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- 1 Ranney ML, Griffith V, Jha AK. Critical supply shortages—the need for ventilators and personal protective equipment during the COVID-19 pandemic. *N Engl J Med* 2020; **382**: e41.
- 2 Mansoor S. California Gov Gavin Newsom says federal government sent '170 broken ventilators'. March 29, 2020. <https://time.com/5812147/california-coronavirus-broken-ventilators> (accessed Jan 5, 2021).
- 3 Proctor N, O'Reilly K. Hospital repair restrictions, manufacturer-imposed barriers to fixing medical equipment cause inefficiencies and delays. July 8, 2020. https://uspirg.org/sites/pirg/files/reports/Hospital_Repair_Restrictions_USPEF_7.8.20b.pdf (accessed Jan 5, 2021).
- 4 European Parliament. Towards a more sustainable single market for business and consumers. March 11, 2020. https://www.europarl.europa.eu/doceo/document/A-9-2020-0209_EN.html# (accessed Jan 5, 2021).
- 5 Robertson A. Massachusetts passes 'right to repair' law to open up car data. Nov 4, 2020. <https://www.theverge.com/2020/11/4/21549129/massachusetts-right-to-repair-question-1-wireless-car-data-passes> (accessed Jan 5, 2021).
- 6 Wyden R. Wyden and Clarke introduce bill to eliminate barriers to fixing critical medical equipment during the pandemic. Aug 6, 2020. <https://www.wyden.senate.gov/news/press-releases/wyden-and-clarke-introduce-bill-to-eliminate-barriers-to-fixing-critical-medical-equipment-during-the-pandemic-> (accessed Jan 2, 2021).

Malnutrition risk in hospitalised COVID-19 patients receiving CPAP

Continuous positive airway pressure (CPAP) that is delivered by face mask or hood is increasingly used in patients with COVID-19 who have been admitted to hospital, often on general or respiratory wards. Oral intake of food and drink in patients with COVID-19 might have been and will often continue to be poor due to disease-associated anorexia, nausea, and impairment of taste. Full-face or hood CPAP also makes it impossible to eat and drink without mask removal,¹ which can be associated with decreased arterial oxygen saturation.

Staff might also fear that the use of nasogastric feeding can cause mask air leaks or promote gastric distension and aspiration due to aerophagia.

Such issues are in fact readily managed, and the British Association for Parenteral and Enteral Nutrition has produced practical guidelines.² However, NHS England and NHS Improvement³ advocate opioid administration when CPAP is used to reduce the sensation of breathlessness and high tidal volumes, an intervention that can impair gut motility.

We received reports of three patients with COVID-19 who were treated with CPAP and developed starvation ketosis and other patients who have gone for extended periods (up to 25 days) without substantial oral intake or initiation of nutritional support. The negative effects of malnutrition can be worsened by the process of muscle wasting, which is common in patients with COVID-19 who are admitted to hospital, and by subsequent admission to an intensive care unit for mechanical ventilation, where gut function might be impaired (eg, by use of opioid analgesia), as dietitians have reported to the Critical Care Specialist Group of the British Dietetic Association.

We were also made aware of the use of 0.9% saline in some health-care centres as the routine (and sole) intravenous crystalloid. Such practice does not comply with the National Institute for Health and Care Excellence clinical guideline 174: although 0.9% saline can be used for replacement of gastrointestinal losses or as a bolus for acute resuscitation, its use is not recommended in terms of routine maintenance.⁴ Use as routine maintenance can increase sodium and chloride load in the body, potentially leading to bowel oedema and further impairment of gastrointestinal function.⁵

We recommend that health-care professionals with expertise in nutrition, especially dietitians, nutrition nurses, physicians, and pharmacists, should be engaged in the assessment

and care of all patients with COVID-19 who receive CPAP and patients who are subsequently admitted to intensive care units for mechanical ventilation. Appropriate nutritional support—including the introduction of parenteral nutrition, if necessary—improves outcomes in analogous cases.⁶

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- 1 Reeves A, White H, Sosnowski K, Tran K, Jones M, Palmer M. Energy and protein intakes of hospitalised patients with acute respiratory failure receiving non-invasive ventilation. *Clin Nutr* 2014; **33**: 1068–73.
- 2 British Association for Parenteral and Enteral Nutrition, British Dietetic Association. Route of nutrition support in patients requiring NIV & CPAP during the COVID-19 response. April 17, 2020. <https://www.bapen.org.uk/pdfs/covid-19/nutrition-in-niv-21-04-20.pdf> (accessed Dec 4, 2020).
- 3 NHS England and NHS Improvement. Guidance for the role and use of non-invasive respiratory support in adult patients with coronavirus (confirmed or suspected). Redditch: NHS England, 2020.
- 4 Intravenous fluid therapy in adults in hospital. Clinical guideline [CG174]. May 5, 2017. <https://www.nice.org.uk/guidance/cg174> (accessed March 16, 2021).
- 5 Li H, Sun S, Yap JQ, Chen J, Qian Q. 0.9% saline is neither normal nor physiological. *J Zhejiang Univ Sci B* 2016; **17**: 181–87.
- 6 Faisy C, Lerolle N, Dachraoui F, et al. Impact of energy deficit calculated by a predictive method on outcome in medical patients requiring prolonged acute mechanical ventilation. *Br J Nutr* 2009; **101**: 1079–87.



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Free licensing of vaccines to end the COVID-19 crisis

The pace of COVID-19 vaccine development, authorisation, and production is unprecedented. Yet all three approved vaccines by Pfizer–BioNTech, Moderna, and AstraZeneca

are already facing manufacturing delays. These delays are creating chaos for many national vaccination programmes, leading to calls for coordinated efforts by governments and manufacturers to increase production.¹

These pharmaceutical companies have benefited greatly from huge sums of public funding for research and development and advance purchase commitments, amounting to between US\$2.2 billion and \$4.1 billion (by Feb 1, 2021) from Germany, the UK, and North America combined (appendix). Yet unfortunately, these governments did not make their support conditional on measures that would enable more vaccine to be produced through, for example, patent pools (eg, the COVID-19 Technology Access Pool) or non-exclusive licensing, which would allow pharmaceutical companies with spare manufacturing capacity to increase supply. So far, most effort has gone into increasing production capacity in the vaccine developers' own facilities or through subcontracts and licensing arrangements with other developers, such as AstraZeneca's agreement with the Serum Institute of India, or Sanofi's support in filling and packing bottles of Pfizer-BioNTech's vaccine.

It is not, however, too late to take bold measures to increase production. Ideally, an agreement could be reached with the patent holders to make the relevant intellectual property available. However, if this agreement is not possible, compulsory licensing is possible (ie, when a government grants permission to someone else to produce a patented product).² Compulsory licensing is permitted in exceptional circumstances: public health emergencies,³ such as the COVID-19 pandemic.

Together, thirteen EU member states account for more than 60% of the world's major facilities for vaccine production and 90% of global vaccine production.⁴ Of course, changes would be needed to refocus production

to COVID-19 vaccines, but this approach could boost production in the immediate future. It would also enable vaccine manufacturers in low-income regions to start producing immediately,⁵ especially benefiting those countries that are far down the list to receive vaccines. Delays in vaccine production and deployment will lead to avoidable morbidity, mortality, and repeated lockdowns with detrimental health, social, and economic consequences that are related to COVID-19. Effective and coordinated roll-out plans are urgently required to speed up deployment of existing vaccines. The EU should also use all instruments that are available, including compulsory licensing, to overcome the delays in vaccine production and to protect public health in this unprecedented crisis.

Throughout the pandemic, things that were once considered to be impossible, such as lockdowns and other severe restrictions on personal and economic liberty, have become accepted. There is no reason why our approach to vaccine development and manufacture should be any different.

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- 1 Lancet Commission on COVID-19 Vaccines and Therapeutics Task Force Members. Urgent needs of low-income and middle-income countries for COVID-19 vaccines and therapeutics. *Lancet* 2021; **397**: 562–64.
- 2 Wong H. The case for compulsory licensing during COVID-19. *J Glob Health* 2020; **10**: 010358.
- 3 WHO. The Doha Declaration on the TRIPS Agreement and Public Health. Nov 20, 2015. https://www.who.int/medicines/areas/policy/doha_declaration/en (accessed Feb 24, 2021).

- 4 European Vaccine Manufacturers. Vaccine's contribution to Europe's future. March 15, 2010. <https://www.vaccineseuropa.eu/wp-content/uploads/2012/12/Vaccines-contribution-to-Europes-future-March-2010.pdf> (accessed Feb 24, 2021).
- 5 Usher AD. South Africa and India push for COVID-19 patents ban. *Lancet* 2020; **396**: 1790–91.

Guidelines should not pool evidence from uncomplicated and severe COVID-19

The WHO Global Development Group guidelines on COVID-19 therapeutics are meant to provide evidence-based advice to all countries on the medical management of patients with COVID-19.^{1,2} The only small-molecule drug to show unequivocal benefit to date is dexamethasone. In the largest randomised controlled trial in patients who were admitted to hospital with COVID-19 (ie, the RECOVERY trial), dexamethasone at a low dose reduced mortality in the prospectively defined subgroups of patients requiring medical oxygen (rate ratio 0.82 [95% CI 0.72–0.94]) or being ventilated (0.64 [0.51–0.81]) but not in patients not receiving respiratory support at randomisation (1.19 [0.91–1.55]).³ The current WHO living guideline on COVID-19 therapeutics¹ recognises this important difference in therapeutic response in relation to stage of the disease by recommending use of corticosteroids in patients requiring respiratory support but conditionally recommending against their use in patients not requiring respiratory support. By stark contrast, largely on the basis of inpatient studies, the guideline has recommended strongly against hydroxychloroquine (87.4% [9549 of 10 921] of studied patients were inpatients⁴) and lopinavir-ritonavir (all 7429 patients were inpatients⁵) in patients with any disease severity. There is convincing evidence that these drugs do not



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See Online for appendix