

# OBESITY AND COVID-19

## Key Points

- » Evidence continues to emerge highlighting an association between obesity and COVID-19 severity and death
- » Obesity has not yet been formally recognised by the World Health Organization (WHO) as an independent risk factor for COVID-19; however, it has been highlighted as leading to an increased risk of COVID-19 severity by other public health organisations, including Public Health England (PHE) and the US Centres for Disease Control and Prevention (CDC)
- » Observations made in UK studies are consistent with international evidence; evidence consistently highlights the association between obesity and COVID-19 hospitalisation, severity, admission to ICU, and death
- » Multiple potential and plausible mechanisms have been suggested including: immune frailty, increased baseline inflammation, increased risk of comorbidities and impaired pulmonary function
- » There is emerging evidence linking COVID-19 severity to particular societal groups, including by ethnicity and area deprivation, highlighting a link to inequalities. Further work is required to explore to what extent such factors contribute to increased severity and death from COVID-19
- » Though findings continue to be consistent in identifying a link between obesity and COVID-19 severity, limitations remain, reducing the strength of conclusions and recommendations that can be made by public health organisations



**Obesity Action  
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## Background

Alongside older age, male sex, Asian and black ethnicity and certain pre-existing conditions/co-morbidities (including diabetes), obesity has been implicated as a potential risk factor for COVID-19 severity, research on which continues to emerge. NHS Inform in Scotland<sup>1</sup> and PHE<sup>2</sup> are amongst those who list 'a BMI of 40kg/m<sup>2</sup> or above' in the higher risk group at risk of severe illness in COVID-19 and they are therefore advised to follow strict physical distancing measures. Since our previous report, the CDC has updated their guidance relating to vulnerable groups, revising their listing of BMI  $\geq 40\text{kg/m}^2$  to a BMI  $\geq 30\text{kg/m}^2$ , to take into account "consistent evidence" suggesting increased risk of severe COVID-19 in this group<sup>3</sup>. Additionally, the European Commission and the European Centre for Disease Prevention and Control launched a joint short-term action plan for COVID-19 outbreaks<sup>4</sup>. Notably, obesity was recognised in the plan, for the first time, within the category of medically vulnerable groups.

Despite this, obesity has not been formally recognised by WHO as an independent risk factor for COVID-19. The World Obesity Federation believes this may be due to obesity itself not being classified as a main disease or risk factor across WHO's "five by five" non-communicable diseases (NCD) framework, despite being a risk factor for major NCDs<sup>5</sup>. However, a recent presentation from the WHO Working Group on NCDs acknowledged that "people living with NCDs may experience more severe disease and poorer outcomes when infected, and various risk factors exist, such as obesity and smoking."<sup>6</sup> The group also highlighted an advocacy plan which included briefing the media on the risk of becoming severely ill with COVID-19 for people living with, or at risk of, NCDs, including obesity<sup>6</sup>.

It is of vital importance that risk factors for morbidity and mortality in COVID-19 be recognised, to both inform prevention strategies and identify high-risk groups for future immunisation programmes.

*This briefing considers the emerging evidence linking obesity to increased risk of severe illness from COVID-19, providing an update to our May 2020 briefing.*

## COVID-19 and obesity: early findings

### Common comorbidity

The ISARIC-4C study<sup>7</sup> characterised the clinical features of 16,749 hospitalised COVID-19 patients across 166 hospitals in Scotland, England and Wales, findings obesity to be one of the ten most common comorbidities on hospitalisation. A large study from New York City found obesity to be one of the three most common comorbidities on hospitalisation (41.7% of patients)<sup>8</sup>.

### Hospitalisation

In the US, much of the early evidence stemmed from New York City, an area that was badly hit initially. Studies found that patients with COVID-19 and obesity were more likely to be admitted to hospital than those without<sup>9</sup>.

### ICU admission

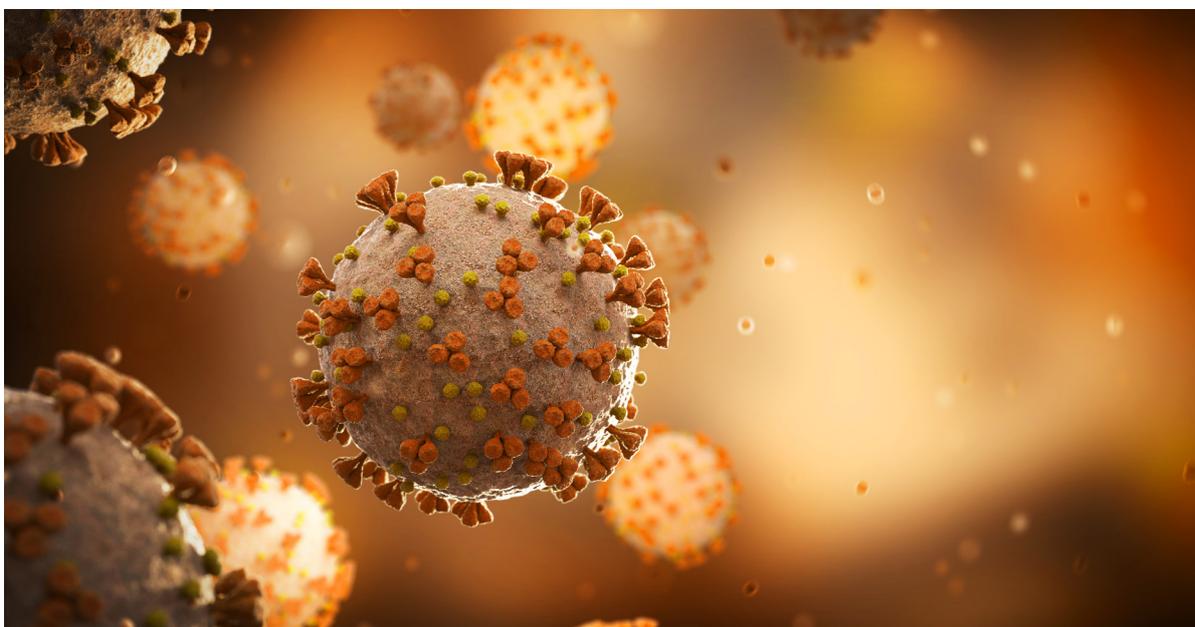
In the UK, early data released on a weekly basis by the Intensive Care National Audit and Research Centre (ICNARC) highlighted overweight and obesity as a factor in ICU admission, with close to three quarters of ICU patients recording BMIs in the overweight or obesity categories<sup>10</sup>. A higher BMI was also implicated in the requirement of advanced respiratory or renal support. This report continues to be published weekly, however, it should be noted that it only includes patients in ICU and not in other settings in hospital or the community.

## Risk of mortality

A large UK study of 20,133 UK patients in hospital with COVID-19 recorded obesity as one of several factors associated with higher hospital mortality (HR 1.33; 95% CI 1.19-1.49,  $p < 0.001$ )<sup>11</sup>. This was also evidenced in another large UK study using the same protocol, after adjustment for other comorbidities, age and sex (HR 1.37; 95%CI: 1.16-1.63;  $p < 0.001$ )<sup>7</sup>. It is important to note, however, that obesity was recorded 'as recognised by clinical staff' and was not stratified by BMI. In the largest UK study, using the linked electronic medical records of 17 million adult NHS patients<sup>12</sup>, increasing risk of hospital death was seen with increasing levels of obesity, from HR 1.27 (95% CI 1.18-1.36) in those with a BMI of 30-34.9kg/m<sup>2</sup>, to HR 2.27 (95% CI 1.99-2.58) in those with a BMI  $\geq 40$ kg/m<sup>2</sup>. Death from COVID-19 was also found to be strongly associated with several prior medical conditions related to obesity, including uncontrolled diabetes (HR 2.36, 95% CI 2.18-2.56), severe asthma (HR 1.25, 95% CI 1.08-1.44) and chronic heart disease (HR 1.27, 95% CI 1.20-1.35)<sup>13</sup>. It should be noted that BMI was determined from weight measurements recorded within the last 10 years, therefore, may not have been up to date. There is also a difficulty measuring height in seriously ill patients, due to lying kyphosis and flexed legs.

## Link with severity in younger age groups

Early data from the CDC highlighted a relationship between younger COVID-19 patients and obesity<sup>14</sup>, with obesity recorded as the most prevalent underlying condition in the 18-49 age group, at 49% of cases. This finding was in agreement with another study which found that patients under the age of 60, with a BMI between 30kg/m<sup>2</sup> and 34kg/m<sup>2</sup> were twice as likely to be admitted to acute care, and 1.8 times as likely to be admitted to critical care, than those with a BMI  $\leq 30$ kg/m<sup>2</sup>(<sup>15</sup>). These findings implicated obesity as a risk factor for hospitalisation and critical care for COVID-19 patients under the age of 60 and aligned with evidence from the Italian National Institute of Health which found that obesity was reported as a factor in deaths in those under the age of 40<sup>16</sup>.



## COVID-19 and obesity: new evidence

Since our initial briefing, new evidence has continued to emerge, strengthening the links between COVID-19 severity and increasing BMI. At the end of July, PHE published its most recent document on the topic, 'Excess weight and COVID-19: insights from new evidence', findings from which can be viewed in Box 1.

## Box 1. Public Health England: Insights from new evidence<sup>17</sup>

On 24th July 2020, PHE released a report providing evidence-based insights into the relationship between excess weight and COVID-19, garnered from new evidence. The report highlighted key insights under four categories, finding:

### Laboratory confirmed COVID-19

- » An increased association with testing positive for COVID-19 as BMI increases above a healthy range, with a stronger relationship observed in BAME groups than in White ethnic groups (authors note that these findings may be a result of selection bias, owing to the testing strategy in place at time of study)

### Hospitalisation

- » Stronger likelihood of hospitalisation in COVID-19 patients with BMI in the overweight or obesity categories, compared to those with BMI in the healthy range
- » Patients with a BMI in the overweight or obesity categories are at a progressively increased risk of being hospitalised than patients with BMI in the healthy range or below

### Admission to intensive/critical care and treatment

- » Patients with a BMI in the overweight or obesity categories are more likely to be admitted to intensive/critical care than those with BMI in the healthy range or below. They are also more likely to require advance treatment for severe symptoms

### Risk of mortality

- » A potentially higher risk of COVID-19 related death with increasing BMI, which has persisted in studies adjusted for confounding factors such as age, sex, measures of socio-economic status (SES), ethnicity and co-morbidities



The report concluded that while the emerging evidence consistently indicates a higher risk of COVID-19 severity and death in those with BMI in the overweight or obesity categories, a more definitive conclusion cannot yet be drawn<sup>17</sup>. This is due to several limitations highlighted within the report, including sampling and testing strategies, sample sizes and unequal exposure to COVID-19. In the UK, recent ICNARC data<sup>18</sup> has continued to report a relationship between critical illness from COVID-19 and obesity, with 31.4% of ICU patients with COVID-19 recording a BMI between 30kg/m<sup>2</sup> and 40kg/m<sup>2</sup>, and 7.9% over 40kg/m<sup>2</sup>. This is higher than is seen in the age and sex-matched population, of which 28.9% and 2.9% fall into the respective BMI categories. The data also shows that three quarters of those receiving advanced respiratory support or any renal support had a BMI within the overweight or obesity categories.

Testing positive for COVID-19 has also been found to be associated with obesity, as demonstrated in a study utilising UK Biobank data<sup>19</sup>. After adjustment for confounding factors, researchers identified a dose-response association between testing positive and increasing BMI categories, with an adjusted odds ratio of 1.31, 1.55 and 1.57 in those with a BMI in the overweight, obesity and severe obesity categories, respectively. As detailed previously, several studies have indicated that those with BMI in the overweight or obesity categories are more likely to require hospitalisation than those with a BMI in the healthy weight category. A further study has emerged since our pre-

vious briefing that highlights similar findings, after adjustment for confounding factors including age, sex and ethnicity<sup>20</sup>. Similarly, a large study of over 10,000 patients with COVID-19 in Brazil found patients with COVID-19 and obesity had 1.74 greater odds of hospitalisation, than those without<sup>21</sup>.

Elsewhere, a systematic review and meta-analysis of nine studies, seven from China and one each from France and US, found that patients with severe COVID-19 illness had a higher BMI than those with less severe illness<sup>22</sup>. Additionally, patients with COVID-19 and obesity were more likely to have worse outcomes than those in the healthy weight category. However, disease severity was not defined and only two of the studies identified comorbidities, thus confounding may be an issue. Another meta-analysis of 14 studies, the design of some unclear, but including research from Korea, China, Italy, US, found obesity to be significantly associated with death following COVID-19 infection.

Similarly, international evidence continues to emerge which aligns with UK findings. In Brazil, a study of comorbidities in over 17,000 patients who died with COVID-19 found obesity to be one of the top ten comorbidities, present in 4.4% of deaths studied<sup>23</sup>. Obesity-related conditions were prevalent, with the most-recorded comorbidity being chronic heart disease (35.1%), followed by diabetes (28.7%). A similar finding was recorded in a Swiss study, reporting a high prevalence of obesity (27%) in patients hospitalised with COVID-19<sup>24</sup>. A study from Greece reported 34.4% obesity in patients hospitalised in ICU with COVID-19 – most prevalent in those under the age of 55<sup>25</sup>. However, it is important to note the small sample sizes (n=99, n=90, respectively) of these studies. In Mexico, a study of over 200,000 people with confirmed COVID-19 found a significantly increased risk of death in COVID-19 patients with obesity (OR 1.42), as well as obesity increasing the risk of ICU admittance and likelihood of intubation<sup>26</sup>. Similarly, a retrospective study in Italy found visceral fat to be the strongest predictor of the need for ICU in COVID-19 patients; visceral fat was significantly higher requiring intensive care (p=0.032), than in those who did not require it<sup>27</sup>.

## Suggested mechanisms linking obesity to COVID-19 severity and/or death

**There are a number of reasons why people with obesity may be at increased risk of severe illness from viruses or respiratory illnesses (Figure 1):**

### Increased state of inflammation

» Obesity and severe obesity cause a chronic inflammatory state in the body, which holds systemic implications for immunity<sup>5,28,29</sup>. This may explain the lower immunisation success rates observed in individuals with obesity<sup>30,31,32</sup>. The inflammation at baseline observed in patients with obesity is likely to contribute to the 'cytokine storm' observed in many hospitalised COVID-19 patients.

### Increased comorbidity risk

» In people with obesity, the risk of comorbidities is increased, for example type 2 diabetes and ischaemic heart disease. It is also common for people with obesity to have multiple comorbidities that increase the risk of complications related to viral infection. Many of the underlying conditions listed by Public Health England within their guidance on social distancing during COVID-19 are conditions associated with obesity, such as asthma, heart disease and chronic kidney disease<sup>33</sup>.

### Impaired pulmonary function

» In obesity and severe obesity, there is an increased risk of restrictive respiratory failure, pulmonary embolism and acute respiratory distress syndrome (ARDS)<sup>34</sup>. People with obesity have also been found to have reduced lung volume and capacity compared to those without<sup>35</sup>. In the current pandemic, it has been found that patients maintain higher oxygen saturation when nursed in the prone position. This has meant that many have not required non-invasive or invasive ventilation. People with obesity are more difficult to turn and are more likely to have restrictive defects due to abdominal splinting<sup>36</sup>. There is also an increase thromboembolic risk in individuals with obesity; COVID-19 favours thromboembolism, particularly in severe disease<sup>5,37</sup>.

## Sedentary activity

» Physical activity and exercise are positively associated with more favourable outcomes in metabolic and immunological health. Similarly, sedentariness and low physical activity levels have been associated with an impaired immune response to viral infection throughout different stages of the response<sup>38</sup>. This has also been seen in reduced physical activity mediated by insulin resistance<sup>39</sup>. People with obesity and those with sedentary lifestyles have a higher incidence of thromboembolic phenomena. A key issue in people treated for COVID-19 is the higher incidence of thrombosis and embolism<sup>5</sup>.

## Practical Healthcare-related difficulties

» Obesity or severe obesity in a patient may lead to difficulties with prone nursing, ventilation and intubation, taking blood samples and some examinations. Severe obesity might make transportation more difficult and equipment such as MRI scanners may not be adapted in some units.

## Obesity and prolonged virus shedding

» The time that the infected individual continues to 'excrete' the virus by any means is known as the period of 'virus shedding'. In individuals with obesity, this timeframe has been found to be prolonged<sup>40</sup>. A 2018 study investigating the effect of obesity on Influenza A virus shedding within households in Nicaragua, found that symptomatic adults with obesity shed the virus 42% longer than those of a normal BMI<sup>41</sup>. Similar observations were found for those who had the virus, but were not displaying any symptoms<sup>41</sup>.

## Stigma

» Individuals with obesity experience stigma and discrimination due to their weight, as recognised by Public Health England in its most recent report on COVID-19 and obesity<sup>17</sup>. Weight stigma is associated with a reluctance to seek healthcare, can affect quality of treatment received, and result in worse outcomes<sup>42</sup>. This may have implications for severe complications from COVID-19.

## Hormonal dysregulation

» Satiety-regulating hormone leptin, secreted in proportion to body fat, connects metabolism to the immune response. Individuals with obesity have higher levels of circulating leptin, associated with leptin resistance. Researchers have suggested that due to its link with pulmonary immunity, leptin dysregulation may have serious consequences during COVID-19 infection through compromised immune response<sup>43-45</sup>.

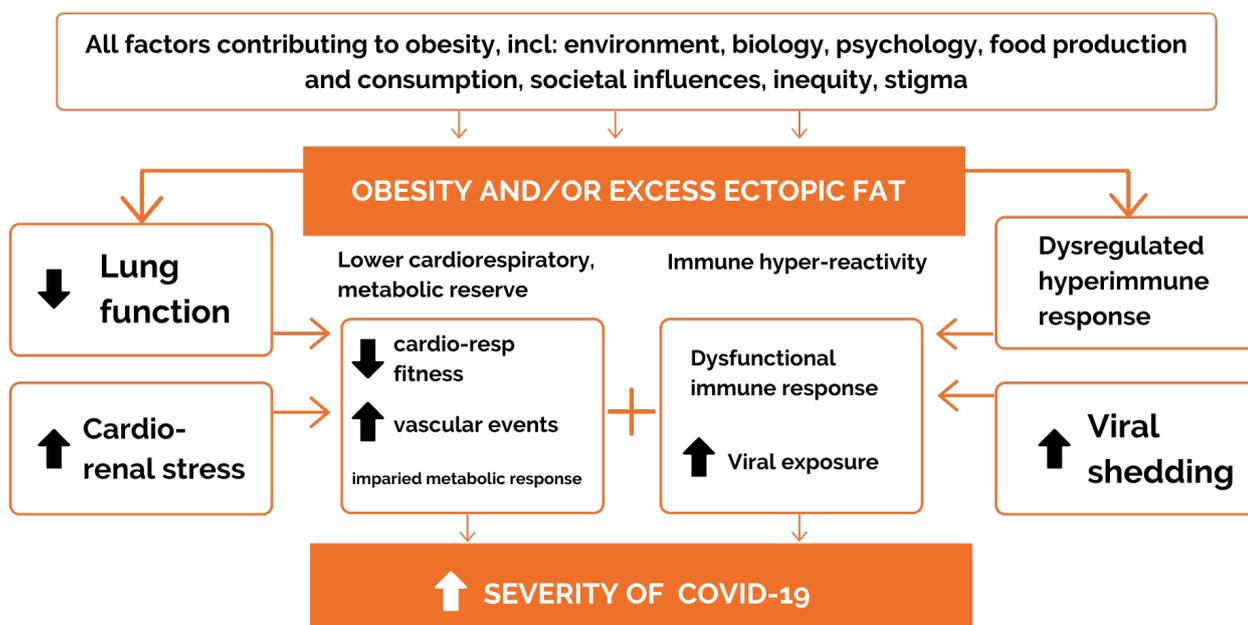


Figure 1. Potential mechanisms explaining the link between obesity and COVID-19 severity. Adapted from Sattar et al (2020)

# Inequalities

There are long-standing health inequalities in the UK that researchers believe have been exacerbated by the coronavirus pandemic, including those related to ethnicity and socio-economic deprivation.

The proportion of children at risk of obesity in the most deprived areas of Scotland is now more than double that of those in the least deprived areas (13.7% vs 6.5%)<sup>46</sup>, with a similar gap seen amongst children in England<sup>47</sup>. In adults in Scotland, obesity prevalence is 19% in the least deprived areas and 38% in the most deprived areas<sup>46</sup>. Similarly, in England in 2018, adult obesity prevalence was 20% and in the most deprived areas was 36%<sup>47</sup>.

Evidence is emerging for an association between obesity, socioeconomic status and COVID-19, showing a social gradient with poorer outcomes for those from more socio-economically deprived areas, which is likely multifactorial:

1. *Increased susceptibility due to poor pre-existing health,*
2. *Increased exposure due to living and working conditions (poorer housing and air quality, lower paid jobs),*
3. *Increased stress during lockdown due to adverse social conditions*

Recent ICNARC data shows that over a quarter (25.7%) of patients diagnosed with COVID-19 and in ICU were from the most deprived fifth of the population, compared to 14.4% in the least deprived fifth<sup>18</sup>. This disparity is evident across all ethnic groups, however is much more pronounced in those of Non-White ethnicity compared to White individuals. The socioeconomic trend is also reflected in those requiring and receiving long-term critical care (for 28 days or more); however, is not shown in outcome (discharged alive vs died in critical care)<sup>18</sup>.

In the latest report of the National Child Measurement Programme in England, obesity prevalence was highest for Black children across both year groups measured (reception and year 6)<sup>48</sup>. In year 6 children, obesity prevalence was 28.9% in Black children, compared to 18.4% in White children, over 10% difference<sup>48</sup>. In Scotland, Primary 1 BMI measurement data indicates that, in general, Black children are more likely than White children to have a high BMI, and children of Asian ethnicity are more likely to have low BMI<sup>49</sup>.

In adults in England, differences in prevalence of overweight and obesity are present between ethnic groups, with the highest prevalence seen in those of Black ethnicity at 73%, versus 63% in those of White ethnicity<sup>50</sup>. Cardiometabolic health risks of obesity present at lower BMI for certain BAME groups and as such, BMI thresholds for intervention are lower.

Two UK studies have used UK biobank data, a large prospective cohort of over half a million individuals, to investigate disparities amongst ethnic groups in relation to BMI and COVID-19. Razieh et al found that whilst the risk of testing positive for coronavirus was associated with BMI both in BAME and White ethnic groups, the dose-response relationship with increasing BMI differed between groups<sup>51</sup>. At a BMI of 30 or 35, the odds of testing positive were 1.75 and 2.56 higher in BAME individuals than in white individuals: a difference that was not evident at a BMI of 25<sup>51</sup>. Sattar et al recorded the same findings, and additionally found that BMI was more strongly related to COVID-19 death (Pinteraction = 0.002) in Non-White individuals (predominantly South Asian and Afro-Caribbean), in comparison to White individuals<sup>52</sup>. Both studies were limited by the low number of biobank participants who tested positive for coronavirus and in the Sattar study, a low number of deaths relative to that. Nevertheless, it indicates an association that should be further explored.

Evidence cited in PHE 'beyond the data' report on COVID-19 and ethnicity highlights further inequalities such as area deprivation - often minority groups live in more deprived areas and may be exposed to a higher likelihood of infection through living conditions, e.g. larger households - and employment in public-facing roles<sup>53</sup>.

## Conclusion

Obesity has well-established links with adverse health outcomes from a range of co-morbidities. Evidence emerging during the coronavirus pandemic suggests similar associations; obesity has been consistently linked to increased severity of COVID-19 and increased risk of death, with multiple potential and plausible mechanisms identified. Nevertheless, there are limitations in the evidence which should be taken into account when making recommendations<sup>17</sup>.

First, while there is increasing data showing links between BMI, ethnicity and deprivation, further research is required to explore the extent to which such factors contribute to increased severity and risk of death from COVID-19.

Second, as more data on co-morbidities and demographics of patients with confirmed COVID-19 is analysed, risk factors can be determined and groups most at risk from the virus can be identified clearly. This information can be used to tailor prevention measures toward groups who require the most protection. For instance, factors such as a reduced response to influenza vaccine in those with obesity have implications for future immunisation programmes.

Finally, excess weight has been highlighted as a potentially modifiable risk factor for COVID-19<sup>17</sup> but the effect of weight loss on decreasing COVID-19 severity is not yet known. We question, therefore, the potentially stigmatising framing of the UK Government's new obesity strategy, positioned as losing weight "to beat coronavirus (COVID-19) and protect the NHS"<sup>54</sup>. Obesity remains a complex, heterogeneous condition, with multiple causes requiring a cross-sectoral approach to reducing population prevalence. While it is important that Government's recognise and act on unhealthy food environments, care must be taken not to stigmatise or blame individuals.

There is, however, much to applaud in the UK Government's obesity strategy. We welcome measures to target the food environment with policies including a 9pm watershed on 'junk food' media advertising, regulations surrounding promotion of unhealthy foods, and the introduction of mandatory kcal labelling on menus in out of home businesses in England. These evidence-based measures will have population health benefits regardless of their direct impact on COVID-19.

*To the best of our knowledge, the content of this briefing is up to date as of 1st August 2020*



*Obesity Action Scotland produces a series of briefings covering a wide range of obesity-related topics.*

*Obesity Action Scotland provides clinical leadership and independent advocacy for a multifactorial approach on preventing and reducing overweight and obesity in Scotland, recognising the multiple causes of obesity.*

*For more information, or to read our range of briefings and blogs, visit our website at: [www.obesityactionscotland.org](http://www.obesityactionscotland.org)*



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