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## The effect of COVID-19 on routine diabetes care and mortality in people with diabetes



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The COVID-19 pandemic has had a disproportionate effect on the health of people living with diabetes. SARS CoV-2 affects many aspects of metabolism, creating the potential for biological interplay and bidirectional negative influence.<sup>1</sup> Data from many countries have consistently shown that people with diabetes with COVID-19 have an excess risk of hospital admission, increased disease severity, and increased mortality.<sup>2-4</sup>

New data, reported by Jonathan Valabhji and colleagues in *The Lancet Diabetes & Endocrinology*,<sup>5</sup> provides evidence that people with diabetes were affected by the pandemic in more ways than one. Their results show that pandemic-related reductions in care have increased non-COVID-related mortality among people with diabetes.

Valabhji and colleagues<sup>5</sup> determined the mortality occurring in people with type 1 and type 2 diabetes in a defined 15-week period from July to October 2021 (2021 cohort) and compared it with that from the same period in 2019. During the observation period in 2021, there were 30 118 non-COVID-related deaths observed, and in the same period in 2019 there were 27 132; an increase of 11%. Additionally, the authors were able to show that there had been a dramatic reduction in the provision of routine diabetes care processes between 2019 and 2021 and that there was a strong association between non-completion of the care processes and mortality. In the 12 months preceding March, 2021, only 853 660 (26.5%) of 3 218 570 people with diabetes in England received all eight of the care processes recommended by the National Institute for Health and Care Excellence (NICE) compared with 1 547 240 (48.1%) in the 12 months to March, 2020, preceding the first pandemic lockdown; a reduction of 44.8% (95% CI 44.7–45.0). The individual care process for which the reduction was most marked was foot surveillance checks, which were reduced by 37.5% (95% CI –37.7 to –37.4), perhaps reflecting the fact that, of the eight, this is the care process that requires the most personal contact. There were also greater decreases in the number of people receiving all eight care processes among those from the most deprived quintile than among those in the least deprived quintile. There was also a clear association between the excess mortality

observed in 2021 and the completion of the routine care processes in the 2 years preceding. Non-COVID-related mortality in the 2021 cohort was greater in those who did not receive all eight care processes in either of the two previous years (OR 2.67 [95% CI 2.56–2.77];  $p < 0.001$ ) and was greater among those who received all eight care processes in 2019–20 but not in 2020–21 (OR 1.66 [95% CI 1.59–1.73];  $p < 0.001$ ).

These data highlight the continuing negative effect of the pandemic on people with diabetes and the outcomes of inequalities of care. Even before the pandemic, there were difference in mortality among people with diabetes according to completeness of the care processes; an effect that has been amplified by the disruption to routine care that has occurred since March, 2020. However it should be noted that the current study had insufficient data to show the effect of COVID-19 on other aspects of morbidity due to diabetes, such as hospital admission or progression of diabetes complications. Future work assessing the broader effect of COVID-19-related disruption on morbidity is important. Furthermore, given the time course for progression of diabetes complications, the effect of the disruption of care due to the pandemic on diabetes outcomes will probably persist for some years. Therefore ongoing prospective evaluation of rates of diabetic microvascular and macrovascular complications and mortality in the coming years will be desirable to determine the true effect of the pandemic and the related disruption to care.

The study by Valabhji and colleagues<sup>5</sup> is a stark reminder that diabetes remains a serious and potentially deadly disease. The effect in mortality according to completeness of the care processes could remain an issue in pandemic times and beyond if not dealt with appropriately. There is a risk that restoration of both routine (mostly provided in a primary care setting) and specialist diabetes care might receive less attention than present major areas of focus of recovery planning: restoring elective surgery and diagnostic procedures, particularly around cancer pathways. A 2021 survey of 1070 UK primary care health-care professionals, with a 91% response rate, found that 79% considered their provision of routine diabetes services had been

impacted by the pandemic.<sup>6</sup> Additionally, there are also concerns that the pandemic might have a disproportionate negative effect on other aspects of metabolic health, including provision of metabolic surgery. Despite evidence that metabolic surgery can reduce diabetes-related morbidity and mortality, access to metabolic surgery has historically been undermined compared with other elective surgery due to barriers, including weight stigma.<sup>7</sup>

There is therefore an urgent need to restore both routine and specialist diabetes care as quickly as possible as part of the recovery from the pandemic to prevent further ongoing harm.

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## Impact of BMI on COVID-19 vaccine effectiveness

COVID-19 and obesity are two overlapping pandemics.<sup>1</sup> Individuals with obesity are at risk of developing more severe clinical outcomes as a result of SARS-CoV-2 infection than those without obesity.<sup>2,3</sup> Obesity is also associated with known risk factors for severe COVID-19, such as diabetes and hypertension. Irrespective of comorbidities, excessive weight results in biomechanical and systemic factors that increase the risk of adverse outcomes. Increased abdominal pressure and upward displacement of the diaphragm result in decreased expiratory reserve volume, functional capacity, and respiratory system compliance. Furthermore, obesity-associated alterations in systemic metabolism include insulin resistance, altered adipokines (eg, increased leptin and decreased adiponectin), and chronic low-grade inflammation.<sup>3</sup> Increased inflammatory chemokines might lead to endothelial dysfunction and exacerbate a prothrombotic state. Preliminary research has shown that mice with obesity have an increased duration of viral shedding due to delayed viral clearance, increased number of secondary bacterial infections, and heightened damage to the respiratory epithelium.<sup>4</sup> In addition, COVID-19 vaccine effectiveness might be lower in people with obesity as baseline alterations in systemic cytokine production

might lead to blunted and delayed innate and adaptive immune responses to vaccination.<sup>1</sup> Reduced vaccine effectiveness in people with obesity has been observed for influenza vaccination<sup>5</sup> and preliminary results were suggestive of lower anti-SARS-CoV-2 spike IgG antibody concentrations after two doses of the BNT162b2 mRNA vaccine.<sup>6</sup>

To address the effect of bodyweight on vaccine effectiveness, Carmen Piernas and colleagues<sup>7</sup> in *The Lancet Diabetes & Endocrinology* used a large representative population-based cohort from England of 9 171 524 individuals to investigate severe COVID-19 outcomes after COVID-19 vaccination and associations with BMI. The authors applied multivariable Cox proportional hazard models to estimate the risk of COVID-19 outcomes associated with BMI. Vaccine protection was assessed through a nested matched case-control design to estimate odds ratios in vaccinated versus non-vaccinated people.

Consistent with the findings from phase 3 company-led efficacy trials,<sup>8</sup> the protection of COVID-19 vaccines against severe disease outcomes was high across all BMI categories when comparing people who were vaccinated against those who were unvaccinated. There was a 40–74% lower odds of hospital admission or death after



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