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Short Communication

COVID-19 mortality and the overweight: Cross-Country Evidence

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ABSTRACT

Objective(s): The objective is to study the role, if any, of excess body weight in COVID-19 mortality. Study design: This is a cross-country study of plausible associations between COVID-19 mortality and the proportion of overweight among adults, controlling for age, gender, and income.

Methods: Parametric and non-parametric regression analysis.

Results: We observe a statistically significant positive association between COVID-19 mortality and the proportion of the overweight in adult populations spanning 154 countries. This association holds across countries belonging to different income groups and is not sensitive to a population's median age, proportion of the elderly, and/or proportion of females. The estimated elasticities of COVID-19 mortality, with respect to the proportion of the overweight in adult populations, are consistently higher for sub-samples of countries that belong to a higher income group. On an average, every percentage point increment in the proportion of the overweight in adult populations contributes to an additional 3.5% points to COVID-19 mortality for high income countries: the limits of confidence intervals around this point estimate range between 1.5 and 5.4.

Conclusions: A positive association between COVID-19 mortality and the proportion of the overweight in a country's adult population is robust, subject to alterations in the conditioning information set on age, gender, and income. Our findings call for an effective alignment of public policy regulations with public health priorities.

1. Introduction

A striking association between being overweight and mortality has surfaced since the earliest pandemic of the 21st century. It is not surprising that such a pattern has been confirmed during subsequent outbreaks of influenza, since excess body weight can predispose to a greater viral shedding that leads to a higher exposure. Cell has unveiled a molecular architecture of the severe acute respiratory syndrome coronavirus 2 (COVID-19) that can be linked to body weight, and *Nature* has reported that the risk of dying from COVID-19 is linked to excess body weight [1,2]. While scientific research identifying the role of excess body weight in mortality among patients diagnosed with COVID-19 is at its infancy, emerging evidence points to a reasonable hypothesis that a population suffering from excess body weight is likely to experience a higher mortality from COVID-19. Our primary point of reference is the relevant medical literature while our main contribution is in conducting, to the best of our knowledge, the first cross-country analysis of a plausible association between COVID-19 mortality and the share of the overweight in nearly 5.5 billion adults around the globe.

In the next section, we lay out the methods of analysis we have used. In section 2 we present our findings. We discuss our contribution in the context of the relevant literature, in section 3. The final section concludes with due caution and a recommendation for aligning public policy with public health priorities. As described in the appendix, all data used are publicly available.

2. Methods

Since mortality is likely to be higher among older populations, due to a decline in immune and inflammatory responses with aging (*ceteris paribus*), we begin by constructing a regression surface to detect any association that COVID-19 mortality (M) bears with our key variable of interest i.e. percentage of the overweight in the adult population (O) alongside the median age of the population (A). To construct this regression surface, with ε capturing any error(s), we estimate the following non-parametric model

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$$\log M = f(\log O, \log A) + \varepsilon$$

for which a multivariate neighborhood around a focal point $(\log O_0, \log A_0)$ is defined using Euclidean distances

$$D = \sqrt{\sum_{j=1}^{c} \left(\log \widehat{O}_{j} - \log O_{0} \right)^{2} + \sum_{j=1}^{k} \left(\log \widehat{A}_{j} - \log A_{0} \right)^{2}}$$

where c is the number of countries (observations) indexed by j; and $(\log \widehat{O}_i, \log \widehat{A}_i)$ represents vectors of standardized regressors. A weighted polynomial regression is run, with weights $\left(\frac{D}{h}\right)$ where h is the halfwidth of the neighborhood. This procedure is repeated for representative combinations of predictor values to build up a plot of the regression surface. We create a data frame containing combinations of values of logO and logA: Using the expand.grid function in R, we take 50 values, for each regressor, evenly spaced along the range of the variable. Next, the corresponding fitted values on the regression surface are compute. These predicted values are then reshaped into a matrix which, along with the values of the predictors, are used to generate the regression surface. While an association between COVID-19 mortality and the proportion of the overweight in a country's adult population transpires from the regression surface, it is apparent that a partial regression in the direction of either of the regressors is not likely to be affected much by a variation in the other. To circumvent any limitation that non-parametric estimation may impose (e.g. the commonly confounding "curse of dimensionality" with expanding continuous variable space) we present,

in the next section, the results from a parametric estimation of

$$\log M = \beta_0 + \beta_1 \log O + + \beta_2 \log A + \varepsilon$$

3. Results

Table 1 confirms that the partial correlation between COVID-19 Mortality and the proportion of the overweight in adult populations is positive and significant. The sign and significance of this association remain robust to reasonable alterations in the conditioning information set, such as, inclusion of the proportion of elderly, proportion of females, and/or a dummy variable for income groups among potential regressors, as well as interaction terms. Such a sensitivity check, of course, lends credibility to our findings to the extent that the sign and significance of the coefficient of our variable of interest are not fragile. Limits of confidence intervals around the point estimates of elasticities, with respect to the proportion of the overweight in adult populations, range between 0.2 and 5.4.

and are consistently higher for the sub-sample of countries that fall in a higher income group: every percentage point increment in the proportion of overweight in the adult population, on an average, contributes to an additional 3.5% points to COVID-19 mortality in high income countries.

4. Discussion

Evolving research suggests that outcomes with COVID-19 are worse among those suffering from excess body weight while hospital reports, though not conclusive, have been indicative of the fact that the likelihood of survival is relatively low among the overweight COVID-19 patients [3,4]. In the absence of any previous analysis of associations between COVID-19 mortality and the proportion of the overweight in adult populations across countries, anecdotal evidence aside, our contribution may be placed at the intersection of clinical studies and the relevant literature on public health.

Since the outbreak of the recent pandemic, several clinical studies

Table 1COVID-19 mortality and proportion of the overweight in adult population: Robustness.

Regression	1	2	3	4	5	6	7	8	9	10	11	12
log (percentage of overweight adults in the population)	2.571***	2.391***	2.468***	2.431***	2.449***	2.417***	2.463***	2.369***	2.488***	2.528***	2.534***	2.567***
Income group dummy (1 = high income; 2 = upper middle income; 3 = lower middle income; 4 = low income)		-0.098	-0.169	-0.063	-0.083	-0.077	-0.128	0.017	-0.033	-0.039	0.004	-0.005
log (median age)			-0.374		-0.096		-0.507		-2.291	-75.828	-1.875	-71.269
log (percentage of female in the population)				-0.656	-0.606			-1.406	-4.087	-68.287	-1.888	-62.642
log (percentage of elderly in the population)						-0.001	0.122	0.170	1.049	0.865	11.316	10.188
log (median age)*log (percentage of female in the population)										18.844		17.773
log (percentage of elderly in the population)*log (percentage of female in the population)											-2.648	-2.402
Constant	3.231***	3.298***	4.765*	5.801	5.984	3.261***	4.864	8.171	24.771*	275.699	14.969	252.539
Sample size	154	154	154	153	153	153	153	153	153	153	153	153
Adjusted R-squared	0.370	0.367	0.364	0.364	0.360	0.363	0.359	0.361	0.365	0.368	0.365	0.368
F-statistic	90.84	45.40	30.22	29.96	22.33	29.82	22.29	22.44	18.44	15.76	15.58	13.65

Notes: Dependent variable is log of COVID-19 Mortality.

^{***} indicates that a regression coefficient is statistically significant at 1% level;

^{**} indicates that a regression coefficient is statistically significant at 5% level; and

^{*} indicates that a regression coefficient is statistically significant at 10% level.

have explored plausible pathological mechanisms through which excess body weight can affect COVID-19 mortality. Clinically, excess body weight is related to several comorbidities that can lead to an increasingly severe course of and consequent death from COVID-19: metabolic disorders (such as hypertension, insulin resistance, dyslipidemia or prediabetes, which frequently occur in overweight patients) predispose to a poorer COVID-19 outcome. Since excess body weight can result in a greater volume and longer duration of viral shedding, it can lead to a higher level of exposure as well.

The most recent meta-analysis, conducted by Hussain et al. (July--August 2020), documents that a vast majority of COVID-19 studies did not include excess body weight, not even obesity, as a mortality risk factor in their reports [5]. The authors attribute such apparent oversight to a lack of awareness and/or an absence of access to reliable data on body mass index (BMI). We draw attention to the clinical studies, relevant to our work, that have identified mechanisms linking COVID-19 mortality and excess body weight. Simonnet et al. (2020) were among the earliest to point out the conspicuous absence of any mention of high BMI in clinical reports on significant risk factors for COVID-19. They conducted a retrospective cohort study to analyze the relationship between BMI and the requirement for invasive mechanical ventilation, involving 124 patients in intensive care at a French center for COVID-19, and concluded that the severity of COVID-19 increased with BMI [6]. Subsequently, in a population cohort study, Ho et al. (2020) analyzed clinical observations on 340 confirmed COVID-19 patients and detected high BMI as a risk factor for COVID-19 mortality. Their study identified a dose-response relation between excess body weight and severity of COVID-19: the relative risk of critical illness from COVID-19 increased by 44% for people who were overweight [7]. Sattar et al. (2020) studied a subsample of UK Biobank participants and reported consistent findings on a strong positive association between BMI and the risk of death related to COVID-19 [8]. Tartof et al. (2020), based on observed patterns in data from an integrated health care system, also reported a strong association between BMI and risk for death among patients diagnosed with COVID-19 [9].

Collectively, these studies point toward multiple mechanisms that can clinically link COVID-19 mortality to excess body weight. For instance, the mass of human angiotensin-converting enzyme II (a putative receptor for the entry of COVID-19) is relatively high among the overweight. Moreover, being overweight impairs immunity by altering the response of cytokines. This results in a decline in the cytotoxic cell response of immunocompetent cells which have a key anti-viral role in addition to causing an imbalance between endocrine hormones affecting the interplay between metabolic and immune systems. Excess body weight can also trigger the involvement of adipose tissue-specific molecules in the generation of an environment that is favorable for diseases with an immune cause. There are negative impacts, as well, on the ability of dendritic cells (that link innate and adaptive immunity) to mature and elicit appropriate responses from white blood cells in the face of a general stimulus (such as, a viral infection like COVID-19).

5. Conclusion

In sum, the positive association between COVID-19 mortality and the proportion of the overweight in a country's adult population is alarming. The current pandemic has, on an average, been more fatal for adult populations residing in parts of the world characterized by excess body weight. While our findings can be used to make a case for stratified lockdowns, it is no less important to turn the spotlight on the food industry which has been profiting from the sale of products that are often ultra-processed, high in salt, sugar, and saturated fat to an extent that can lead to an accumulation of excess body weight exacerbating the fatal consequences of COVID-19. As the World Health Organization underscores, companies should reduce the fat, sugar, and salt content of processed food and beverages and ensure that healthy and nutritious choices are available and affordable to all consumers. On the contrary,

some firms in the food industry have taken the liberty of using the pandemic as a platform for marketing in ways that are all but conducive to restraining body weight. But for some scattered instances (e.g. taxes on sweetened beverages in the United Kingdom), a comprehensive regulation of the food industry is conspicuous in its absence while public policy is far from being aligned with public health priorities. Our observed association, between COVID-19 mortality and the share of the overweight in nearly 5.5 billion adults residing across 154 countries that host almost 7.5 billion people around the globe, serves as a caution against putting more lives at stake: in hindsight, with the death toll from the current pandemic exceeding four and a half million, our findings call for immediate and effective regulations (e.g. restrictions on "serving" the market for food and beverages with items, the intake of which can result in the accumulation of excess body weight) that are long overdue.

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Ethical approval

Not required, since all data used are publicly available.

Declaration of competing interest

There is no conflict of interest with respect to the submission of "COVID-19 Mortality and the Overweight: Cross-Country Evidence," accepted for publication at *Public Health in Practice*.

Appendix

COVID-19 mortality: The European Centre for Disease Prevention and Control (ECDC) provides data on COVID-19 mortality. The Epidemic Intelligence team of the ECDC, as described on the relevant web pages (https://www.ecdc.europa.eu/en/covid-19/data-collection), has been collecting the number of COVID-19 deaths, based on reports from health authorities worldwide, since the beginning of the coronavirus pandemic. The ECDC follows a comprehensive and systematic process in data collection in order to insure the accuracy and reliability of the data: a team of epidemiologists screens up to 500 relevant sources to collect the latest figures, every day between 6.00 and 10.00 CET. ECDC receives regular updates from European countries through the Early Warning and Response System (EWRS), The European Surveillance System (TESSy), the World Health Organization (WHO) and email exchanges with other international stakeholders. This information is complemented by screening up to 500 sources every day to collect COVID-19 figures from 196 countries. This includes websites of ministries of health (43% of the total number of sources), websites of public health institutes (9%), websites from other national authorities (ministries of social services and welfare, governments, prime minister cabinets, cabinets of ministries, websites on health statistics and official response teams) (6%), WHO websites and WHO situation reports (2%), and official dashboards and interactive maps from national and international institutions (10%). In addition, ECDC screens social media accounts maintained by national authorities, including Twitter, Facebook, YouTube or Telegram accounts run by ministries of health (28%) and other official sources (e.g. official media outlets) (2%). Several media and social media sources are screened to gather additional information which can be validated with the official sources previously mentioned.

Percentage of overweight adults in the population: The Global Health Observatory (GHO) repository, WHO's gateway to health-related statistics for its Member States, provides data on the percentage of overweight adults in populations based on estimates of the prevalence of overweight men and women aged 18 and above by country. As described on the relevant web pages (https://www.who.int/data/gho), these

estimates are based on data from random sampling of the general population of each country.

Median age: The World Population Prospects, of the United Nations Population Division, provides data on the 2019 median age of populations residing in countries around the world. As described on the relevant web pages (https://population.un.org/wpp/), median age (expressed in years) divides the population distribution so that there are as many persons with ages above the median as there are with ages below the median.

<u>Population proportion of elderly</u>: Estimates of the proportion of elderly (65 years or older) in populations, across countries, are based on the 2019 revision of age distributions provided by the World Population Prospects, of the United Nations Population Division (https://population.un.org/wpp/).

<u>Population proportion of females</u>: Estimates of the proportion of females in populations, across countries, are based on the 2019 revision of sex distributions provided by the World Population Prospects, of the United Nations Population Division (https://population.un.org/wpp/).

Income groups: We follow the World Bank Atlas method of classification of countries by income groups (https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups) on the basis of 2019 per capita Gross National Income (GNI). Low income countries are defined as those with a per capita GNI of

\$1035 or less; lower middle income countries are those with a per capita GNI ranging from \$1036 to \$4045; upper middle income countries are those with a per capita GNI ranging from \$4046 to \$12,535; and high income countries are those with a per capita GNI of \$12,536 or more.

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