

databases kept by pharmaceutical companies. To gather detailed long-term safety data in a comprehensive broad-based fashion, a group of eminent paediatric endocrinologists set up a European consortium (Safety and Appropriateness of Growth hormone treatments in Europe [SAGhE]) that involved eight countries (Belgium, France, Germany, Italy, the Netherlands, Sweden, Switzerland, and the UK) and merged datasets on around 24 000 young adults treated with recombinant human growth hormone during childhood and adolescence.<sup>4</sup>

In *The Lancet Diabetes & Endocrinology*, Lars Sävendahl and colleagues<sup>6</sup> present the first large international population-based cohort study of patients treated with recombinant human growth hormone during childhood. The study reports overall and cause-specific mortality data for all eight participating SAGhE countries, with more than 400 000 patient-years and up to 25 years of follow-up. All-cause mortality data only showed increased mortality in children with an inherent increased mortality risk due to their underlying disorder, whereas in patients who did not have any such predisposing disorder, overall mortality was not increased. The authors found no association between mortality and recombinant human growth hormone dose, irrespective of risk at the outset of treatment.

These findings are reassuring, both for clinicians and the families of those treated with recombinant human growth hormone during childhood. Further analysis is required to explore the interaction between

various predisposing underlying disorders in susceptible children, recombinant human growth hormone therapy, and mortality risk. Additionally, with larger numbers and longer follow-up, the CIs around the safety statements will hopefully be narrowed.

The balance between benefit and safety for recombinant human growth hormone therapy for short stature has contrasting time constraints. Benefit, in terms of final height gain, can be estimated using a prediction model<sup>7</sup> after a few years of therapy, but safety requires decades of follow-up.

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## Obesity and COVID-19: a call for action from people living with obesity

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See Online for appendix

Data from France and the UK have showed a disproportionately higher prevalence of obesity in patients with COVID-19 admitted to Intensive Care Units (ICUs) compared with general population data.<sup>1,2</sup> About 10% of ICU patients in the UK have a BMI of 40 kg/m<sup>2</sup> or more, and evidence shows increased mortality among this group.<sup>2,3</sup> The UK Government advice for those with a BMI of at least 40 kg/m<sup>2</sup> is to be particularly stringent in following social distancing measures. This message has created confusion and fear among many people living with obesity because of uncertainty about their risk or what actions they should take, including people with a

BMI of 30 kg/m<sup>2</sup> or more, who are also over-represented in ICU but not listed as at risk.<sup>3</sup>

We consulted with people living with obesity and summarise in this Comment the main reflections, formulated into a call for action (appendix pp 2–5). It is a candid account of the impact of COVID-19 during the peak of the pandemic in the UK. The reported effects were both physical and mental, and are likely to have a lasting impact for many years.

Overwhelmingly, we heard of genuine, all-consuming fears of contracting COVID-19, with many people afraid of not getting medical support if they were admitted to

hospital, amid the accumulating reports that they are at greater risk of dying. Clearly, an immediate need exists for clarity regarding risk, both in terms of contracting the virus and its probable impact.

People showed considerable anxiety about the capacity of the health-care system to provide appropriate equipment, gowns, and beds. Anxiety about accessing health care is not a new phenomenon,<sup>4</sup> but it is likely to be greater exposed during the current crisis. From the perspective of Obesity UK and Obesity Empowerment Network members, this anxiety relates not only to a physical challenge, but also to one of dignity if they were to be hospitalised. These fears are not without cause; patients who require sedation do need to be moved, and proning appears to be important in the successful treatment of acute respiratory distress.<sup>5</sup> There is also a fear that access to obesity treatments (particularly National Health Service multidisciplinary therapy and bariatric surgery) will be affected by austerity policies in response to the economic crisis, at a time when demand will increase because of increased waiting lists due to delayed treatment and a potential increase in the number of people who require support following lockdown.

Another recurring theme was stigma, largely related to comments on social media and fuelled by the media. We suggest that media speculation is underpinned by societal norms permitting the discussion and referencing of body shape and size by anyone, perpetuating existing stigma. Many people expressed that such comments led to feelings of shame, a perception of being “less of a priority than any other condition,” and a reluctance to seek help. Respondents were acutely aware of the impact that language has on stigma, with many citing the poor use of “unscientific” words. Such language (mis)use is not new to the COVID-19 pandemic, but it has been exacerbated during this time.<sup>6</sup> Stigma has a lasting and negative impact on the mental and physical health of people living with obesity.<sup>7</sup> It can be conscious or unconscious and delivered from multiple sources, including health professionals.<sup>6</sup> One consequence can be avoidance of health care, probably worsening COVID-19 outcomes. Obesity UK and some Royal Colleges, charities, advocacy groups, clinicians, and patients have been striving hard for many years to reduce weight stigma, and guidance and position statements are available.<sup>6,8</sup>

In every response, we learnt about mental health concerns. Although some of these were linked to the fear of contracting COVID-19, many related to the impact of isolation, shielding, or social distancing. Resilience appears to relate to mental health before lockdown; those who reported coping better often expressed that they were in a “good place mentally” before the COVID-19 outbreak. Worryingly, this was not the case for many, particularly those who recently underwent (or are waiting for) bariatric surgery. Lockdown presents substantial challenges to maintaining healthy behaviours for anyone; however, people living with obesity have often had years of battling with weight and experiencing feelings of guilt from perceived failure.<sup>9</sup> Representatives in our consultation reported having a fear of weight gain during lockdown, related to the effect of anxiety on eating behaviours (often compounded by scrutiny from family members). For many, this fear related to stigma or shame and prevented them from exercising or shopping for food in ways that did not make them feel self-conscious. Lockdown has had a profound influence on self-efficacy, and increased episodes of secret eating or binge eating have been commonly reported within the Obesity UK support groups during this time. Like many stigmatised populations, people living with obesity have often developed coping strategies over many years,<sup>10</sup> and this was highlighted in our consultation. Many people reported using focused and dedicated approaches to protect their physical and mental health, including attending remote support groups.

We have formulated a call for action using our consultation. Immediate action is needed to clarify the risk of adverse COVID-19 outcomes for people living with obesity, with specific recommendations for those at greatest risk and the health-care professionals who support them. This includes supporting research to define the risk of infection and subsequent mortality in people living with obesity, in addition to providing clear guidance on managing risk. Essential to this initiative is careful consideration of messaging, to prevent the perpetuation and exacerbation of stigma. In the long term, the current pandemic offers an opportunity to consider ways to improve the health-care system for people living with obesity and to tackle obesity-related stigma. In addition to providing appropriate equipment, we advocate specific training for health-care professionals

that empowers them to support people living with obesity, minimise unconscious bias, and prevent stigma. Although we welcome the recent UK Government focus on obesity, any action must be considered in the context of the experiences of people living with obesity, and an understanding of obesity as a complex chronic disease. Accordingly, we call on the UK Government to work with people living with obesity when developing guidance and COVID-19 recovery plans who are in frequent contact with the health-care system and have expertise on the barriers to accessing healthcare.<sup>6</sup>

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## COVID-19 and Cushing’s syndrome: recommendations for a special population with endogenous glucocorticoid excess

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Over the past few months, COVID-19, the pandemic disease caused by severe acute respiratory syndrome coronavirus 2, has been associated with a high rate of infection and lethality, especially in patients with comorbidities such as obesity, hypertension, diabetes, and immunodeficiency syndromes.<sup>1</sup>

These cardiometabolic and immune impairments are common comorbidities of Cushing’s syndrome, a condition characterised by excessive exposure to endogenous glucocorticoids. In patients with Cushing’s syndrome, the increased cardiovascular risk factors, amplified by the increased thromboembolic risk, and the increased susceptibility to severe infections, are the two leading causes of death.<sup>2</sup>

In healthy individuals in the early phase of infection, at the physiological level, glucocorticoids exert immunoenhancing effects, priming danger sensor and cytokine receptor expression, thereby sensitising the immune system to external agents.<sup>3</sup> However,

over time and with sustained high concentrations, the principal effects of glucocorticoids are to produce profound immunosuppression, with depression of innate and adaptive immune responses. Therefore, chronic excessive glucocorticoids might hamper the initial response to external agents and the consequent activation of adaptive responses. Subsequently, a decrease in the number of B-lymphocytes and T-lymphocytes, as well as a reduction in T-helper cell activation might favour opportunistic and intracellular infection. As a result, an increased risk of infection is seen, with an estimated prevalence of 21–51% in patients with Cushing’s syndrome.<sup>4</sup> Therefore, despite the absence of data on the effects of COVID-19 in patients with Cushing’s syndrome, one can make observations related to the compromised immune state in patients with Cushing’s syndrome and provide expert advice for patients with a current or past history of Cushing’s syndrome.