) and Alzheimer's disease (HR 2.03 (1.79 to 2.31)) at one year post-illness.[105] A large international study (n=1 487 712) compared patients with covid-19 with a contemporaneous cohort of matched patients with other respiratory infections: it found an increased risk of cognitive deficit (HR 1.36 (1.33 to 1.39)) and dementia (HR 1.33 (1.26 to 1.41)) remained at two years post-infection in those with a history of covid-19.[58]

A recent systematic review and meta-analysis of 43 studies of those with a history of covid-19 and/or long covid underscores the wide variability in prevalence of subjective cognitive dysfunction, with reports ranging from 15% to 80% at 12 or more weeks after diagnosis and an overall prevalence of 18%.[99] Finally, in one of the few studies to have statistically adjusted for pre-

covid-19 health status and differentiated between covid-19 history and long covid, an estimated 2.2% (95% uncertainty interval (UI) 0.3% to 7.6%) of individuals who experienced a symptomatic SARS-CoV-2 infection and 35.4% (9.4% to 75.1%) of those with long covid reported cognitive difficulties three months after acute illness.[27]

Despite substantial research, a consistent cognitive profile associated with long covid has not emerged. Specific cognitive domains, such as attention/concentration,[142 147] executive functioning,[115 138 147 148] processing speed,[107 146 148] and memory[115 147] have each been identified as the most prominent areas of cognitive dysfunction associated with long covid.

Overall, the long covid literature indicates that, when present, the magnitude of objective neurocognitive dysfunction tends to be mild.[90 151]

As the majority of covid-19 cases are now of mild to moderate severity, there is particular concern about the cognitive consequences of these milder acute illnesses.[151 152] A meta-analysis of data published through June 2023 examined cognitive outcomes across 54 studies (>75% of which focused on individuals with long covid or post-acute sequelae of SARS-CoV-2 infection (PASC)) at an average six months from mild to moderate acute covid illness while also exploring mental health outcomes.[152] A small but statistically significant overall effect was observed, with the covid group performing more poorly than healthy controls and/or normative data (g=−0.36 (95% CI −0.45 to −0.28)).

Cognitive performance validity testing is recommended in long covid clinical care and research as it is a standard of practice for neuropsychological assessment and provides objective evidence regarding an examinee's cognitive scores.[21 153] Clinically, the use of performance validity testing is essential in demonstrating the veracity of low cognitive scores and guiding appropriate care.

Mental health outcomes

The global covid-19 pandemic was associated with an increase in mental health symptoms such as depression and anxiety.[58 105] Against this backdrop, psychiatric symptoms have emerged as a significant contributor to long covid related disability.[145]

Studies have generally reported increased rates of psychiatric diagnoses following an acute covid-19 illness. A systematic review of 151 studies published through September 2021 estimated depression and post-traumatic stress disorder (PTSD) prevalences to be 18.3% and 17.9%, respectively, when assessed between four and 20 weeks from covid symptom onset.[9] UK BioBank data from one year after illness similarly demonstrated increased incidence of mental health diagnoses among 26 101 individuals with a history of covid-19 compared with 380 621 contemporary controls (hazard ratio 1.54 (95% CI 1.42 to 1.67)).[157] Electronic health record data from the US Department of Veterans Affairs have shown comparably elevated risk (1.43 (95% CI 1.38 to 1.47)) for a mental health disorder composite one year after covid-19 among 154 068 affected individuals compared with roughly 11 million contemporaneous and historical covid negative controls. While hospitalisation generally increases risk for psychiatric diagnoses both independent of and in the context of covid-19,[105 158 159] several studies report that rates of psychiatric complications after hospitalisation for covid-19 do not differ from those observed following hospitalisation for a similarly severe non-covid illness.[83 160]

Despite substantial research, a consistent cognitive profile associated with long covid has not emerged

Evidence from studies examining rates of elevated psychiatric symptoms, rather than formal diagnoses, is mixed, and few have focused on symptoms persisting ≥12 weeks. A systematic review of 23 studies published through October 2021 included individuals with symptoms persisting ≥4 weeks and found marked variability in the prevalence of elevated psychiatric symptoms.[113] Rates of anxiety ranged from 6.8% to 47.8%, depression from 4.6% to 35.9%, and PTSD from 13.0% to 42.8%. A review of 33 studies assessing 6743 people one to six months after a covid diagnosis found no compelling evidence of poorer mental health outcomes relative to the general population, with 12.2% reporting PTSD, 11.1% reporting anxiety, and 10.4% reporting depression at >12 weeks after illness.[161] The most informative data to date come from a nationally representative US sample of 25 122 adults.[162] A higher prevalence of moderate symptoms of depression (16.8% *v* 7.1%; adjusted odds ratio (AOR) 1.96 (95% CI 1.51 to 2.55)) and anxiety (16.7% *v* 6.3%; AOR 2.21 (1.53 to 3.19)) was observed in those with long covid of ≥3 months' duration compared with non-long covid controls.

Neuropsychiatric symptom trajectories

Considerable heterogeneity exists with respect to the reported longitudinal course of cognitive and mental health outcomes associated with both symptomatic covid-19 and long covid. Thus far, studies have variably demonstrated remission of neuropsychiatric issues over time, symptom persistence or fluctuation, delayed emergence of such issues, or a deteriorating clinical picture for at-risk populations.

In a population based cohort of adults in Ecuador, declines in MoCA cognitive scores at six months were observed among those with a prior covid-19 illness while scores of unaffected individuals remained stable. Scores rebounded in the covid group by 12 months' follow-up, suggesting cognitive recovery.[163] Conversely, a cohort study of adults age ≥60 years who had been hospitalised for covid-19 in Wuhan, China, early in the pandemic compared their cognitive functioning against that of unaffected spouses. At six and 12 months after discharge, a greater proportion of covid survivors with severe acute illness demonstrated mild cognitive impairment (26.5% and 26%, respectively) or dementia (10% and 15%, respectively) compared with those with milder illness and controls (<5.4% across time points).[110 164] However, deterioration may be time limited. When followed from 12 to 30 months after

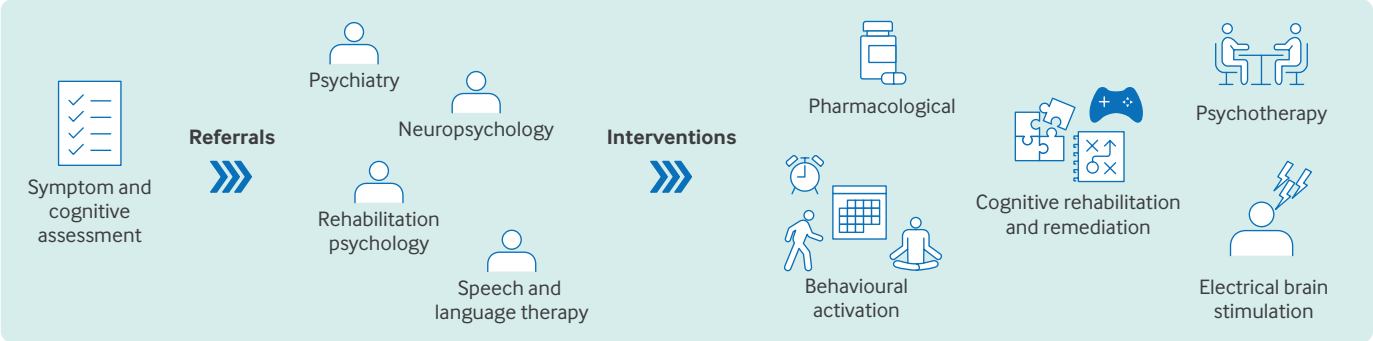

Fig 2| Optimal clinical care of patients with long covid

discharge, covid survivors showed less steep cognitive decline relative to control groups, and a small proportion (8%) improved over this period.[165] Wang and colleagues similarly demonstrated increased risk of receiving an Alzheimer's disease diagnosis among older adults in the year following a covid illness compared with those with other respiratory illnesses.[166] However, a recent meta-analysis found that, although dementia risk is elevated among older adults after covid-19, this risk does not exceed that observed for other respiratory infections.[168]

Symptom management

Given the phenotypic variability of long covid neuropsychiatric presentations, a patient centred or individualised treatment approach is recommended.[35 137] Clinical care ideally occurs in multidisciplinary clinical settings with access to medical providers, mental health specialists (such as neuropsychologists, rehabilitation or health psychologists), speech and language therapists, and physical and occupational therapists with expertise in long covid (see fig 2).[169-171]

Before initiating management of neuropsychiatric symptoms, a thorough assessment should gather information on acute covid-19 symptoms, vaccination status, symptom course, pre-existing conditions and symptoms, and potential contributing factors.[175] Examinations to reveal or rule out other causes of cognitive dysfunction or mental health symptoms may be useful (such as thyroid functioning, vitamin B_{12} levels, polysubstance use). It is recommended that neuropsychiatric symptoms and functioning be assessed using validated measures that allow for tracking of progress over time.[170 176 177] Although a Delphi consensus study failed to identify optimal tools for long covid neuropsychiatric assessment,[177] the GAD-7,[178] PTSD Checklist for DSM-5,[179] Cognitive Failures Questionnaire,[180] and the Montreal Cognitive Assessment-Telephone version[181] were most highly rated. The NeuroCOVID International Neuropsychology Taskforce has recommended a harmonised, flexible set of tools for assessing both subjective and objective cognition in adults with long covid, including incorporation of cognitive performance validity testing.[176] The American Academy of Physical Medicine and Rehabilitation (AAPMR) and long covid neuropsychology experts have issued similar guidance concerning instruments for use in this population.[170 175]

Limited evidence exists to guide management of long covid neuropsychiatric symptoms. A 2023 scoping review found only four of 17 mental health intervention studies were controlled trials,[182] and a 2024 review reported just 7% of psychological trials specifically targeted long covid related mental health concerns.[183] Encouragingly, the 2022 National Health Interview Survey found most US adults with long covid related depression (71.8%) or anxiety (65.1%) had received mental health treatment in the previous year.[162]

Interventions for cognitive dysfunction recommended by WHO and/or AAPMR include cognitive rehabilitation, self-management strategies, use of compensatory and assistive technology, and environmental modifications.[137 170] Suggestions for addressing mental health symptoms include cognitive behavioural therapy (CBT), with additional components of acceptance and commitment therapy (such as validating the patient experience), mindfulness approaches, physical activity, and peer support as well as consideration of pharmacological intervention. Providing psychoeducation regarding biological, psychological, and social contributions to symptoms and their persistence is also emphasised.

Of the relatively few non-pharmacological trials in long covid, most have applied CBT principles and/or multidisciplinary programmes and have targeted symptoms of anxiety, depression, and cognitive concerns.[184] A randomised clinical trial compared CBT versus usual care to tackle severe fatigue in 114 adults with long covid.[185] The intervention significantly improved both fatigue and subjective cognitive functioning at six months' follow-up. In one of the largest intervention trials to date, an eight week structured online group physical and mental health programme was compared with care as usual among 585 formerly hospitalised individuals with physical and/or mental health symptoms of long covid.[186] The intervention was associated with improved symptoms of depression (adjusted mean difference 1.39 (95% CI 0.06 to 2.71)) but not subjective cognitive dysfunction, with benefits that persisted at 12 months. Other promising non-pharmacological approaches include neuromodulation via direct current stimulation (tDCS), transcranial pulse

stimulation, or transcranial magnetic stimulation.[187]

There is little controlled evidence to guide the choice of medications. However, an eight week randomised controlled trial found that selective serotonin reuptake inhibitors effectively reduced depressive symptoms in those with long covid related depression, including among those with pre-covid psychiatric symptoms.[189] Low dose naltrexone has been widely used to target long covid fatigue, with studies suggesting more widespread benefit.[190-192]

Emerging treatments

A 2022 review of clinicaltrials.gov, a trial registry by the US National Library of Medicine, and the International Clinical Trials Registry, showed 41 long covid mental health interventional trials, ranging from nutritional supplements to CBT and neurorehabilitation.[193] Several promising ongoing pharmacological interventions are evaluating C1 esterase inhibitor, atorvastatin, donepezil, vortioxetine, nirmatrelvir/ritonavir (Paxlovid), and marrow stromal cell infusion.[194]

Guidelines

As an evidence based pathway for managing long covid neuropsychiatric symptoms has yet to emerge, NICE, WHO, and AAPMR have published guidelines for providing long covid care in community settings.[35 137 169 170] Most recently in February 2025, the CDC issued an updated Clinical Overview of Long COVID.[196] Common themes across guidelines include the importance of applying a person centred approach and establishing a supportive and collaborative therapeutic milieu while also referring patients to specialists. The NICE, WHO, and AAPMR guidelines note the importance of using validated instruments to capture cognitive functioning and mental health symptoms.[137 170] WHO, AAPMR, and CDC recommend implementing psychological and behavioural treatment strategies with an existing evidence base built on the treatment of other post-viral illnesses and medical conditions with high rates of mental health and cognitive sequelae (such as post-treatment Lyme disease syndrome, fibromyalgia).[137 169 170]

Conclusions

Long term cognitive and mental health sequelae of covid-19 remain prevalent, with nearly one in five affected adults demonstrating or reporting persistent cognitive, mood, or anxiety symptoms at ≥12 weeks after an acute covid illness. While objective cognitive deficits are largely modest in magnitude, both cognitive and psychiatric symptoms serve as substantial contributors to reduced functioning and employment among those with long covid. Evidence based treatments are lacking, and existing guidelines recommend interventions with empirical support for use in other patient populations.

Competing interests: None declared.

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HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

The perspectives of long covid patients and caregivers were shared with author MM, whose moderated discussion of patients' lived experience with long covid is freely available online.[198]

A patient with long covid and associated cognitive and mental health concerns provided a critique of our review before submission. Their input highlighted issues related to the challenges of living with symptoms for which there may not be a clearly identifiable cause or definitive diagnostic test. Their input led us to highlight concerns regarding stigma from society and the potential for patients to feel dismissed by care providers. Our patient shared the importance of supportive provider communication. This specifically included the value of providers acknowledging that much remains to be learnt about treating long covid related neuropsychiatric symptoms and the value of sharing the scientific basis for implementing interventions that are lacking evidence in long covid but have been shown to improve symptoms or functioning in other health conditions.

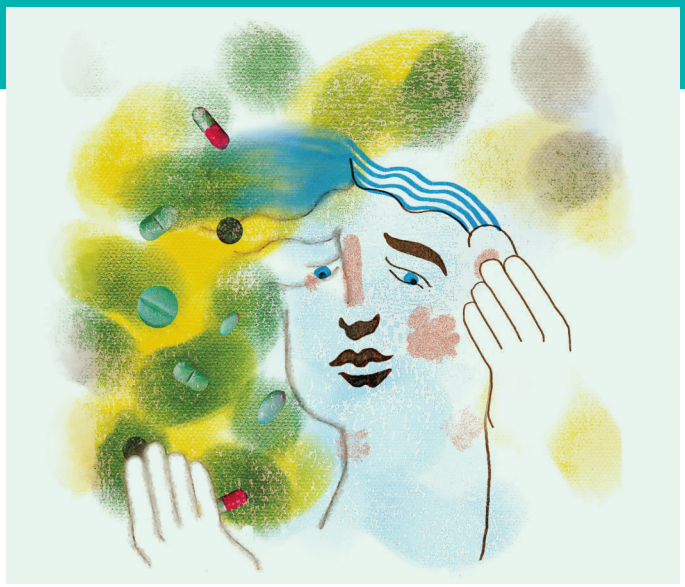
Knowledge synthesis

- There is no reliable diagnostic marker for neuropsychiatric symptoms of long covid
- Methodological heterogeneity and the evolving nature of the pandemic have contributed to discrepant findings concerning long covid related neuropsychiatric symptoms
- These symptoms are associated with functional, occupational, and economic burden and may be more pronounced in elderly people and those who had severe acute covid-19
- Potentially interactive pathways include immune and inflammatory responses, endothelial disruption, and vascular processes. Symptoms may also arise due to, or be complicated by, co-occurring symptoms, conditions, and interventions. For a subset, they may reflect a manifestation or exacerbation of pre-existing symptoms or vulnerabilities and may be influenced by early life adversities and expectancies
- Risk factors include female sex, vaccination status, emergence of new variants, and physical and psychiatric comorbidities. Increased age and severity of acute illness are generally associated with greater objective cognitive dysfunction, while less severe acute illness and younger age are common features among those presenting for neuropsychiatric treatment
- Cognitive testing provides a more direct measure of brain function relative to symptom reports, and recommended instruments and batteries have been developed
- A consistent cognitive profile has not emerged. When deficits are present, effect sizes tend to be small to moderate across domains of attention, processing speed, executive functioning, and memory and more pronounced in the context of severe acute illness, fatigue, and psychiatric symptoms
- There is evidence for symptom remission, persistence, fluctuation, and delayed emergence, which is consistent with current case definitions of long covid. Preliminary data suggest the early recovery period may reflect a window of opportunity for mitigating negative long term neuropsychiatric outcomes
- Clinical care should take a person centred approach, gather a comprehensive history, consider contributing factors, use validated screening and assessment instruments, and refer to specialists
- Providers should aim to form a trusting therapeutic alliance that validates the patient experience while providing psychoeducation, implementing interventions with empirical evidence from other health conditions, and focusing on functioning rather than causality
- Interventions may include cognitive rehabilitation and compensatory strategies, psychotherapy (such as CBT, ACT), mindfulness, physical activity, peer support, and pharmacotherapy (such as SSRIs, LND). These, as well as non-invasive brain stimulation and a range of pharmacological agents, are under active investigation as potential tools to address neuropsychiatric symptoms of long covid

WHAT YOUR PATIENT IS THINKING

Living with an intolerance to medication

CPD READING
0.5 HOURS



PRIYA SUNDRAM

Steven Comyns describes living with an intolerance to many medications and how he would like health professionals to help him find a solution

I am 61 years old and have lived with an intolerance to many medications for the past 15 years. The problems began after an increase in my medication; within weeks, I had developed debilitating flu-like symptoms. After a month I stopped all my medication until I felt better.

The intolerance is intermittent, which means that at times I can tolerate medications, and then suddenly I cannot. Periods of intolerance can last up to 18 months.

Debilitating symptoms

Before the problem began I had been taking the same drug treatments for 16 years, experiencing some common side effects that I was able to tolerate. Then, in my mid 40s I started gradually to increase the doses of those same medications for blood pressure, diabetes, and overactive bladder. This began a life altering sensitivity to tablets, liquid medication, patches, and even vitamin sprays.

The reactions are not immune based allergic in the usual sense, like anaphylaxis or rashes. For me, symptoms usually start within a day or two of taking medication, and can range in severity from those resembling a cold to a debilitating flu. I can experience extreme fatigue, brain fog, night sweats, nasal congestion, swollen glands, and at times earache. In recent years, I have experienced brain fog and felt unwell, even sort of semi-conscious. It feels as if my system becomes overloaded by medication until it crashes. These reactions don't seem logical to me at all.

Living with uncertainty

I have tried around 30 blood pressure medications in oral, liquid, and transdermal forms, all of them with the same debilitating side effects. The same adverse reactions also occurred with antidepressants and neuropathic pain medications. I have found only a handful of medications tolerable so far.

The result is that I live with multiple unmanaged health conditions, including high blood pressure, depression, neuropathic neck pain, and plantar fasciitis. For over a year, my blood pressure hovered around 180/120 mm Hg before I underwent renal denervation. Some health professionals have questioned whether my symptoms are psychosomatic. Initially, this made me feel as if I were being accused of making it up, which made me question myself. Part of me even hoped that might be the case, as it would mean there was at least an explanation.

Shared decision making

I would like my doctors to be more aware of the complexity of my health problems when we are discussing solutions, and for decisions about my care to be made jointly by my healthcare team and me. For example, with plantar fasciitis, cortisone injections are extremely effective, yet some foot and ankle specialists are reluctant to offer them and, as a patient, I don't understand why. Not having access to this intervention means I have to rely on painkillers, which I often cannot tolerate. If I do manage to take painkillers, I worry that it might reduce my ability to metabolise other medication, such as for hypertension.

As a result of the symptoms I experience after taking medication, I assume that every tablet causes some level of damage to my system.

Ideally, I would like my treatment plans to be discussed and decided jointly by the consultants, GP, and myself. I do understand that prescribing decisions might be more difficult when a doctor cannot swiftly prescribe the pill they usually would to solve a problem. Patients like me can require more time in the consultation and careful consideration of the treatment approach.

Patient author
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WHAT YOU NEED TO KNOW

- If a patient is experiencing side effects with several medications, consider the possibility of multiple drug intolerance syndrome
- Take the time to explain why a non-medication intervention might not be offered, particularly in the context of multiple drug intolerances
- Patients who have experienced multiple unexplained reactions to medications might value being involved in treatment decisions, with a clear mechanism for timely review should any side effects occur

EDUCATION INTO PRACTICE

- What information or support could you give a patient who is experiencing an intolerance to a medication?
- How might you ensure you are working with patients to make the decisions around medications together?
- When might you ensure you are working collaboratively with other specialties best to support patients with complex medication intolerances?

ADDITIONAL INFORMATION

Multiple Drug Intolerance Syndrome – https://pubmed.ncbi.nlm.nih.gov/25362509/

CASE REVIEW

A boy with swollen and painful hands

A 6 year old boy presented to the dermatology department with a two day history of progressively swollen and painful hands and wrists. He had no fever, abdominal pain, or knee or ankle swelling or pain. Topical corticosteroid and mupirocin ointment were initially prescribed for possible insect bites, but there was minimal improvement. He had a history of upper respiratory tract infection five days before the hand swelling. He had no other medical history or relevant family history.

Observations including blood pressure were within normal limits. On physical examination, there was considerable non-pitting oedema of both hands, and patchy ecchymoses were present on the back of the hands and wrists (fig 1). No oedema was noted in the lower extremities. Ecchymoses were also seen on the thighs and buttocks (fig 2). Routine laboratory tests included urine analysis, which was normal, and full blood count, which showed elevated neutrophils: 14.53×10^9/L cells (normal range (1.3 to 6.7×10^9/L).

1 **What are the differential diagnoses?**
2 **What is the most likely diagnosis?**
3 **What is the management?**

Submitted by Wu Guo and Xiao qiong Li

Parental consent obtained.

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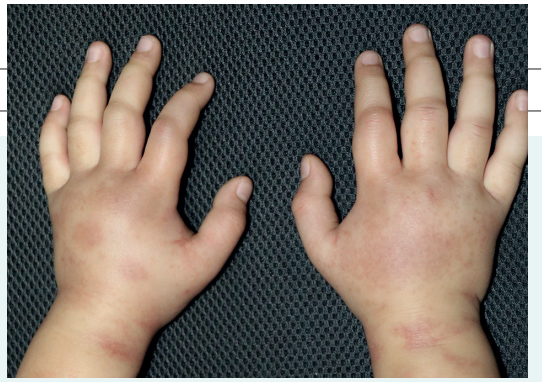

Fig 1 | Swelling and scattered ecchymoses to hands and wrists

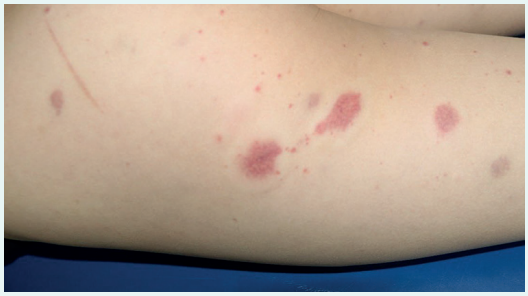

Fig 2 | Petechiae and ecchymoses scattered over the buttocks and lower limbs

answers

CASE REVIEW **A boy with swollen and painful hands**

1 What are the differential diagnoses?

Differential diagnoses include immune thrombocytopenia (ITP), Kawasaki disease, and immunoglobulin A (IgA) vasculitis (previously known as Henoch-Schönlein purpura). ITP is an autoimmune disease that leads to a low platelet count, purpura, and spontaneous bleeding episodes, but is not normally associated with joint pain or swelling. Kawasaki disease is a paediatric vasculitis that usually presents with erythematous oedema of the hands and feet, diffuse erythematous polymorphic rash, and unremitting fever beyond five days. It is not likely in this case given the absence of fever. The clinical features of IgA vasculitis include palpable purpura of the lower extremities and buttocks, arthritis or arthralgia, abdominal pain, gastrointestinal bleeding, and renal involvement with haematuria and/or proteinuria. Some children may also present with non-pitting oedema of the scalp, face, or dorsum of the hands and feet.

2 What is the most likely diagnosis?

IgA vasculitis.

IgA vasculitis is an IgA-mediated small-vessel leucocytoclastic vasculitis that occurs mainly in children under 10 years of age. Approximately half of cases occur after upper respiratory tract infections.

Diagnosis is based on criteria developed by the Paediatric Rheumatology European Society (PRES), including petechiae or purpura primarily involving the lower extremities and at least one of: abdominal pain, arthritis or arthralgia, renal involvement manifested by proteinuria or haematuria, or histopathological confirmation.

3 What is the management?

Management of IgA vasculitis is generally supportive with rest, adequate hydration, and pain relief. Systemic steroids can be considered if the patient has persistent unrelieved abdominal pain or arthralgia. As IgA vasculitis nephritis can be a late feature, patients should be regularly monitored with urine analysis screening for proteinuria or haematuria.

PATIENT OUTCOME

The patient received supportive care, and his symptoms gradually resolved. He was monitored with blood and urine tests with no long term complications.

LEARNING POINTS

- **IgA vasculitis can present with localised or diffuse subcutaneous oedema in addition to the characteristic rash**
- **The diagnosis of IgA vasculitis is generally clinical based on PRES criteria**
- **In addition to supportive care, periodic urine analysis should be used to monitor for IgA vasculitis nephritis as it may be a late feature**

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

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