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So is there cause for concern? Clearly, variability in the spike glycoprotein can affect the efficiency of antibody neutralisation. The role of spike protein variability in T cell immunity is likely to be elucidated in experimental studies in the next few months; a priori, the enhanced repertoire of T cell epitopes makes the loss of cytotoxic activity or recognition improbable. But only ongoing clinical trials will show whether vaccinated individuals recognise SARS-CoV-2 variants differently, and whether mutations decrease vaccine protection in some vaccinated individuals. The ongoing phase 3 trial of an adenovirus-vectored spike-based vaccine (Johnson & Johnson, NCT04505722) in South Africa, where the 501Y.V2 (B.1.351) strain with the Glu484Lys substitution is rapidly replacing pre-existing variants,¹¹ might provide an opportunity to examine this question. Ultimately, most vaccines are based on a recombinant spike protein sequence. Thus if evidence emerges that particular variants do appear to influence vaccine efficacy, it should be possible to periodically reformulate the vaccines so that they better match the circulating strains.

Importantly, the overall effectiveness of immunisation will correlate with rates of vaccine uptake. We therefore encourage researchers, health-care providers, and policy makers to act as advocates for immunisation, and to advise individuals with questions about vaccines to seek this information from reliable sources. The higher the proportion of a population vaccinated, the lower the number of susceptible individuals, and the fewer opportunities SARS-CoV-2 will have to spread and mutate.

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Improving family access to dying patients during the COVID-19 pandemic

In response to the COVID-19 pandemic, most health-care organisations have implemented policies to restrict visitor access. Although there are exceptions to some of these policies, including limited visiting for patients

nearing the end of life, they still have profound effects on the dying and their family members. We are still in the midst of the pandemic, but there are compelling reasons to expand access of family members to their



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Panel: Proposed elements of an end-of-life visitor policy

- 1 The policy would apply to anyone admitted to an inpatient palliative care facility, or any inpatient with a plan of care focused on comfort, and when the patient is expected to die in the coming weeks or short months. The policy should be applied consistently across a given region.
- 2 Visitors should be allowed during normal visiting hours; when physical circumstances allow, one family member can remain with the patient outside of these hours.
- 3 The number of visitors allowed at the bedside should be limited only by the size of the room. In practice, this would mean up to four visitors in a private room, and up to two visitors in a semiprivate room if another patient is present in that room.
- 4 Cycling of visitors should be avoided. Family members should be allowed to remain at the bedside throughout visiting hours. However, once they leave the hospital, they should not return to the bedside until the next day or unless they are remaining overnight. If more than four visitors in a group wish to attend, the visit should be scheduled in advance with the ward.
- 5 Visitors have a responsibility to observe proper infection prevention and control procedures to limit the risks to patients, staff, and to themselves. Visitors who are unwilling or unable to comply with these procedures would not be able to visit, but would be offered virtual visits instead.
- 6 Although longer visits would be permitted, we recommend that family members limit their visits to 1 h at a time, to reduce the risk of asymptomatic transmission of COVID and to allow patients and family members to rest.



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loved ones as they near the end of life, despite the risk of infection.

Hospital visitor policies represent an attempt to balance two competing priorities. Restrictions reduce the chance of harm from infection, but increase the chance of harm from isolation or separation. Exemptions can reduce isolation and allow for a more compassionate response to patients nearing the end of life, but they potentially increase the risk of COVID-19 transmission.

It is too early to assess the burden of complex grief of family members who endure the loss of a loved one

during the pandemic, and we have little bereavement data from previous pandemics.¹ We know that restrictive visitor policies are associated with a higher frequency of delirium and anxiety in patients.² We also know that separation from the patient, the absence of normal death rites, and the disruption of social support networks are risk factors for poor bereavement outcomes.³ Virtual communication is not feasible for some family members, and might be distressing if the patient is dyspnoeic, delirious, or intubated.

There are also little data on the harms of liberalising visitor policies. Liberal visitor policies in intensive care units do not appear to be associated with an increased risk of nosocomial infection, but they do increase the risk of burnout among staff.² Zhou and colleagues⁴ studied rates of nosocomial infections in the early days of the COVID-19 outbreak in Wuhan, China, before visitor restrictions and routine personal protective equipment were implemented, and found that nosocomial infections accounted for a third of all cases, but only 2% were due to people other than hospital staff.

The scarcity of good data is frustrating, but ultimately not relevant. Even if we knew the precise risks of different approaches to visitor policies, we would not be any closer to finding a balanced approach because the risks cannot be compared directly. How much psych morbidity is justified by the prevention of a single COVID-19 infection?

Neither the risk of transmission nor the harm of isolation can ever be reduced to zero. Hospital outbreaks occur due to asymptomatic staff, even when there are no visitors, and unrestricted visitor policies would not address isolation in individuals with distant or no family. But the harms of isolation are clearly amplified for people approaching the end of life. Faced with a choice between having acute hospital care or having unrestricted access to family members, some dying patients choose to remain at home, even if that means uncontrolled symptoms and an unsustainable burden on family members and community care services that are already stretched by the pandemic.

Even end-of-life visitor exemptions can be harmful, if they apply only to people in the final days of life. Prognostication is challenging, and patients can sometimes deteriorate suddenly without any of the usual warning signs. Such occurrences have led to situations in which family members were forced to leave

the bedside of patients who appeared to have months to live, and were then unable to return quickly enough after a sudden deterioration. Moreover, patients in their final days and hours are often minimally responsive and unable to interact with family members; the opportunity to spend so-called quality time has passed. Otani and colleagues⁵ found that being present at the time of death was not associated with any difference in the incidence of complicated grief among family members, but having the opportunity for meaningful conversation (eg, being able to say goodbye) was associated with reduced symptoms of depression and complicated grief.

Limiting the number of visitors allowed at one time might seem a reasonable compromise, but it can also lead to problems. Considering that cohabiting family members often visit at the same time, separating them at the bedside does not reduce the chances of transmission to each other or to the patient. Instead, they often choose to take turns, cycling between being at the bedside and being outside the hospital multiple times in a single day. Because the greatest risk of transmission occurs during the removal of personal protective equipment and transit within the hospital (eg, encountering other staff, travel in elevators), this cycling is likely to increase the risk of transmission substantially more than simply allowing all visitors to remain at the bedside for the duration of their visit (space permitting).

We have also found that inconsistent visitor policies among different sites can be problematic. Patient transfers are very common as patients near the end of life and are transferred from acute care to palliative settings. But if the receiving facility has stricter limits on visiting than the sending facility, patients often refuse the transfer, which increases the burden on the acute care facilities by adding to the population of those classed in the so-called alternate level of care.

The broad visitor restrictions put in place by many health-care facilities at the start of the pandemic were reasonable responses to a new and previously unknown pathogen. With the benefit of experience, and provided that sufficient personal protective equipment is available, we propose that health-care organisations adopt a new end-of-life visitor policy (panel) that would reduce restrictions overall without necessarily putting patients, staff, and family members at a substantially increased risk of COVID-19 transmission. Elements of this policy might be reasonable outside the end-of-life context, and Munshi and colleagues⁶ recently proposed more general relaxation of visitor policies. This proposal is not intended as a criticism of those who recommended more rigid restrictions at the start of the pandemic. But the threats of COVID-19 must be placed in context of other threats to health, including those that are harder to appreciate in the short term.

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α1-Antitrypsin deficiency and the risk of COVID-19: an urgent call to action

The COVID-19 pandemic is a global emergency. Identifying populations who are at risk of severe complications is crucial in developing special measures to prevent or reduce severe illness and mortality in

vulnerable patients.¹ Emerging evidence indicates that alpha₁-proteinase inhibitor might inhibit infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). α1-Antitrypsin also has anticoagulation



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