The business of bundles in sepsis
A new study from the US looked at the effect of a sepsis management bundle on treatment and patient outcomes. The longitudinal study of repeated cross sectional cohorts within 11 hospitals in one integrated US healthcare system looked at data from two years before adherence to the sepsis bundle had to be reported to Medicare to two years after. These are observational data with a historical comparison rather than a contemporaneous control group, so changes cannot be attributed to reporting of bundle adherence. However, the finding was that rates of early lactate measurement and, somewhat more moderately, antibiotic administration increased over time, but rates of death and discharge to home didn’t change.

The authors suggest revising the sepsis bundle measure, but I am not hopeful for that being more effective. There may not be scope to improve outcomes further using a bundle because outcomes may be limited by other factors—such as staffing levels or the fact that, even when all elements of a bundle are adhered to, sepsis still causes adverse outcomes.

Hospital at home for people over 65 with frailty
I don’t think I’ve ever said this before, but I’m in love with a trial. It’s a large randomised trial, set in the UK. The study population is a critical one—older people. The primary outcome is a relevant one—living at home six months down the line. And the intervention is something that does get used but hadn’t been properly tested until now. Now we can be confident that “admission avoidance hospital at home” (provision of hospital level care with comprehensive geriatric assessment) had similar outcomes to hospital admission. This shows there is an alternative to admission in these patients. The problem possibly requiring admission was usually infection, but falls and COPD were also common, and most of the participants had a degree of cognitive impairment.

Magic mushrooms for depression?
Psilocybin was compared with escitalopram (a selective serotonin reuptake inhibitor) in a six week double-blind randomised trial of 59 people with moderate to severe depression. It was intended to be exploratory and look at efficacy and mechanisms, but I’m not sure it provided much evidence of either. The functional MRI data were not reported here. Patients were highly selected (no comorbid psychiatric conditions, no immediate family or personal history of psychosis, and no history of serious suicide attempts). They had to have not used escitalopram before, but more than a quarter of participants had used psilocybin before. The study found similar reductions in depression scores in both groups.

With no placebo group, it’s impossible to know if these effects were placebo effects in both groups (or simply the effect of the psychological support both groups received). This trial was short—the natural course of depression means we should be looking for sustained response, and six weeks doesn’t give escitalopram time to work. Blinding was also an issue: the psychedelic effect of psilocybin and the known side effects of escitalopram meant that patients could easily guess which group they were in, thus biasing the outcome measure (guessing the treatment arm could also have affected the clinician rated assessment of depression).

Covid-19: single dose vaccine effective
The Ad26.COV2.S vaccine (Johnson & Johnson vaccine) was found to prevent moderate to severe covid-19 with onset at least 14 days after administration with 67% efficacy, and up to 77% for severe infection alone in the double blinded randomised Ensemble trial. It was conducted in eight countries worldwide, including Brazil, US, and South Africa. A reasonable level of efficacy was seen against the South Africa variant of SARS-CoV-2. Aside from needing only a single dose for vaccination, the vaccine can be stored in a standard freezer for up to two years and up to three months in a fridge, making it more accessible. And efficacy against symptomatic disease was demonstrated across age groups.

Treating vaso-occlusive episodes in sickle cell disease
Casella and colleagues performed a randomised trial in 388 children and adults across 66 hospitals comparing intravenous poloxamer 188 (a non-ionic block polymer surfactant, whatever that is) with placebo in a double-blind fashion. The aim was to shorten the duration of vaso occlusive episodes, supposedly by reducing blood viscosity and improving microvascular blood flow. The effect was judged by the time to the last dose of parenteral opioids. There was no evidence of benefit with poloxamer 188. This contradicts findings from an earlier trial that suggested the drug might be beneficial (which used the more subjective “time to resolution of the episode” as an endpoint and had a lot of incomplete data). The authors, and the journal, should be congratulated on their persistence in ensuring this negative trial from 2016 saw the light of day.
CLINICAL UPDATES

Postural hypotension

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Postural hypotension, also called orthostatic hypotension, is an abnormal drop in blood pressure on standing. It impairs quality of life and increases risk of falls, cardiovascular disease, depression, dementia, and death.1  -  4 Primary care providers play an important role in screening and detection of postural hypotension and in helping patients make shared treatment decisions to improve symptoms and reduce risk.

How common is it?

The prevalence of postural hypotension increases with age. One in five community-dwelling adults over 60 years old and one in four people in long term residential care have postural hypotension, as per a systematic review and meta-analysis.5 Two large population based studies in the US suggest it is found in <5% of people aged 45-49 years, almost 15% in those aged 65-69 years, and over 25% of those aged >85 years.6

How is it caused?

Postural hypotension occurs with an inadequate or delayed response to fluid shifts in the body on standing. This leads to an exaggerated drop in systolic blood pressure (≥20 mm Hg) and/or diastolic blood pressure (≥10 mm Hg) on standing.7 The figure depicts the mechanism. “Classic” postural hypotension occurs within three minutes of standing, “delayed” postural hypotension occurs after three minutes.

Box 1 lists the neurogenic or non-neurogenic conditions that may cause postural hypotension. About a quarter of patients with diabetes have postural hypotension.13 High HbA1c, hypertension, and diabetic neuropathy increase its likelihood. About a third of patients with Parkinson’s disease have postural hypotension.14 Medications can cause postural hypotension as an adverse reaction. Individual susceptibility, age, comorbidities, and polypharmacy determine whether a patient develops postural hypotension.15 16

1. Blood is evenly distributed throughout the body when lying flat
2. On standing, blood pools in the legs
3. Pooling blood causes reduction in venous return, and therefore cardiac output, so pressure falls
4. The drop in blood pressure is detected by specialised cells (baroreceptors; shaded area) in the aortic arch and carotid sinus, these respond by increasing sympathetic and reducing parasympathetic outflow (this is known as the baroreflex)
5. As a result, peripheral vascular resistance is increased, which causes venous return, cardiac output, and therefore blood pressure, to increase, thereby limiting the drop in blood pressure that occurs as a result of standing
6. If this response is inadequate or delayed, then the fall in blood pressure is not corrected and postural hypotension occurs

The normal physiological response to change of position from lying to standing: the response is coordinated through neuronal and non-neuronal mechanisms

How do patients present?

Symptoms are triggered by changes in posture and usually resolve with lying down or sitting. Patients may present with lightheadedness or dizziness, transient loss of consciousness, or falls. Symptoms may occur first thing in the morning, as the patient gets up from bed, or throughout the day, as they change position from lying to standing, sitting to standing, or even lying to sitting.

Some patients have no symptoms and postural hypotension is detected incidentally on clinical examination. The clinical significance of asymptomatic postural hypotension is not established.

What to cover on clinical assessment?

Ask about the nature of symptoms, their onset in relation to changes in posture and if they are persistent/recurrent or isolated. Factors such as diurnal variability, food intake, hydration, ambient temperature, prolonged recumbency, and deconditioning can affect symptoms. Seek to identify the cause(s) of postural hypotension, which may be multifactorial. Medication history is important, particularly if symptoms appeared after initiation of a drug.

Tailor clinical examination to identify features related to symptoms and probable causes. A patient with palpitations may have a murmur suggestive of structural abnormality of the heart, while a patient who describes slowness of movement and tremor may have hypomimia and rigidity, suggestive of Parkinson’s disease.

Postural blood pressure measurement

Take lying and standing blood pressure measurements and check for a drop in systolic blood pressure ≥20 mm Hg and/or diastolic blood pressure ≥10 mm Hg within three minutes of standing. Measurement beyond three minutes of standing may be necessary if a patient reports symptoms occurring after this time, otherwise delayed postural hypotension may be missed. It is advisable to take multiple lying and standing measurements.

For convenience or practical reasons, sitting and standing (and occasionally lying and sitting) measurements are sometimes used. The optimal thresholds for a diagnosis based on these measurements are not known. If an exaggerated drop in blood pressure is not found, lying and standing measurements may be more likely to detect postural hypotension. Measuring postural hypotension can be time consuming in a busy practice. Involve allied healthcare professionals in taking postural measurements on the day of the appointment, as is done in falls clinics.

Repeating measurements at a later point in time increases detection rates. Serial home postural blood pressure measurements (morning and evening), either by patients themselves or their carers, may be considered if feasible and the patient is sufficiently mobile.

Note changes in heart rate when taking lying and standing blood pressure measurements. If postural hypotension is found, an accompanying increase in heart rate of <15 beats per minute may suggest a neurogenic cause, and an increase in heart rate of >15 beats per minute may suggest a non-neurogenic cause.

Box 1 | Conditions that can cause postural hypotension

Neurogenic causes

- Neurodegenerative disease—Such as Parkinson’s disease, Parkinson-plus syndromes
- Peripheral neuropathy—Such as diabetes, vitamin B12 deficiency, renal failure, amyloidosis, rheumatological, autoimmune, and paraneoplastic conditions

Non-neurogenic causes

- Volume depletion—Anaemia, dehydration, haemorrhage, hyperglycaemia
- Cardiovascular disease—Aortic stenosis, hypertension, heart failure, atherosclerosis or vascular stiffening, arrhythmias
- Other—Adrenal insufficiency, physical deconditioning, ageing

Either mechanism

- Medications—α blockers, antihypertensives, nitrates, diuretics, selective serotonin reuptake inhibitors, tricyclic antidepressants, antipsychotics, β blockers
- Alcohol consumption
- Short term: diuretic effect, impairment of vasoconstriction
- Long term or chronic: neurotoxic effects

Idiopathic

Whom to screen for postural hypotension?

The UK National Institute for Health and Care Excellence (NICE) guidelines advise checking for postural hypotension in patients who have hypertension alongside type 2 diabetes or who have hypertension and are aged 80 years and over. The American Diabetes Association recommends assessment for postural hypotension during initial evaluation of hypertension in all patients with diabetes, and periodically at follow-up even in the absence of symptoms. Consensus recommendations by an expert panel suggest screening in patients suspected of, or diagnosed with, any neurodegenerative condition associated with autonomic dysfunction (such as Parkinson’s disease) and in patients with peripheral neuropathies known to be associated with autonomic dysfunction (such as diabetes).

What differential diagnoses to consider?

Patients may experience similar symptoms triggered by meals in post-prandial hypotension. Vasovagal syncope (commonly referred to as a “faint”) may be accompanied by an acute drop in blood pressure when standing. It is usually precipitated by emotional stress, pain, heat, dehydration, or a period of prolonged sitting or standing and tends to occur in younger, otherwise healthy adults. There may be prodromal symptoms such as sweating, nausea, and pallor before the transient loss of consciousness.

Carotid sinus syndrome causes syncope, near-syncope, or unexplained falls due to carotid sinus hypersensitivity. Like postural hypotension, it is more common in older people and is difficult to distinguish clinically. The two conditions cause similar symptoms and may coexist. Tilt-table testing may help in a diagnosis. This is done in a specialist cardiology setting for patients with syncope of uncertain origin. The patient is put under positional or orthostatic stress in a controlled and monitored setting.
What are the investigations?

Investigations are chosen on a case-by-case basis because of the wide range of possible causes, but they may not be necessary if a drug related cause is suspected. Depending on the history, tests in primary care may include:

- **Bloods**—full blood count if the patient has chronic bleeding or anaemia, urea and electrolytes, HbA1c for diabetes, vitamin B12
- **Electrocardiography**—if an arrhythmia is suspected
- **Echocardiogram**—if a structural heart problem is suspected

How is it managed?

The aim of treatment is to reduce symptoms and risk of injury, not to try to normalise the magnitude of the postural fall in blood pressure. Asymptomatic postural hypotension is not currently treated. Some patients may not meet the defined criteria for a diagnosis of postural hypotension despite having symptoms and home measurements showing a postural drop in blood pressure. Their symptoms are managed as those with confirmed postural hypotension.

**Address reversible causes**

Address reversible causes such as drugs, infection, dehydration, and anaemia. Consider stopping or reducing the dose of an offending drug or using a modified-release preparation. The withdrawn drug may be replaced by another drug, or the underlying condition may be adequately managed without the drug.

**Conservative measures to improve symptoms**

Help patients understand what postural hypotension is, what causes it, and what may make it worse. Prolonged standing, eating large meals, drinking alcohol, deconditioning, dehydration, hot environment, taking hot baths or showers, and straining may worsen symptoms in some patients. Box 2 lists common non-pharmacological measures that may be suggested in practice. Lower limb and abdominal compression therapy may offer some benefit, but the evidence is of very low quality.

**Referral and medications**

Offer referral to a specialist if symptoms are not controlled or are persistent and frequent, or if the cause is unexplained. Specialist referral is based on the patient’s age, symptoms, and medical conditions. For example, a young patient with repeated unexplained syncopal symptoms and palpitations would be referred to a cardiologist, and an elderly frail patient with multimorbidity and polypharmacy with recurrent falls would be referred to a geriatrician.

Pharmacological treatment is usually started by a specialist if symptoms are not well controlled by conservative measures. Treatment may be continued or modified in primary care. Prescribing practices vary and are governed by local guidelines. In the UK, for example, the use of fludrocortisone for postural hypotension is off-label. Midoxydine is indicated only for people with postural hypotension due to autonomic dysfunction, and its use for other types of postural hypotension is off-label. Droxidopa does not yet have market authorisation for use in postural hypotension in the UK.

**Special considerations in hypertensive patients**

Clinicians may worry that tight control of blood pressure in a hypertensive patient may cause or worsen postural hypotension. It may not be necessary to compromise blood pressure targets in people with postural hypotension, rather uncontrolled hypotension may worsen postural hypotension. In a large randomised controlled trial, more intensive blood pressure targets (systolic blood pressure ≤120 mm Hg) were not more likely to cause postural hypotension than standard targets (systolic blood pressure ≤140 mm Hg), but syncope was more common. A recent systematic review and meta-analysis showed that lower blood pressure treatment goals decreased the risk of postural hypotension.

Different drug classes confer different risk of postural hypotension, and reports linking particular antihypertensive drugs to postural hypotension are inconsistent. The number of drugs taken may be more predictive of postural hypotension than individual drug classes. Competing interests: None declared.

Cite this as: BMJ 2021;378:n922

Find the full version with references at http://dx.doi.org/10.1136/bmj.n922

**HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE**

A patient partner through the Patient and Family Advisory Council at Beth Israel Deaconess Medical Center reviewed the manuscript and provided feedback on sections related to education, management, and goals of therapy for postural hypotension. She was instrumental in creating the box on what patients need to know. We are grateful for her input.

**EDUCATION INTO PRACTICE**

What is the protocol for taking postural blood pressure measurements at your clinic? How would you approach a patient with postural hypotension related to a medication?
Chronic pain—defined as pain that lasts for more than three months—is common, debilitating, and often difficult to treat. Chronic pain is classified in ICD-11 as being either primary or secondary. In chronic primary pain there is no clear underlying condition that adequately accounts for the pain or its impact; chronic secondary pain is pain linked to an underlying condition. Clinical judgment is required to determine whether the pain is primary, secondary, or a combination of the two.

This article summarises recommendations from the National Institute for Health and Care Excellence (NICE) guideline for chronic pain (primary and secondary) in people over 16 years old for use in all NHS settings where pain is managed. The guideline, published in April 2021, covers assessment for people living with primary or secondary chronic pain and management of chronic primary pain.

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This article summarises recommendations from the National Institute for Health and Care Excellence (NICE) guideline for chronic pain (primary and secondary) in people over 16 years old for use in all NHS settings where pain is managed. The guideline, published in April 2021, covers assessment for people living with primary or secondary chronic pain and management of chronic primary pain.

The evidence demonstrated the pivotal importance of an empathic and supportive therapeutic relationship between people with pain and healthcare professionals.

Assessing all types of chronic pain (chronic primary pain, chronic secondary pain, or both)

Qualitative evidence demonstrates shortcomings in people’s experience of healthcare consultations. Evidence reviewed in the guideline highlights that the principles of best practice in supporting people with long-term conditions are central in supporting people with pain. The Guideline Committee therefore agreed that this should be addressed within the guideline and several recommendations were made for clinicians assessing people with chronic pain.

The evidence demonstrated the pivotal importance of an empathic and supportive therapeutic relationship between people with pain and healthcare professionals that underpins decision making and care and support planning. Other recommendations address developing an understanding of the experience of the person with pain and providing advice and information.

**Person-centred assessment**

- Offer a person-centred assessment to those presenting with chronic pain (chronic primary pain, chronic secondary pain, or both) to identify factors contributing to the pain and how the pain affects the person’s life.
- Foster a collaborative and supportive relationship with the person with chronic pain.

**Thinking about possible causes for pain**

- Think about a diagnosis of chronic primary pain if there is no clear underlying (secondary) cause or the pain or its impact is out of proportion to any observable injury or disease, particularly when the pain is causing significant distress and disability.
- Recognise that chronic primary pain can co-exist with chronic secondary pain.

**Talking about pain**—how this affects life and how life affects pain

- Ask the person to describe how chronic pain affects their life, and that of their family, carers, and significant others, and how aspects of their life may affect their chronic pain. This might include:
  - Lifestyle and day-to-day activities, including work and sleep disturbance
Managing chronic primary pain (CPP)

The guideline makes recommendations for managing chronic primary pain. When chronic primary and secondary pain coexist, management should be guided by both the recommendations in this section and the NICE guideline for the secondary pain condition. The Guideline Committee agreed that shared decisions to inform a care and support plan should be based on discussion of risks and benefits of potential options known to be effective for chronic primary pain.

There was consistent evidence of benefit for non-pharmacological approaches, which the committee agreed could be considered as treatment options according to individual needs and preferences. Evidence was particularly strong for group exercise, which the committee agreed could be offered to all people with chronic primary pain. In contrast, the committee recommended not initiating medicines for chronic pain (with the exception of antidepressants, which can be considered after a full discussion of the benefits and harms). The evidence review found that most medicines do not demonstrate a benefit compared with placebo in the management of chronic primary pain; some demonstrate a risk of harm, such as the risk of misuse and dependence with opioids and gabapentinoids.

Offer a supervised group exercise programme to people aged 16 years and over to manage chronic primary pain. Take people’s specific needs, preferences, and abilities into account.

Consider acceptance and commitment therapy or cognitive behavioural therapy for pain for people aged 16 years and over with chronic primary pain delivered by healthcare professionals with appropriate training.

• Consider a single course of acupuncture or dry needling, within a traditional Chinese or Western acupuncture system, for people aged 16 years and over to manage chronic primary pain, but only if the course:
  – Is delivered in a community setting and
  – Is delivered by a healthcare professional at band 7 equivalent or lower with appropriate training and
  – Is made up of no more than 5 hours of healthcare professional time (the number and length of sessions can be adapted within these boundaries) or
  – Is delivered by another healthcare professional with appropriate training and/or in another setting for equivalent or lower cost.

• Do not offer any of the following to people aged 16 years and over to manage chronic primary pain because there is no evidence of benefit:
  – TENS (transcutaneous electrical nerve stimulation)
  – Ultrasound therapy
  – Interferential therapy.

• Consider an antidepressant—either amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine, or sertraline—for people aged 18 years and over to manage chronic primary pain, after a full discussion of the benefits and harms.

• If an antidepressant is offered to manage chronic primary pain, explain that this is because these medicines may help with quality of life, pain, sleep, and psychological distress, even in the absence of a diagnosis of depression.

• Do not initiate any of the following medicines to manage chronic primary pain in people aged 16 years and over:
  – Antiepileptic drugs, including gabapentinoids, unless gabapentinoids are offered as part of a clinical trial for complex regional pain syndrome (see research recommendations)
  – Antipsychotic drugs
  – Benzodiazepines
  – Corticosteroid trigger point injections
  – Ketamine
  – Local anaesthetics (topical or intravenous), unless as part of a clinical trial for complex regional pain syndrome (see research recommendations)
  – Local anaesthetic-corticosteroid combination trigger point injections
  – Non-steroidal anti-inflammatory drugs
  – Opioids
  – Paracetamol.

If a person with chronic primary pain is already taking any of the medicines in the recommendation above, review the prescribing as part of shared decision making:

• Explain the lack of evidence for these medicines for chronic primary pain and
• Agree a shared plan for continuing safely if they report benefit at a safe dose and few harms or
• Explain the risks of continuing if they report little benefit or significant harm and encourage and support them to reduce and stop the medicine if possible.

• When making shared decisions about whether to stop antidepressants, opioids, gabapentinoids, or benzodiazepines, discuss with the person any problems associated with withdrawal.

Competing interests: See bmj.com.
Cite this as: BMJ 2021;373:n895
Find the full version with references at http://dx.doi.org/10.1136/bmj.n895
Post-acute complications of severe covid-19

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This abridged State of the Art review was created by The BMJ with input from the authors and appears as a summary for non-specialists. The full version (doi:10.1136/bmj.n436) discusses the epidemiological and clinical features of covid-19, the pathophysiological mechanisms, inpatient respiratory support, drug treatments, and long term management of patients with severe covid-19 pneumonia.

The current article is the third of three summaries of the review and focuses on post-acute complications of severe covid-19. The first summary covers respiratory care (BMJ 27 March 2021) and the second covers drug treatments (BMJ 24 April 2021).

Table 1 | Post-acute covid-19 complications by system

<table>
<thead>
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<th>System</th>
<th>Complications</th>
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| Physical impairment     | • Seen in up to 80% after any critical illness and includes loss of muscle mass, neuromuscular weakness, fatigue, dyspnea, decreased exercise tolerance, joint contractures, and sexual dysfunction.190-192  
• Substantial muscle wasting and neuromuscular weakness are common following non-covid ARDS and can last for months or years,193 with major risk factors being corticosteroid use and intensive care unit length of stay194  
• Recent study from Italy of covid-19 patients with more than half reporting 3+ persistent symptoms, including fatigue (53%), dyspnea (43%), joint pain (22%), and reductions in quality of life (44%)195 |
| Mental health impairment| • For non-covid patients who were in intensive care unit, these include anxiety, depression, or post-traumatic stress disorder (PTSD) in 8% to 57% of cases196-198  
• Can also occur in family members of patients who were in intensive care units (known as PICS-family)  
• Unique to covid-19 which increase the risk for mental health impairment include social isolation, loneliness, the stigma of the disease, limited hospital visitation policy, and the psychological effect of the pandemic itself199  
• In a study of 402 survivors of covid-19, a significant number of patients reported PTSD (28%), depression (31%), anxiety (42%), obsessive-compulsive symptomatology (20%), and insomnia (40%200 |
| Pulmonary impairment     | • Persistent pulmonary symptoms are common after covid-19195  
• In a 3 month follow-up study in China of covid-19 patients (n=55), 71% had radiological abnormalities including interstitial thickening and fibrosis, and 25% had impaired diffusing capacity for carbon monoxide at three months following discharge201  
• An observational study from China of 51 covid-19 patients showed that 45% had abnormal computed tomography scans four weeks after discharge202 |
| Cardiac impairment       | • Evidence for long term sequelae from covid-19 has been noted, including evidence of myocardial inflammation on magnetic resonance imaging 12-92 days following infection203  
204 |
| Neurological impairment  | • While the occurrence of stroke due to covid-19 is relatively rare, other conditions including impairment of consciousness, encephalitis, seizure, encephalopathy, and “brain fog” have been reported 2-3 months after initial illness onset205-207  
• Cognitive impairment is typically seen in 30-80% of patients who were in intensive care and includes memory loss as well as difficulty with concentration, comprehension, and critical thinking208 |

Current estimates are that 91.5 million patients worldwide have recovered from SARS-CoV-2 infection. For those who survive covid-19, emerging reports have identified persistent symptoms beyond the acute phase of illness. These symptoms, which can affect multiple organ systems (table 1), are not due to persistent viral infection but instead sequelae of severe inflammation from the disease.

“Post-acute covid-19” is defined as the presence of symptoms extending beyond three weeks, and chronic covid-19 extends beyond 12 weeks. We know from studies before the pandemic that a high percentage of patients who require intensive care develop post-intensive care syndrome (PICS), which is the constellation of new or worsening physical, mental health and cognitive impairments that develop following critical illness. These impairments often last beyond a year and have a profound impact on quality of life.

Patients who were in intensive care are particularly at risk to develop PICS given the high incidence of ARDS, prolonged mechanical ventilation, higher exposure to sedatives, higher incidence of delirium, limited physical therapy owing to concern for disease transmission, and constraints on social and emotional support owing to limited visits.
Mitigation of post-ICU syndrome

Prevention and mitigation of PICS can be accomplished by following the “ABCDEF” bundle and other guidelines, which focus on managing pain, early ventilator liberation, assessing and treating delirium, appropriate usage of sedative agents, early mobility and exercise, and family engagement to prevent long term impairments. Early physical therapy and mobilisation interventions are paramount, and should be continued as an outpatient with home based physical therapy. Other interventions include ICU diaries, early psychological intervention, animal visitation, peer support groups for patients and families, and utilising digital technology to bridge social distance. Healthcare providers should acknowledge the difficulty of covid-19, the unique stressors covid-19 patients and families are facing, and tailor their communication and behaviour accordingly.

Patients who spent time in intensive care, especially patients with ARDS, are at high risk for PICS development. Without appropriate recognition, impairments go undiagnosed and can persist for months to years and profoundly affect quality of life. An interdisciplinary approach is essential to assist with diagnosis and management of critical illness recovery.

Post-ICU recovery programmes staffed by a team of providers (i.e., pulmonologists, intensivists, pharmacists, advanced practice providers, nurses, physical and occupational therapists, respiratory therapists, social workers, case managers, and mental health providers) can diagnose and treat PICS impairments. These clinics also facilitate access to necessary subspecialties (tables 1, 2). The comprehensive approach of post-ICU clinics mirrors the magnitude that critical illness affects multiple domains of a patient’s health. By bringing together various subspeciality healthcare workers, these clinics promote mind, body, social, and spiritual recovery to survivors of critical illness.

The need for ongoing ambulatory care for these vulnerable patients, also known as “long haulers,” is imperative. Long term longitudinal observational studies and clinical trials will be critical to clarify the durability and extent of health consequences attributable to covid-19 and define best practices for covid-19 survivors.

Table 2| Assessment of patients in post-ICU recovery clinics adapted to post-acute covid-19 patients

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Assessment</th>
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<tbody>
<tr>
<td>Activities of Daily Living and Instrumental Activities of Daily Living</td>
<td>Functional status</td>
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<tr>
<td>Physical therapy and occupational therapy evaluation</td>
<td>Functional assessment, mobility, strength</td>
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<tr>
<td>European Quality of Life Five Dimension (EQ-SD)</td>
<td>Health related quality of life, mobility, pain</td>
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<td>Hospital Anxiety and Depression Scale (HADS)</td>
<td>Anxiety, depression</td>
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<td>Impact of Event Scale-Revised (IES-R)</td>
<td>Post-traumatic stress disorder</td>
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<td>Montreal Cognitive Assessment (MoCA)</td>
<td>Cognition</td>
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<tr>
<td>Pulmonary function testing</td>
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</tr>
<tr>
<td>6 Minute walk test</td>
<td>Lung function, functional status</td>
</tr>
<tr>
<td>Chest radiograph</td>
<td>Lung parenchyma</td>
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<tr>
<td>Echocardiogram and electrocardiogram</td>
<td>Cardiac function</td>
</tr>
</tbody>
</table>

Competing interests: UH reports receiving royalties from Wolters Kluwer Health for his work as section editor for UpToDate.

Cite this as: BMJ 2021;372:n436

Find the full version with references at http://dx.doi.org/10.1136/bmj.n436

By bringing together various subspecialty healthcare workers, these clinics promote mind, body, social, and spiritual recovery to survivors of critical illness.
My mother developed rheumatoid arthritis in her twenties and had joint replacements for knees and elbows. After a series of infections at the age of 70, her prostheses were all progressively removed to save her life, and she could no longer walk or feed herself. She asked to be cared for at a nursing home. Although she later had cancer and a minor stroke, she was generally in good spirits.

One Sunday, my mother refused her favourite spicy noodles. She commented that everything tasted worse than before. The following week, she refused another favourite, braised pork with vegetables. My mother had not been eating much. She could not swallow. She felt nausea, as if something were pressing against her throat. She calmly told me she was going to die soon.

Tests and investigations
I took my mother to see a health professional she knew well and trusted. My mother’s eyes no longer sparkled. She looked tired, thin, and fragile. The doctors were deeply concerned and admitted her for observation. We discussed the possible causes and the battery of tests began. The medical team diligently went about their investigations but it troubled me that there seemed to be little thought or questioning about whether the tests were reasonable with her condition.

The tests and treatments all caused her pain. My mother was so thin that every attempt to draw blood or to insert a drip caused even more pain. The process of giving the tests seemed automatic. There seemed to be little consideration of alternative means of obtaining the information needed. I kept wondering, could there have been less invasive or painful ways to help my mother?

Time to go home
After two months there was still no diagnosis and my mother’s condition had not improved, even after multiple efforts by the medical team. With my sister and a close friend, I made the decision to cease my mother’s treatment. My mother had entrusted me to make her decisions for her, partly because she did not speak much English, and also because she felt I was better able to make these decisions. This is common in Singapore, where I live.

The drips, blood tests, scans, and attempts at 'scopes were stopped and it was time to go home. Her medical team found this decision hard to accept. They pressed me to persuade her to allow just one more test. I told them my mother had suffered enough and needed to rest. She received palliative care and died peacefully a week later.

Accepting death
During my mother’s care I had a good rapport with her doctors. They kept me informed through everything. But the only times we had discussed death and dying were before her surgeries. Perhaps, in our minds, dying was something that would occur suddenly, during an intervention. We had not imagined it could instead happen gradually, over several months. Why did we not see that my mother was right? Her symptoms were consistent with the signs of dying. Perhaps we were unwilling to accept death because there was no diagnosis. As we had to learn, “dying” is a diagnosis, too.

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Cite this as: BMJ 2021;373:n920

WHAT YOUR PATIENT IS THINKING

Why is dying not seen as a diagnosis?

Audrey Chia explains why seeing dying as a diagnosis is important for patients at the end of life.

WHAT YOU NEED TO KNOW

- Recognising when a patient is dying and having open conversations will help patients and their families better prepare and feel involved
- Understanding a patient’s values, goals, and preferences will help ensure that care is appropriate and in line with their wishes
- Ensure patients and their families are involved in decision making around what tests should be conducted

EDUCATION IN PRACTICE

- Think of a patient in your care who is approaching the end of life. How might you better understand their needs and preferences about their care?
- How would you approach a conversation about death and dying with a patient and their family?
- How can you ensure that patients and their families are involved in the decision making around investigations and that their input is considered?
Infections and multiple sclerosis

Evidence shows that infection with Epstein Barr virus in adolescence increases the risk of multiple sclerosis. A register-based study from Sweden, which linked recorded diagnoses of multiple sclerosis after age 20 with hospital diagnosed infections before age 20, confirms this. But Epstein Barr virus may not be the only culprit. After exclusion of infectious mononucleosis, pneumonia, and infections of the central nervous system, other infections in adolescence also increased the risk of a later diagnosis of multiple sclerosis (Brain doi:10.1093/brain/awab100).

Internet searches

Each day, millions of people search the internet to find out what’s causing their symptoms. Although many doctors believe that these searches lead to misdiagnosis, an online survey of 5000 US adults who were given case vignettes to assess found that diagnostic accuracy was better in those who searched the internet (JAMA Netw Open doi:10.1001/jamanetworkopen.2021.3287). However, decisions about whether the symptoms required medical advice weren’t improved.

Covid-19 and clinical trials

Inevitably, social distancing and lockdowns during the pandemic have affected researchers’ ability to finish clinical trials. Study completion rates dropped worldwide in 2020 (Clin Transl Sci doi: 10.1111/cts.13034). Trials with a pharmaceutical sponsor were more likely to reach a successful conclusion than trials with academic or government funding.

Hearing loss in older people

A longitudinal study of older adults finds that those with hearing loss showed a faster rate of cognitive decline than those whose hearing was normal. By contrast, no association was found between vision loss and deterioration in cognitive function (J Am Geriatr Soc doi:10.1111/jgs.16933). The question is whether hearing loss is a modifiable risk factor. Would giving older people better hearing aids reduce the risk of cognitive decline?

Physical activity

Among 100 000 adults taking part in the Copenhagen General Population Study, cardiovascular events and all-cause mortality were lower in those who were physically active in their leisure time. That’s no surprise. What is surprising, however, is that the opposite relation was seen with occupational physical activity, where higher levels were associated with an increased risk of heart disease (Eur Heart J doi:10.1093/eurheartj/ehab087). The reason isn’t clear but the results persisted after stratifying by lifestyle and socioeconomic factors.

Prefer subtraction to addition

When trying to improve stuff—whether objects, ideas, or situations—people show a systematic bias in favour of addition and a tendency to ignore the benefits of subtraction and simplification. That’s the conclusion of a series of experiments in which subjects were asked to solve a range of intellectual and practical problems. The investigators think that this default setting of add, rather than take away, is part of the reason for red tape, overcrowded diaries, and the sort of explanations where you can’t see the wood for the trees (Nature doi:10.1038/s41586-021-03380-y).

Benefits of breastfeeding for mothers

Women who breastfeed have a lower risk of cardiovascular disease and diabetes. Some of this protective effect may be because of the influence of lactation on the presence and distribution of fat. A longitudinal study of 1000 women finds that those who breastfed for longer had lower volumes of visceral adipose tissue and pericardial adipose tissue when measured by computed tomography around 15 years after their last birth (J Clin Endocrinol Metab doi:10.1210/clinem/dgaa980).