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Therapeutic Advances in Endocrinology and Metabolism

COVID-19 and obesity: an opportunity for change

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Keywords: COVID-19, obesity, type 2 diabetes, physical activity

The recent hospitalisation and admission to the intensive care unit (ICU) of the British Prime Minister, Boris Johnson, with severe COVD-19 infection has starkly brought obesity into the public conscience, emerging as a major risk factor for poor outcome and death after COVID-19 infection.¹ Boris weighed ~111kg (17 $\frac{1}{2}$ stone) on admission to Guy's and St Thomas's Hospital, London. Assuming a height of 1.75 m, his body mass index (BMI) was 36 kg/m². Several weeks later, having emerged from the ICU clearly and understandably emotional from his near-death experience, he returned to 10 Downing Street somewhat lighter and announced to the nation his determination finally to tackle Britain's obesity pandemic.²

Obesity is defined by the World Health Organisation (WHO) as abnormal or excessive fat accumulation that may impair health.³ Obesity (defined as a BMI \geq 30 kg/m²) is very common in the UK with a prevalence of 28% amongst adults in 2018.⁴ The impacts of obesity on the metabolic, physical and psychological components of health, the healthcare system and the wider economy are well established.⁵ Weight loss, however achieved, *via* lifestyle and behavioural interventions, pharmacotherapy or bariatric surgery, has beneficial effects on obesity-related complications.^{6–10}

COVID-19 is a disease caused by the SARS-C0V-2 virus and on 11 March 2020 the World Health Organisation declared the outbreak as a global pandemic.¹¹ Initial data suggested that older adults are at particular risk of severe complications of COVID-19. However, the recent report by Public Health England commissioned by the UK Government, namely *Disparities in the risk and outcomes of COVID-19*, showed the stark reality of health disparities across the UK and factors such as ethnicity, obesity, socioeconomic status and sex can disproportionately affect the outcome of COVID-19 on health.

Data demonstrated a higher risk of severe COVID-19 in Black, Asian and minority ethnic (BAME) groups than in White ethnic groups.¹² Indeed, death rates from COVID-19 were highest among people of BAME groups.¹² Ethnic minorities in hospital are more likely to be admitted to critical care and receive invasive mechanical ventilation than Whites, despite similar clinical characteristics and being younger with fewer comorbidities (Harrison *et al.* 2020, *Lancet*, preprint). South Asians had a higher mortality than White people, mediated by a higher prevalence of pre-existing diabetes (Harrison *et al.* 2020, *Lancet*, preprint).

Data from China, Italy, Spain, the US and now the UK show that obesity is a major predisposing factor for severe COVID-19 complications. Recent research from France showed that the age- and sex-adjusted prevalence of obesity in patients with severe COVID-19, and those who were admitted to the critical care unit (CCU), was greater than obesity prevalence in the general French population [odds ratio (OR) 1.35, 95% confidence interval (CI) 1.08-1.66; and 2.88, 2.19-3.66, respectively]. These associations remained significant despite additional adjustment for type 2 diabetes (T2D), hypertension, dyslipidaemia, and chronic obstructive lung disease.13 Data from National Health Service England demonstrated that a BMI of $\geq 40 \text{ kg/m}^2$ conferred an increased risk of COVID-19-related death (compared with BMI 25-29.9 kg/m²) in patients with type 1 diabetes (T1D) and T2D [hazard ratio (HR) 2.15, 95% CI 1.37-3.36; and 1.46, 1.50–1.79, respectively].¹⁴

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Recent data support a commonality of factors linking the development of obesity with an increased risk of COVID-19 infection, which may be directly or indirectly mediated. Directly mediated mechanisms may include obesity-associated respiratory dysfunction, characterised by impaired gas exchange, increased airway resistance, low lung volumes and low muscle strength.¹⁵ Differences in angiotensin-converting enzyme 2 (ACE2) expression between those with lower and with higher BMIs may also represent a putative explanation for the increased risk of severe COVID-19 with obesity. COVID-19 utilises the ACE2 receptor on epithelial cells to bind, gain entry and to infect cells.^{16,17} ACE2 is expressed in a number of tissues including cardiac, kidney and lung. However, ACE2 expression is higher in adipose tissue than in the lungs18 and may theoretically result in greater viral proliferation in individuals with greater adipose tissue mass. The renin-angiotensin (RAS) pathway is also differentially expressed in the subcutaneous and visceral fat depots.19

Indirectly, obesity-associated impaired metabolic health and comorbidities such as diabetes (T1D and T2D), hypertensive disease, chronic kidney disease and dementia have all been identified as predictors of poor outcomes.²⁰ Obesity contributes to the development of all these diseases, while obesity treatments, including lifestyle intervention, pharmacotherapy or bariatric surgery, have all had a significantly favourable impact on the management of T2D, hypertension and cardiovascular disease.^{7,21–23} Thus, tackling obesity will have a potential (direct and indirect) impact on future outcomes from COVID-19 infections.

Other drivers of poor outcomes include social inequalities that also play an important role in the high prevalence of obesity in the UK:²⁴ in the UK, people who are most socioeconomically deprived are more likely to develop COVID-19 compared with those least deprived (adjusted OR 2.03, 95% CI 1.51–2.71).²⁵ In addition, obesity prevalence is higher in Black adults²⁶ and there are lower BMI thresholds (23 kg/m² and 28 kg/m²) for the development of overweight and obesity complications in South Asians.²⁷

Clearly, the cornerstones of maintaining a healthy body weight are maintaining the energy balance between nutritional intake and physical activity. Furthermore, there is clear evidence of the effects of regular physical activity and higher cardiorespiratory fitness on reducing the burden of cardiovascular and metabolic disease, dementia and improving survival regardless of weight loss. Even a small amount of physical activity brings significant health gains. A study of over 40,000 people in Taiwan, followed for an average period of >8 years, noted that just 15 min/day of moderate exercise such as fast walking (or even 5 min of vigorous exercise such as running) was enough to reduce all-cause mortality by 14% and confer a 3-year longer life expectancy, compared with sedentary people. Furthermore, every additional 15 min of daily exercise, beyond this initial 15 min/ day, further reduced all-cause mortality by 4% and all cancer mortality by 1%.28 As we are advised to avoid public transport to reduce viral transmission, and adopt different ways of commuting to work, the health benefits of incorporating increased levels of physical activity as part of the commute to work would reduce obesity, cardiovascular disease, cancer and all-cause mortality.^{29,30}

Physical inactivity is common in the general population, especially during periods of self-isolation. We have previously highlighted the negative metabolic and musculoskeletal impact of physical inactivity and sedentary behaviour even over a short time scale.^{31,32} Inactivity, combined with overfeeding, has a synergistic effect. Opportunities presented with lockdown have included for many (but not all) an increased emphasis on physical activity: encouraging walking and cycling, promotion of bike lanes and home-based fitness programmes. There have also been changes in eating patterns with increased home cooking. For others, there have been reductions in physical activity, increased comfort and convenience food eating (higher consumption of snacks and sugary drinks) and limited access to fresh food. Concerns have been raised particularly regarding the impact of lockdown on childhood obesity reflecting on data from the National Child Measurement Programme that already places UK school children amongst the most overweight/obese in Europe.

However an individual's or family's own lifestyle patterns may have evolved during lockdown with the many competing economic, family and societal pressures, the pandemic may provide societal opportunities. A significant opportunity to improve the health of the nation with renewed awareness of the risks of obesity (including a higher risk of COVID-19 complications), increased appreciation of the mental and physical benefits of physical activity with infrastructural changes to facilitate these changes. We need to focus on improving treatment access and options for people with obesity and addressing some of the driving factors such as social inequalities and sedentary life behaviour that are drivers for being overweight or obese.

Clearly, we are facing an unholy interaction between two pandemics, COVID-19 and obesity. Such future planning for society living with COIVD-19 (because at the time of writing there is an absence of an effective treatment or vaccine available to prevent COVID-19 disease) will require wider engagement with people with obesity to overcome the barriers and stigma that exist in the current healthcare system, in society and within the political systems. There is also an urgent need to address some of the other health inequalities in society including the disproportionately increased risk in BAME groups and those of lower socioeconomic groups. No one will ever forget 2020 with a legacy from COVID-19 for decades to come. We have had our wake-up call; now it's time for us all to reshape the future with the impetus to develop new obesity strategies.

Author contribution(s)

Dan J. Cuthbertson: Conceptualisation; Writingoriginal draft; Writing-review & editing.

Uazman Alam: Conceptualisation; Writing-original draft; Writing-review & editing.

Abd Tahrani: Conceptualisation; Writing-original draft; Writing-review & editing.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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