Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

However, before self-testing for infectious diseases can become the norm, there is a need to empower patients to understand and manage their self-diagnosis with appropriate resources. This approach requires a clear objective from the patient, transparent and efficient reporting of results, and rapid communication with health professionals using telemedicine or other virtual methods to maximise the advantages of self-testing. Furthermore, psychological support must be readily available to ensure that patients are prepared to receive their results and engage in appropriate management. Beyond COVID-19, the patient should become the centre of infectious diseases management, especially in LMICs.

We declare no competing interests.

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1 Ondoa P, Kebede Y, Loembe MM, et al. COVID-19 testing in Africa: lessons learnt. *Lancet Microbe* 2020; **1:** e103–04.
2 Ministère de la Santé Publique. Epidémie de Coronavirus (COVID-19). Minsante, 2020. https://www.minsante.cm/site/?q=fr/epid-mie-de-coronavirus-covid---19- (accessed March 17, 2021).
3 WHO Africa. New COVID-19 rapid tests a game changer for Africa. World Health Organization Regional Office for Africa, 2020. https://www.afro.who.int/news/new-covid-19-rapid-tests-game-changer-africa (accessed March 17, 2021).
4 Boum Y, Fai KN, Nikolay B, et al. Performance and operational feasibility of antigen and antibody rapid diagnostic tests for COVID-19 in symptomatic and asymptomatic patients in Cameroon: a clinical, prospective, diagnostic accuracy study. *Lancet Infect Dis* 2021; published online March 25. https://doi.org/10.1016/S1473-3099(21)00132-8.
5 Tsang NNY, So HC, Ng KY, et al. Diagnostic performance of different sampling approaches for SARS-CoV-2 RT-PCR testing: a systematic review and meta-analysis. *Lancet Infect Dis* 2021; published online April 12. https://doi.org/10.1016/S1473-3099(21)00146-8.
6 Stevens DR, Vrana CJ, Dlin RE, Korte JE. A global review of HIV self-testing: themes and implications. *AIDS Behav* 2018; **22:** 497–512.

Lack of detail in population-level data impedes analysis of SARS-CoV-2 variants of concern and clinical outcomes

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The SARS-CoV-2 lineage B.1.1.7 is characterised by a suite of defining mutations in the immunodominant spike protein, including a signature Asp501Tyr substitution in the receptor-binding domain.[1] First reported in December 2020, in the UK, the variant's discovery coincided with a substantial surge in case numbers and fatalities in the UK, raising concerns that this variant was both more infectious and virulent than previous variants. Epidemiological and modelling studies have yielded good evidence that B.1.1.7 is more transmissible than other variants.[1,2] However, conclusions as to the effects of B.1.1.7 on disease severity are less certain. Confounding factors including health-care resource use, demographic changes, and socio-behavioural trends affect clinical outcomes, including mortality, and are difficult to adjust for without detailed, robust, patient-level data.

In *The Lancet Infectious Diseases*, Dan Frampton and colleagues[3] report their findings from such a study. Analysing a cohort of 341 patients, including 198 (58%) with B.1.1.7 infections, the authors correlated outcomes with granular clinical data. Their observation that B.1.1.7 infections were associated with increased viral loads corroborates findings from two other studies[4,5] and provides a mechanistic hypothesis that increased transmissibility is via increased respiratory shedding. Yet, disease severity and clinical outcomes between patients with B.1.1.7 and non-B.1.1.7 infections were similar after adjusting for differences in age, sex, ethnicity, and comorbidities. Importantly, this study was done from Nov 9, to Dec 20, 2020, before the late-December peak in UK COVID-19 infections, avoiding any confounding effect of the availability of health-care resources on mortality.

This finding is in contrast with three studies that reported increased mortality associated with lineage B.1.1.7 (table).[6–8] Several factors might explain this discordance. Two of these studies were based on a community-based testing dataset, whereas Frampton and colleagues studied a cohort of patients admitted to hospital, which included substantially more older adults than the other studies did. Although the proportion of patients with severe illness was not reported by the other studies, this proportion was probably much lower than that in Frampton and colleagues' study. Hence, although these large community studies found a significant difference in mortality at a population level, the absolute risk increase affecting individual patients is probably minimal.

Furthermore, instead of whole-genome sequencing as used by Frampton and colleagues, these studies

	Frampton et al[3]	Challen et al[6]	Davies et al[7]	Grint et al[8]
Patient recruitment	Hospitalised patients with confirmed COVID-19	Public health data from community-based testing dataset	Public health data from community-based testing dataset	Public health data from both community and hospital-based testing dataset
Study dates	Nov 9, to Dec 20, 2020	Oct 1, 2020, to Jan 28, 2021	Nov 1, 2020, to Jan 23, 2021	Nov 16, 2020, to Jan 11, 2021
Number of participants	341 (69%) included of 496 available patients screened	109 812 (11·6%) included of 941 518 available patients screened	1 146 534 (51·1%) included of 2 245 263 available patients screened	184 786 (41·9%) included of 441 161 available patients screened
Age of participants, years	Median 60 (IQR 47–75)	Mean 46·3 (SD 11·0)	1–34 (513 726/1 14 6534 [44·8%]); 35–54 (403 313/1 14 6534 [35·2%]); 55–69 (175 983/1 14 6534 [15·3%]); 70–84 (440 46/1 14 6534 [3·8%]); ≥85 (9446/1 14 6534 [0·8%])	Median 38·0 (IQR 24·0–52·0); mean 38·2 (SD 18·1)
Detection of lineage B.1.1.7	Whole-genome sequencing and matching to COG-UK Mutation Explorer database	Surrogate measure using S-gene negativity on Thermo TaqPath COVID-19 multiplex PCR assay	Surrogate measure using S-gene negativity on Thermo TaqPath COVID-19 multiplex PCR assay	Surrogate measure using S-gene negativity on Thermo TaqPath COVID-19 multiplex PCR assay
Controls	Non-B.1.1.7 infections	S-gene positive patients	S-gene positive patients	S-gene positive patients
Primary outcome	Clinical severity as defined by WHO ordinal scale ≥6; mortality at 28 days	Mortality at 28 days	Mortality at 28 days	Mortality at 28 days
Overall rate of severe disease	36·9%	Data not available	Data not available	Data not available
Overall mortality rate	16·2%	0·3%	0·9%	0·5%
Effect on mortality	No significant difference	HR 1·64 (95% CI 1·32–2·04)	HR 1·55 (95% CI 1·39–1·72)	HR 1·67 (95% CI 1·34–2·09)

HR=hazard ratio.

Table: **Comparison of studies assessing the effect of lineage B.1.1.7 on disease severity and clinical outcomes**

used S-gene target failure (SGTF) on PCR assay as a surrogate measure for detection of lineage B.1.1.7. The B.1.1.7 variant is associated with nucleotide deletions that prevent S gene target amplification by several commercial tests. This method gave rise to notable selection bias because S-gene data were unavailable in certain areas because of assay availability, with half of patients in both studies having unknown S gene status. Crucially, missing SGTF status was associated with older age and place of residence, with most patients in care homes having absent S-gene data, where mortality rates from COVID-19 are highest.

Thus, although limited by a much smaller dataset, the study by Frampton and colleagues has important advantages over the three community studies. These advantages include the use of whole-genome sequencing, recruitment of hospitalised patients, and a population reflective of the spectrum of severity in whom increased virulence will have the greatest effect on outcomes. The finding that lineage B.1.1.7 infection did not confer increased risk of severe disease and mortality in this high-risk cohort is reassuring but requires further confirmation in larger studies.

These differences between B.1.1.7 and non-B.1.1.7 lineages mirror those of other virological sub-groups of SARS-CoV-2. Similarly conflicting data was initially reported when variants carrying the Asp614Gly substitution emerged and became the dominant variants worldwide over the first few months of the pandemic in 2020. Early population-level data suggested that this substitution was associated with increased COVID-19 mortality but later cohort studies found no effect on disease severity.[9,10] In a study we did in Singapore comparing different SARS-CoV-2 clades, Asp614Gly was associated with increased viral loads without changes in severity or transmission.[11]

Genetic drift and selection pressures (in particular with passive antibody treatments and vaccination) will continue to engender changes in SARS-CoV-2 and might result in the emergence of variants of high consequence—variants that are more virulent, escape from host immunity, or are resistant to treatment. Active, timely, and broad-based genomic surveillance is crucial for their early detection. But careful epidemiologic and clinical assessment, coupled with a healthy scepticism, is important when assessing claims of the effect of these variants.

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1 Davies NG, Abbott S, Barnard RC, et al. Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. *Science* 2021; published online March 3. https://doi.org/10.1126/science.abg3055.
2 Leung K, Shum MH, Leung GM, Lam TT, Wu JT. Early transmissibility assessment of the N501Y mutant strains of SARS-CoV-2 in the United Kingdom, October to November 2020. *Euro Surveill* 2021; **26:** 2002106.
3 Frampton D, Rampling T, Cross A, et al. Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study. *Lancet Infect Dis* 2021; published online April 12. https://doi.org/10.1016/S1473-3099(21)00170-5.
4 Kidd M, Richter A, Best A, et al. S-variant SARS-CoV-2 lineage B1.1.7 is associated with significantly higher viral loads in samples tested by ThermoFisher TaqPath RT-qPCR. *J Infect Dis* 2021; **223:** 1666–70.
5 Calistri P, Amato L, Puglia I, et al. Infection sustained by lineage B.1.1.7 of SARS-CoV-2 is characterised by longer persistence and higher viral RNA loads in nasopharyngeal swabs. *Int J Infect Dis* 2021; published online March 5. https://doi.org/10.1016/j.ijid.2021.03.005.
6 Challen R, Brooks-Pollock E, Read JM, Dyson L, Tsaneva-Atanasova K, Danon L. Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study. *BMJ* 2021; **372:** n579.
7 Davies NG, Jarvis CI, Group CC-W, et al. Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7. *Nature* 2021; published online March 15. https://doi.org/10.1038/s41586-021-03426-1.
8 Grint DJ, Wing K, Williamson E, et al. Case fatality risk of the SARS-CoV-2 variant of concern B.1.1.7 in England, 16 November to 5 February. *Eurosurveillance* 2021; **26:** 2100256.
9 Eaaswarkhanth M, Al Madhoun A, Al-Mulla F. Could the D614G substitution in the SARS-CoV-2 spike (S) protein be associated with higher COVID-19 mortality? *Int J Infect Dis* 2020; **96:** 459–60.
10 Volz E, Hill V, McCrone JT, et al. Evaluating the effects of SARS-CoV-2 spike mutation D614G on transmissibility and pathogenicity. *Cell* 2021; **184:** 64–75.e11.
11 Young B, Wei WE, Fong SW, et al. Association of SARS-CoV-2 clades with clinical, inflammatory and virologic outcomes: an observational study. *EBioMedicine* (in press).

Three are better than one—increasing HBV seroprotection by a tri-antigenic vaccine

With an estimated 257 million chronically infected individuals worldwide, hepatitis B virus (HBV) infection and its sequelae are a leading cause of death.[1] As of 2012, 183 WHO member states have implemented universal hepatitis B infant immunisation and 94 member states have introduced vaccination at birth.[1] These strategies have dramatically reduced HBV prevalence, as paradigmatically shown in Taiwan that witnessed a reduction in the HBsAg carrier rate in children (aged 1–10 years) from 10% to less than 1% after the implementation of childhood vaccination in 1984.[2] However, so far universal childhood vaccination had shown minimal impact on decreasing the overall HBV prevalence, as it will take decades for vaccinated birth cohorts to reduce horizontal HBV transmission in adult risk groups.[3]

In this situation, vaccination of adult risk groups represents an important tool for reducing horizontal HBV transmissions. However, vaccination efficacy is compromised in adults of whom 5–30% do not develop protective anti-HB concentrations.[4] Risk factors for non-response to the vaccine include advanced age, immune compromising condition, male sex, *DRB1* and *DQB1* human leukocyte antigen class II alleles, and non-compliance to vaccine administrations.[5]

Although there is no standard approach for handling non-response to vaccination, various strategies such as repeated vaccination, increased antigen doses, or modification of the adjuvant are pursued.[6,7] Timo Vesikari and colleagues[8] report results of a large international randomised phase 3 PROTECT study evaluating the immunogenicity and safety of the tri-antigenic hepatitis B vaccine (TAV) Sci-B-Vac compared with the standard mono-antigenic vaccine (MAV) Engerix-B, with a special emphasis on participants with unfavourable vaccine response characteristics. By contrast with current monovalent hepatitis B vaccines that contain only the small HBV surface antigen, the third generation Sci-B-Vac vaccine contains all three HBV envelope proteins, the small (HBsAg), medium (preS2), and large surface (preS1) antigens. The vaccine can better enhance immunity by the expression of highly immunogenic T and B cell epitopes.[9] 1607 participants were randomly assigned to receive three doses of intramuscular TAV or MAV. Co-primary outcomes were non-inferiority of TAV in seroprotection rates, defined as the percentage of participants having anti-HBs concentrations of more than 10 mIU/mL, 4 weeks after the third vaccination with TAV versus MAV in adults aged 18 years and older, as well as 45 years

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