Olfactory observations
Spinato and colleagues surveyed mildly symptomatic outpatients infected with SARS-CoV-2 in Italy to estimate the prevalence of an altered sense of taste or smell. In people who had tested positive and responded to the survey, 64.4% had some degree of altered sense of taste or smell. The timing of the onset of this symptom was variable: in 18% it came before other symptoms, in 35% it occurred with other symptoms, in 62% it came after, and in the rest it was their only symptom. One limitation of the study was that it was based on questioning the patient about their symptoms rather than objective measures, so there is a chance that symptom prevalence or severity could have been overestimated. However, the methods were pragmatic given the circumstances. This is definitely a symptom worth watching out for, although this type of study doesn’t tell us how specific it is for COVID-19.

Not a good time to be immunosuppressed
Yes, that’s a bit of an understatement. Akalin and colleagues’ letter describes the outcomes of 36 kidney transplant recipients with COVID-19 in Montefiore Medical Center in New York. Ten died, 28 were admitted to hospital, and 11 received mechanical ventilation (of those who died, seven had had ventilation). Of the 28 who were admitted to hospital, 24 had their antimetabolite medication withdrawn. Tacrolimus was withheld in six. These patients had low CD3, CD4, and CD8 counts at presentation, suggesting that reducing immunosuppression could be sensible, but no one really knows what to do about these medications in this context. The key message from this cohort is that kidney transplant recipients have an alarmingly high mortality. Thus they should (continue to) aggressively shield themselves.

Privacy violations in South Korean tracing
The Korea Centers for Disease Control and Prevention was permitted to collect, profile, and share personal data that in the UK I like to think we’d never dream of sharing: including location data from mobile carriers, CCTV from the police, transactions from credit card companies, public transport records, and prescription and medical records. Some would argue that this is justified in view of the pandemic. Others would argue it violates the human right to privacy and that, instead, governments must find another solution. According to Park and colleagues’ letter, public identification of businesses visited by infected people led to loss of business, and the ages, sex, and nationalities of infected people were published on the Ministry of Health website. It went beyond the minimum necessary to achieve tracking goals. The authors present strategies for a more balanced approach—that is, disclosure of less granular data.

Rational rationing?
Ethics expert Armand Antommaria and his colleagues’ survey looked at US “triage” policies in 67 hospitals (because triage sounds better than rationing). OK, only half of those hospitals had policies, and some directors were not able to share the policies with the researchers. Most policies used scoring systems, presumably for the semblance of objectivity. The most frequently cited triage criteria were need, age, conservation of resources, and lottery. Those last two mean (a) denying a ventilator to those who would need a disproportionate amount of resources and (b) allocating resources by choice rather than first-come first-served when survival chances with a ventilator are unclear, respectively. These options aren’t exactly palatable, but there are worse ways of choosing who gets a ventilator when supply is short.

Nor a good time to be in a care home
Arons and colleagues found that SARS-CoV-2 spread rapidly in a nursing home: by 23 days after the first resident tested positive for the virus, 64% of residents had tested positive. More than half of those who tested positive had no symptoms at the time of testing. Such data are invaluable in comprehensively documenting how a facility can be so rapidly decimated by the virus so lessons can be learnt. The most interesting analysis in this study is of viral load and shedding by symptom classification: pre-symptomatic, typical symptoms, atypical symptoms, and (remained) asymptomatic. Pre-symptomatic patients could be retrospectively identified because everyone was tested and followed up to see who developed symptoms. Viral loads were similar between groups. The key lesson is the need for mass testing, especially in care homes, regardless of symptom status.

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The kung fu of covid

One third of a year has passed since the start of the covid-19 pandemic, but there is little sense of shared global wisdom. The Chinese sage Kŏng Qiū (551-479 BCE) would be saddened. Among the many sayings attributed to him are: “All people are the same; only their habits differ.” China, with the largest population in the world, is the only country to have come close to eliminating covid-19 within its borders (with the possible exceptions of New Zealand and Iceland, as we go to press). Among 1.4 billion people, daily deaths are zero. Why then isn’t the rest of the world rushing to adopt the habits of China? Another maxim of Confucius/kung fu is “Learn avidly. Question repeatedly. Analyse carefully. Then put what you have learned into practice intelligently.”

Dialogue concerning the two world systems

Galileo wrote a dialogue to show you could not believe contrary things at once: either the sun revolved around the earth, or the earth revolved around the sun. Unfortunately, the Pope was office-bound to believe the first, and Galileo made him look a fool. Mistake. The pope remained a fool for life, and Galileo remained under house arrest for life.

Now, with covid-19, any containment policy either revolves around the value of individual life, or it revolves around the economy. It cannot do both at the same time. China exemplifies the first, and Britain exemplifies the second. On 12 March our chief medical officer, chief scientific adviser, and Boris Johnson declared in favour of “herd immunity” (www.gov.uk/government/speeches/pm-statement-on-coronavirus-12-march-2020), and nothing that has happened since shows serious intent to prevent the cull which that implies. If we had started by valuing the individual, this would not have happened. And our economy would be less ruined too. Maybe there is time to mend our ways in the second wave.

Natural history

I may have been reading the wrong journals, but so far I’ve found little about the varied natural histories of the illness called covid-19. For sure, there have been plenty of symptom lists and time course diagrams and so forth, but nothing that’s helped me understand the transition from benign covid into malignant covid.

Now a very comprehensive review of the world literature has appeared in medRxiv (www.medrxiv.org/content/10.1101/2020.04.19.20071548v1). This divides covid-19 into three stages: “the time of infection (stage I), sometimes progressing to pulmonary involvement (stage II, with or without hypoxaemia), and less frequently to systemic inflammation (stage III).” The hardworking authors go on to attempt to map therapy on to each stage. That is certainly the central challenge, though it seems hardly addressable in the present state of ignorance.

Richard Lehman is professor of the shared understanding of medicine at the University of Birmingham.
EASILY MISSED?

ANCA associated vasculitis

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ANCA associated vasculitis (AAV) is an umbrella term for a group of multi-system autoimmune small vessel vasculitides that can present at any age and affect 20-25 people per million per year in Europe. 1 A typical GP practice with 8000 patients can expect to see one new case approximately every five years.

AAV diseases include microscopic polyangiitis, granulomatosus with polyangiitis (GPA, previously “Wegener’s granulomatosis”), and eosinophilic granulomatosis with polyangiitis (EGPA, previously “Churg-Strauss syndrome”). 1 The conditions are characterised by the formation of granulomas and inflammation of small arteries, arterioles, venules, and capillaries. 1 Inflamed vessels may rupture (for example, causing alveolar haemorrhage or a purpuric rash) or become occluded (for example, causing segmental glomerular infarction), giving rise to a broad array of clinical symptoms and signs related to a systemic inflammatory response, end organ microvascular injury, or the mass effect of granulomas.

What symptoms do patients develop?

AAV may present with constitutional symptoms suggestive of chronic inflammatory disease (fatigue, weight loss, fever, night sweats, myalgia, or polyarthralgia) or with specific features of end-organ involvement. Almost any part of the body can be affected, but the most commonly affected systems are the upper airways, lungs, kidneys, eyes, and peripheral nerves.

Therefore, presenting symptoms include sinus pain, nasal discharge, or crust, eye pain, or deafness (from upper airways involvement), cough, shortness of breath, wheeze or haemoptysis (from lung involvement), and painful, red eyes (from scleritis). Some patients may have weakness, numbness, or difficulty walking, but many patients do not mention these symptoms, and signs of peripheral neuropathy—such as foot drop or wrist drop—should be specifically sought on examination. A classic “vasculitic” purpuric skin rash is present in a minority of patients. Common presenting symptoms are listed in box 1.

Who gets vasculitis?

Several genetic and environmental risk factors have been identified, but most of the variation in incidence is accounted for by patient age. Incidence rises progressively with age until the mid-late 80s, so that the incidence in the population aged over 70 is 80-90 per million per year 1 and consequently AAV is the leading cause of glomerulonephritis in this age group. 7 However, AAV can present at any age—including in childhood—and affects all ethnicities; the incidence is approximately the same in women and men. Environmental risk factors are absent in most cases but exposure to drugs such as cocaine, hydralazine, and propylthiouracil has been implicated. 1

WHAT YOU NEED TO KNOW

- Consider ANCA associated vasculitis (AAV) in people with chronic systemic symptoms and evidence of renal, pulmonary, ear, nose, and throat, ophthalmic, or peripheral nerve disease
- Perform urinalysis in people presenting with persistent systemic symptoms and in those with specific features of vasculitis (scleritis, chronic dyspnoea, cough, haemoptysis, foot drop) because these individuals have a high probability of multi-system disease
- Patients with haemoptysis plus other features of AAV warrant same day hospital assessment to evaluate for pulmonary haemorrhage

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Nicola Welsh is an author of this article. She was involved in planning the content, writing her perspective and case history, and reviewing the final manuscript.
Diagnosis of AAV is often delayed or missed because the condition has virtually no pathognomonic features, and most of the presenting symptoms are either general—and thus may be misdiagnosed as another systemic disease—or more specific but attributed to more common diseases such as uncomplicated sinusitis, asthma, or scleritis. For example, EGPA may present with shortness of breath and wheeze and is often initially misdiagnosed as refractory or frequently relapsing asthma. People with predominant myalgia may be misdiagnosed as having polymyalgia rheumatica and—because corticosteroid treatment partially treats AAV—correct diagnosis is delayed until the steroid dose is weaned and other symptoms emerge. Granulomatosis with polyangiitis with cavitating lung lesions can be misdiagnosed as lung cancer.

Diagnosis can also be delayed or missed when symptoms in disparate organs are not recognised as manifestations of a single disease. A patient may attend separate clinics: ear, nose, and throat (for nasal crusting), ophthalmology (for scleritis), and neurology (for peripheral neuropathy) without anybody “joining the dots” between these symptoms. Indeed, a UK case-control study found that patients had frequent healthcare encounters in the months before a new diagnosis of GPA, with nearly 20% of patients attending two or more specialist clinic appointments in the year before diagnosis (compared to ~5% of controls).
Why does this matter?

There is a stark difference in patient outcomes when diagnosis is delayed or missed: untreated, only one in 10 patients survives beyond two years—a prognosis that is worse than most cancers. If promptly recognised, however, AAV responds well to immunosuppressive treatment and has a prognosis akin to other chronic inflammatory diseases. In randomised controlled trials, 60–90% of patients enter disease remission, and the 2 year survival is 90–97%.

This difference in survival stems from the degree of irreversible organ damage that occurs before the diagnosis is made (figure). This can also leave patients with long term symptoms—such as painful paraesthesia, dyspnoea, deafness, or facial deformity—or with life-limiting organ dysfunction such as chronic kidney disease. The consequences of late diagnosis are particularly apparent in the subset of people who have renal involvement. In this group, delayed diagnosis and worse renal function at presentation are associated with a higher risk of end-stage renal disease and early mortality.

How is it diagnosed?

Clinical

The diagnosis of AAV is clinical, supported by serological and histological data. There are many possible presenting symptoms—none more important than another for making the diagnosis—and no isolated discriminating symptoms of AAV. Rather, the key to diagnosis is prompt recognition of an inflammatory disease pattern when multiple symptoms emerge, especially if more than one organ system is implicated or in combination with chronic systemic symptoms. Therefore, when two or more of these symptoms develop concurrently, the index of suspicion should be high (box 1).

Two clinical scenarios pose particular diagnostic difficulty. The first is alveolar haemorrhage: it can be hard to recognise and is devastating if missed. Alveolar haemorrhage may present with haemoptysis, but this symptom is absent in up to half of cases. Some patients with extensive airspace bleeding will report only of shortness of breath or cough and have a near normal chest examination. Patients with haemoptysis plus other features of AAV warrant same day hospital assessment to rule out pulmonary haemorrhage without further primary care investigations if these would delay referral (box 2). All other patients with suspected vasculitis and dyspnoea or cough should have a full blood count; if there is a recent drop in haemoglobin (or a low haemoglobin with no historic blood loss in low grade alveolar haemorrhage) or in combination with chronic systemic symptoms. Therefore, when two or more of these symptoms develop concurrently, the index of suspicion should be high (box 1).

The second difficult scenario is AAV presenting as organ limited disease, without systemic symptoms. For example, most patients with isolated glomerulonephritis have no symptoms until renal failure advances to the point of uraemia. Thus, consider AAV in patients with falling eGFR with blood and protein on urine dipstick even if they have no constitutional symptoms and full blood count and C reactive protein results are normal.

The differential diagnosis of AAV includes cancer, chronic infection (particularly bacterial endocarditis), and other autoimmune conditions. Because of the difficulties in diagnosis, discuss patients with possible or suspected AAV early with a specialty service.

Investigations

Investigations can further support a diagnosis of AAV and refute the major differential diagnoses of infection and cancer. As in the case study, urinalysis can rapidly screen for renal involvement in a multi-system disease. Patients with haematuria or proteinuria in this context have a high probability of having AAV. This probability is ~2% if the dipstick findings occur in isolation, rising to 85% if there is concomitant sinus and pulmonary disease.

ANCA testing improves diagnostic certainty for patients with a high pre-test probability of disease. However, up to 10% of patients with small vessel vasculitis clinically test negative for ANCA. Conversely, false positive results can occur in the general population and in association with infections, malignancy, and autoimmune gastrointestinal and renal disease. Given this complexity, ANCA tests are not usually requested in primary care. Kidney or lung biopsies may be taken by specialty services to confirm a diagnosis of AAV or exclude differential diagnoses such as cancer.

How is it managed?

AAV is managed by a specialty service, which may be a rheumatology, renal, respiratory, or dedicated vasculitis service. It is treated with immunosuppressive therapies such as glucocorticoids, cyclophosphamide, rituximab, azathioprine, methotrexate, and mycophenolate mofetil. Adjunctive treatments aim to reduce the risk of infections—particularly pneumocystis, osteoporosis, diabetes, and cardiovascular disease.

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Planned earlier delivery for late pre-eclampsia may be better for mothers

Why was this study needed?
Mild pre-eclampsia affects up to 6% of pregnancies, with severe cases developing in 1% to 2%. Early signs include high blood pressure and having protein in the urine. Symptoms such as ankle swelling and headaches can occur if the condition progresses. In rare cases, there can be serious complications such as convulsions and stroke as well as stillbirth.

The cause is not yet fully understood, but it is thought to be linked to problems with the placenta.

What did this study do?
The PHOENIX randomised controlled trial allocated 448 women to a planned delivery, such as an induction or caesarean section, and 451 women to expectant management (usual care). All had late pre-eclampsia.

The trial took place in 46 consultant led maternity units across England and Wales. Those in the intervention group were scheduled for initiation of delivery within 48 hours of randomisation to enable preparations such as neonatal lung maturity acceleration to take place. Delivery was by induction of labour unless a caesarean section was necessary. Expectant management involved delivery at 37 weeks or sooner, as in the recommendations from the National Institute for Health and Care Excellence (NICE).

Longer term results from this trial are still being collected. For example, it will be useful to know if those infants in the intervention group have a higher incidence of developmental delay.

What did it find?
• Babies in the planned delivery arm were born on average five days earlier than controls, according to their gestational age.
• The primary outcome for the baby was either death or neonatal unit admission. This was higher in the planned delivery group affecting 196 (4.2%) infants compared with 159 (3.4%) infants in the expectant management group (adjusted relative risk 1.26, 95% confidence interval 1.08 to 1.47). However, admission was mainly attributed to prematurity, without excessive respiratory or other morbidity, intensity of care, or length of stay, and there were no deaths.
• The primary maternal outcome was either a recorded high systolic blood pressure or any of the fullPIERS model outcomes (Pre-eclampsia Integrated Estimate of Risk). This includes specific outcomes such as death, stroke, and acute renal failure. The incidence of any of these outcomes was lower in the planned delivery group, affecting 289 (65%) women compared with 338 (75%) women in the expectant management group (adjusted relative risk 0.86, 95% confidence interval 0.79 to 0.94).

What does current guidance say on this issue?
Recent NICE guidance on the diagnosis and management of hypertension in pregnancy recommends that women diagnosed before 34 weeks should be monitored until they reach 37 weeks unless the condition worsens. Intravenous magnesium sulphate and a course of antenatal corticosteroids should be offered in line with the NICE guideline on preterm labour and birth. The advice for women between 34 and 37 weeks is the same, but in addition, it states that if considering a planned delivery, it is important to take into account the condition of woman and baby.

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

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Cannabis-based medicinal products: summary of NICE guidance

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Further information about the guidance, a list of members of the guideline development group, and the supporting evidence statements are in the full version on bmj.com.

In September 2018, in light of the UK chief medical officer’s review and in response to the Advisory Council on the Misuse of Drugs advice, ministers in the UK announced changes to the existing regulations on cannabis-based medicinal products (CBMPs). CBMPs would be rescheduled from Schedule 1 of the Misuse of Drugs Regulations 20011 2 to Schedule 2 controlled drugs and prescribing would be restricted to doctors on the Specialist Register of the General Medical Council (GMC). Rescheduling allows CBMPs to be legally prescribed. However, many CBMPs currently do not have marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA), and so existing prescribing guidance and governance arrangements in place for unlicensed medicines continue to apply. Unlicensed medications should not be considered as first line treatments and should be used only when there is an unmet clinical need.

The Department of Health and Social Care in England asked the National Institute for Health and Clinical Excellence (NICE) to develop guidance on prescribing of CBMPs. This article summarises the recommendations from this guideline. As set out in the guideline scope, NICE looked at four specific conditions: intractable nausea and vomiting, chronic pain, spasticity, and severe treatment-resistant epilepsy.

WHAT YOU NEED TO KNOW

• The rescheduling of cannabis-based medicinal products (CBMPs) allows their prescription when there is an unmet clinical need
• Initial prescription of CBMPs must be made by a doctor on the Specialist Register with a special interest in the condition being treated. For children and young people, the initiating prescriber should also be a tertiary paediatric specialist
• Subsequent prescriptions of CBMPs may be issued by another prescriber, such as a general practitioner, as part of a shared care agreement under the direction of the initiating specialist prescriber
• Offer THC:CBD spray for moderate to severe spasticity in adults with multiple sclerosis if other pharmacological treatments are not effective. Consider nabulone as an add-on treatment for adults with intractable chemotherapy-induced nausea and vomiting. Cannabidiol (CBD) with clobazam is recommended for treating seizures associated with Lennox-Gastaut syndrome and Dravet syndrome
• Do not offer CBMPs to manage chronic pain in adults. Do not offer CBD to manage chronic pain in adults unless as part of a clinical trial

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the guideline committee’s experience and opinion of what constitutes good practice. Evidence levels for the recommendations are in the full version of this article on bmj.com.

Prescribing CBMPs

The guideline makes recommendations about the initiation of CBMPs, and the factors to be taken into account when prescribing CBMPs.

• Initial prescription of CBMPs must be made by a specialist medical practitioner (a doctor included in the register of specialist medical practitioners (the Specialist Register)). They should also have a special interest in the condition being treated.
• For children and young people under the care of paediatric services, the initiating prescriber should also be a tertiary paediatric specialist.
• When prescribing CBMPs, advise people to stop any non-prescribed cannabis, including over-the-counter, online, and illicit products.
• Prescribers should record details of treatment, clinical outcomes, and adverse effects for people prescribed CBMPs, using local or national registers if available.
• When prescribing and monitoring CBMPs, take into account:
  – Current and past use of cannabis (including any over-the-counter and online products)
  – History of substance misuse, including the illicit use of cannabis
  – Potential for dependence, diversion, and misuse (in particular with delta-9-tetrahydrocannabinol (THC))
  – Mental health and medical history (in particular, liver impairment, renal impairment, cardiovascular disease)
  – Potential for interaction with other medicines— for example, central nervous system depressants and other centrally active drugs, antiepileptics, and hormonal contraceptives
  – Pregnancy and breastfeeding.
• When prescribing CBMPs for babies, children, and young people, pay particular attention to the:
– Potential impact on psychological, emotional, and cognitive development
– Potential impact of sedation
– Potential impact on structural and functional brain development.

Shared care
The guideline includes shared care recommendations, which outline the responsibilities for managing CBMP prescribing where shared care between the specialist and a primary care prescriber is being considered.

• After the initial prescription, subsequent prescriptions of CBMPs may be issued by another prescriber as part of a shared care agreement under the direction of the initiating specialist prescriber, if:
  – Shared care is appropriate and is in the patient’s best interest
  – The patient’s clinical condition is stable
  – The other prescriber is confident to make a fully informed prescribing decision about CBMPs.
• Efficacy and safety of CBMPs should be monitored and evaluated, and doses should be adjusted by the initiating specialist prescriber as part of the shared care agreement.
• A shared care agreement for a person prescribed a CBMP should include:
  – The responsibilities of all parties (the initiating specialist prescriber, the other prescriber(s), the patient, and family and/or carers)
  – The nature and frequency of monitoring and how this will be recorded
  – When treatment might be stopped, for example, if it is not effective
  – How suspected or known adverse reactions will be managed
  – How communication will be managed between the initiating specialist prescriber, the other prescriber, the patient, and family and/or carers
  – How the treatment will be funded
  – How care will be maintained when the patient, initiating specialist prescriber, or other prescriber moves location (including transition to adult services).

Shared decision making
The guideline recommends a shared decision making approach to ensure that patients are at the centre of decisions about their own treatment and care.

• Before prescribing CBMPs, discuss with people:
  – The potential benefits and harms, including any risk of dependence or interaction with other medicines
  – The licensing status of the medicines
  – How long they might take the medicine
  – How long it will take to work
  – What it has been prescribed for and how to take it
  – How it may affect their ability to drive (see the advice from the UK Department for Transport)
  – The need to seek advice before travelling abroad about the legality of CBMPs in other countries (see the UK Government’s advice on travelling with medicine containing a controlled drug).
  – The importance of not allowing others to use the prescribed medicine.

GUIDELINES INTO PRACTICE

• How do you ensure that patients get access to the initial prescription of CBMPs by a specialist medical practitioner (that is, listed on the Specialist Register) with a special interest in the condition being treated?
• What system do you have in place to monitor patients under the shared care arrangement after the initial CBMP prescription?

Efficacy and safety of CBMPs should be monitored and evaluated, and doses should be adjusted by the initiating specialist prescriber.
CBMPs for specific conditions
NICE reviewed the evidence for four specific groups. The quality of evidence varies, with most of the higher quality evidence found for treatment of chronic pain and of spasticity. When there was a lack of evidence from randomised controlled trials (for example, regarding the treatment of epilepsy), recommendations were based on the committee’s experience and consensus.

Intractable nausea and vomiting
- Consider nabilone as an add-on treatment for adults (≥18 years old) with chemotherapy-induced nausea and vomiting which persists with optimised conventional antiemetics.
- When considering nabilone for adults with chemotherapy-induced nausea and vomiting, take into account potential adverse drug interactions—for example, with central nervous system depressants and other centrally active drugs.

Chronic pain
- Do not offer cannabidiol (CBD) to manage chronic pain in adults unless as part of a clinical trial.
- Do not offer the following to manage chronic pain in adults:
  - Nabilone
  - Dronabinol
  - Delta-9-tetrahydrocannabinol (THC)
  - Combination of CBD with THC.
- Adults who started CBMPs to manage chronic pain in the NHS before this guidance was published should be able to continue treatment until they and their NHS clinician think it appropriate to stop.

Spasticity
- Offer a four week trial of THC:CBD spray to treat moderate to severe spasticity in adults with multiple sclerosis, if:
  - Other pharmacological treatments for spasticity are not effective (see research recommendations)
  - The company provides THC:CBD spray according to its “pay-for-responders” scheme.
- After the four week trial, continue THC:CBD spray if the person has had at least a 20% reduction in spasticity-related symptoms on a 0 to 10 patient-reported numeric rating scale.
- Treatment with THC:CBD spray should be initiated and supervised by a physician with specialist expertise in treating spasticity due to multiple sclerosis, in line with its marketing authorisation.

Severe treatment-resistant epilepsy
NICE has made research recommendations on the use of CBMPs for severe treatment-resistant epilepsy (see research recommendations).
- NICE has developed technology appraisal guidance on CBD with clobazam for treating seizures associated with Lennox-Gastaut syndrome and Dravet syndrome.

Implementation
The main challenges to the implementation of this guidance for specialist services are:
- Only a limited number of healthcare professionals have experience of prescribing CBMPs. Training will be needed to ensure healthcare professionals have the confidence and knowledge to provide the care needed.
- Access to the initial CBMPs prescription may depend on the availability of doctors on the Specialist Register within a particular local area.
- A multidisciplinary team may need to be involved when decisions need to be made that are in the patient’s best interest, such as the care of babies, children, or young people. However, this may not be feasible in all specialist care settings because staffing and structure of care provision varies.

Training will be needed to ensure healthcare professionals have the confidence and knowledge to provide the care needed.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE
Committee members involved in this guideline update included three lay members who contributed to the formulation of the recommendations summarised here. We thank them for sharing their experiences and expertise and helping to ensure that the guideline took account of the perspective of patients, their families, and their carers.

FUTURE RESEARCH
The Guideline Committee has made the following recommendations for research.
1. For adults with fibromyalgia or persistent treatment-resistant neuropathic pain, what is the clinical and cost effectiveness of cannabidiol (CBD), containing no or only traces of delta-9-tetrahydrocannabinol (THC), as an add-on to standard treatment?
2. For children and young people with intractable cancer-related pain and pain associated with specific diseases (such as epidermolysis bullosa), what is the clinical and cost effectiveness of cannabis-based medicinal products (CBMPs) as an add-on to standard treatment to improve symptoms compared with treatment with standard care?
3. What is the clinical and cost effectiveness of CBD in epileptic disorders in children, young people, and adults?
4. Does the addition of THC to CBD have an effect on seizure frequency, brain structure, and neuropsychological performance when compared with both CBD alone and placebo in epileptic disorders in children, young people, and adults?
5. What is the clinical and cost effectiveness of CBMPs other than THC:CBD spray for children, young people, and adults with spasticity? In particular, what is the impact of spasticity on improvements in quality of life?

Competing interests: Declaration of interests based on NICE’s policy on conflicts of interests (available at http://www.nice.org.uk/ Media/Default/About/Who-we-are/Policies-and-procedures/code-of-practice-for-declaring-and-managing-conflicts-of-interest.pdf). The authors’ full statements can be viewed at https://www.nice.org.uk/guidance/rg144/documents/committee-member-list-3. SCD and CM are NICE staff and have no relevant interests to declare.

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**MINERVA**

**Obesity and type 2 diabetes**

Obesity is the dominant risk factor by far for type 2 diabetes, according to a Danish study that followed 10,000 middle aged people for 15 years. Compared with people of normal weight, those with obesity were almost six times more likely to develop diabetes (Diabetologia doi:10.1007/s00125-020-05140-5). This contrasts with estimates of genetic risk. People with a high score for nearly 200 genetic variants associated with type 2 diabetes were only twice as likely to develop the condition as those with a low score.

**Variation in body mass index**

A study from the US tries to work out the relative importance of environmental variables and genetic influences on body mass index and reaches a surprising conclusion. Among 7,000 young adults who contributed not only detailed information on lifestyle but also samples for genetic analysis, less than 6% of the variation in BMI between individuals could be explained by socioeconomic status and not much more by a polygenic risk score (Am J Epidemiol doi:10.1093/aje/kwaa058). So why are some people thin and others overweight? The investigators don’t know. Most of the individual variation in BMI couldn’t be explained by demographic characteristics, social circumstances, genetic score, or health behaviours.

**Disease as a metaphor**

Susan Sontag’s famous book Illness as Metaphor started life in 1978 as a long essay. Appropriately enough, the New York Review of Books has just made it available again (https://www.nybooks.com/articles/1978/02/23/disease-as-political-metaphor). At a time when we are being assaulted by military metaphors of battles against a viral foe, it’s worth reading. Sontag argued that the most truthful way of regarding illness was one purged of metaphorical thinking. Metaphor encouraged misrepresentations, stupidities, and false ideas. A disease should be regarded as a disease, not as a sign of evil.

**Bariatric surgery**

Likelihood of long term complications is important for patients considering the balance between benefits and harms of bariatric surgery. A large database study from the US finds that it’s common to need further abdominal surgery after the initial operation—although less so after sleeve gastrectomy (9% over five years) than Roux-en-Y gastric bypass (12% over five years). Most of these additional procedures were revisions, repairs of abdominal wall hernias, and operations for internal hernias. Five year mortality was around 9% for both sleeve gastrectomy and Roux-en-Y gastric bypass (JAMA Surg doi:10.1001/jamasurg.2019.5470).

**CINEMA**

CINEMA or Confidence In Network Meta-Analysis is a web based tool for doing exactly what its name suggests. It allows investigators to evaluate the results from network meta-analyses when multiple interventions are being compared. The underlying framework considers six domains of quality: within-study bias, reporting bias, indirectness, imprecision, heterogeneity, and incoherence. The central idea is a percentage contribution matrix, which shows how much information each individual study contributes to the results (https://doi.org/10.1371/journal.pmed.1003082; https://cinema.ispm.unibe.ch/).

**Lessons from pandemics**

Inevitably perhaps, people are using aspects of the covid-19 pandemic to argue in support of something they already believed in. Vegetarians point to the origin of the virus to show the harms of eating meat. Libertarians fear that the pandemic is herding us towards a police state. Religious leaders see it as a timely reminder of eternal truths. Sometimes the evidence points both ways (https://www.spectator.co.uk/article/we-re-all-guilty-of-recruiting-this-virus-to-our-cause). Supporters of the NHS think the pandemic shows the value of socialised medicine. Detractors, on the other hand, say that it reveals a monolithic organisation unable to react fast enough to avoid a population lockdown.

**Vaccine development**

How soon we shall have a safe and effective vaccine against SARS-CoV-2 remains to be seen, but vaccines have been developed quickly in the past. The virologist Maurice Hilleman contributed to the invention of more than 40 vaccines over his career, one of which helped prevent a pandemic of Asian flu in 1957. After isolating the virus in May of that year, Hilleman sent samples to six companies that had previously produced influenza vaccines. Vaccines against the new virus were developed within weeks and more than 40 million doses were given that autumn. Of course, these companies weren’t starting from scratch and safety testing was less demanding than it is now. Even so, it was an impressive achievement (https://www.lastwordonnothing.com/2020/04/15/one-voice-many-vaccines-2/).

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