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RESEARCH ARTICLE

Worldwide Regional Differences in Obesity, Elderly, and COVID-19 Mortality: Do the Exceptions Prove the Rule?

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ABSTRACT

Objectives. Obesity and old age are commonly assumed to be risk factors for COVID-19 mortality. On a worldwide basis, we examine quantitative measures of obesity and elderly in the populations of individual countries and territories, and investigate whether these measures are predictive of COVID-19 mortality in those countries. In particular, we highlight regional differences relative to obesity and elderly metrics, and how these relate to COVID-19 mortality.

Methods. In this retrospective, population-based study, we obtained data relating to percentages of obese or elderly individuals in 199 countries, as well as COVID-19 mortality rates in these countries. We used negative binomial regression analyses to assess associations between COVID-19 mortality rates and the putative risk factors, in six regions – Africa, Asia, Europe, North America, Oceania, and South America.

Results. We found significant differences between regions relative to COVID-19 mortality, as well as obesity and elderly population proportions. There were also substantial differences between countries within regions relative to proportions of obesity and elderly individuals, and COVID-19 mortality.

Conclusions. There are significant differences both between regions and within regions relative to COVID-19 mortality rates, as well as proportions of obese or elderly individuals. A global pronouncement that obesity and elderly constitute definitive risk factors for COVID-19 mortality masks the subtleties engendered by these intra- and inter-regional differences.

Introduction

The COVID-19 pandemic is a global health crisis, resulting in significant morbidity and mortality which has affected millions of people worldwide. The virus disproportionately affects certain populations, in particular, the elderly and those with preexisting health conditions such as obesity. It is commonly accepted that obesity and elderly age are significant risk factors for severe illness and death from COVID-19. Obesity can impair lung function, increasing the risk of respiratory infections such as COVID-19, and is associated with chronic low-grade inflammation, which can weaken the immune system and make it harder to fight off infections. It is often associated with a range of comorbidities, including diabetes, hypertension, and cardiovascular disease, all of which can further increase the risk of severe illness from COVID-19. Similarly, aging is associated with a weakening of the immune system, and elderly individuals are more likely to have underlying health conditions including obesity and associated comorbidities, again increasing the risk of severe illness or mortality from COVID-19.

Relationships between obesity, elderly population, and COVID-19 morbidity and mortality have been extensively investigated¹⁻¹⁶; but here we take a more nuanced approach. On a worldwide basis, we examine quantitative measures of obesity and elderly in the populations of individual countries and territories, and investigate whether these measures are predictive of COVID-19 mortality in those countries. Unlike previous publications, we do not adopt a meta-analytic perspective, as we recognize that there is extensive heterogeneity across countries and regions relative to obesity and elderly population profiles, and how these relate to COVID-19 mortality. We believe this heterogeneity presents challenges to the orthodoxy that obesity and old age are universal risk factors for COVID-19 mortality.

We highlight these regional differences in our synthesis of the obesity and elderly data, and discuss implications of these findings relative to observed COVID-19 mortality.

Methods

All data used in this study are freely available to the public, in a totally anonymized format without

any identifiable information on a personal level. This study was therefore considered exempt from ethical review by our institution.

Data

Cumulative totals of mortality attributable to COVID-19 per country or territory were obtained from the World Health Organization's coronavirus dashboard¹⁷. Elderly population percentages, with elderly constituting individuals aged 65 and above, were obtained from the World Bank DataBank¹⁸, as determined with data from the United Nations Population Division. We used percentages from 2021 in our study. Obesity population percentages, with obesity defined as body mass index of 30 or greater, were obtained from the Bariatrics Report¹⁹, 2022 data.

We merged the three datasets, with country or territory as key. This resulted in a combined dataset representing 199 countries or territories. For some analyses and graphs, we subdivided these data by region: Africa, Asia, Europe, North America, Oceania, or South America.

Statistical Methods

Our study is largely observational, hence we are hesitant to overly analyze these data. Nevertheless, we do utilize regression methodology to tease out any relations between population proportions of elderly or obesity and region, and associations between COVID-19 mortality and regional obesity and elderly proportions. Our main tool in this regard is negative binomial regression²⁰⁻²². We remark in passing that Poisson regression models are commonly used for modeling count data, but we initially found that obesity and elderly proportions as well as COVID-19 deaths across countries are substantially over-dispersed relative to the Poisson assumption that mean is equal to the variance. Thus a Poisson distributional assumption for our endpoints of interest appeared inappropriate, and we chose to adopt negative binomial models, that allow count outcome variables with variance larger than the mean.

Formally, let Y denote a (dependent) variable that is an observed count following a negative binomial distribution. We may write

$$\Pr(Y = y_i | \mu_i, \alpha) = \frac{\Gamma(y_i + \alpha^{-1})}{\Gamma(y_i + 1)\Gamma(\alpha^{-1})} \left(\frac{\alpha^{-1}}{\alpha^{-1} + \mu_i} \right)^{\alpha^{-1}} \left(\frac{\mu_i}{\alpha^{-1} + \mu_i} \right)^{y_i}$$

where $\mu_i = p_i \mu$ and α is sometimes parameterized by $\alpha = 1/v$. The parameter μ is the mean incidence rate of Y per unit of exposure. In our setting, exposure constitutes population size, and we use the symbol p_i to represent the underlying population size (the population at risk) for a particular observation.

Turning to the negative binomial regression model, the mean of Y is determined by the population size p and a set of k regressor variables (conventionally, the x 's in a linear regression $Y = AX + b$). The expression relating these entities is

$$\mu_i = \text{Exp}(\text{Log}(p_i) + \sum_{j=1}^k \beta_j x_{ji}).$$

Here, $\text{Exp}()$ is the exponential function, and $\text{Log}()$ denotes the natural log. Often, we set $x_1 = 1$, and β_1 is termed the intercept. The regression coefficients, the β_j , are unknown parameters that are then estimated from a set of data.

We utilized negative binomial regressions to compare obesity, elderly, and COVID-19 mortality between regions: the Y_i are counts of obesity, elderly, or mortality per country or territory, the p_i are the corresponding populations, and the x_i are indicator variables for the 6 regions of interest.

Within each region, we also utilized negative binomial regressions to examine associations

between COVID-19 mortality and obesity or elderly. In this scenario, the Y_i are counts of mortality for country i , the p_i are corresponding population sizes, $k = 2$, the x_{1i} are all 1 and the x_{2i} are percentages of obesity or elderly per country. Hence for each region we are estimating an intercept and slope of a regression line relating obesity or elderly to COVID-19 mortality for the countries in that region, a regression line that is linear in log (mortality rate).

Results

In Figure 1 we present global choropleths of percentages of obesity and elderly. Relatively high levels of obesity seem common throughout the world, with the exceptions of countries in eastern Asia and central Africa. The elderly profile is quite different: with the exception of the Africa region, countries tend to have a substantial proportion of elderly people. A slightly different perspective of national differences in obesity and elderly is given in Figure 2, where we give scatter diagrams of these percentages by region, namely, Africa, Asia, Europe, North America, Oceania, and South America. We also give in Figure 2 estimated marginal means of regional percentages of obesity and elderly from negative binomial regressions, along with associated 95% confidence intervals. Notably, compared to other regions, Africa overall exhibits significantly less obesity and elderly, and Europe has a significantly higher percentage of elderly. In each region, there is less variability in elderly compared to obesity proportions.

Figure 1A

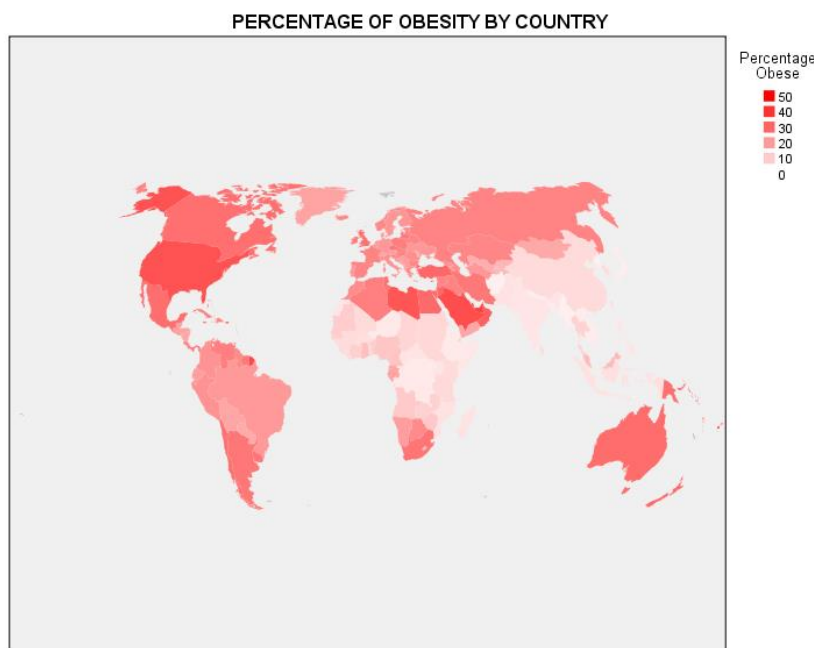


Figure 1B

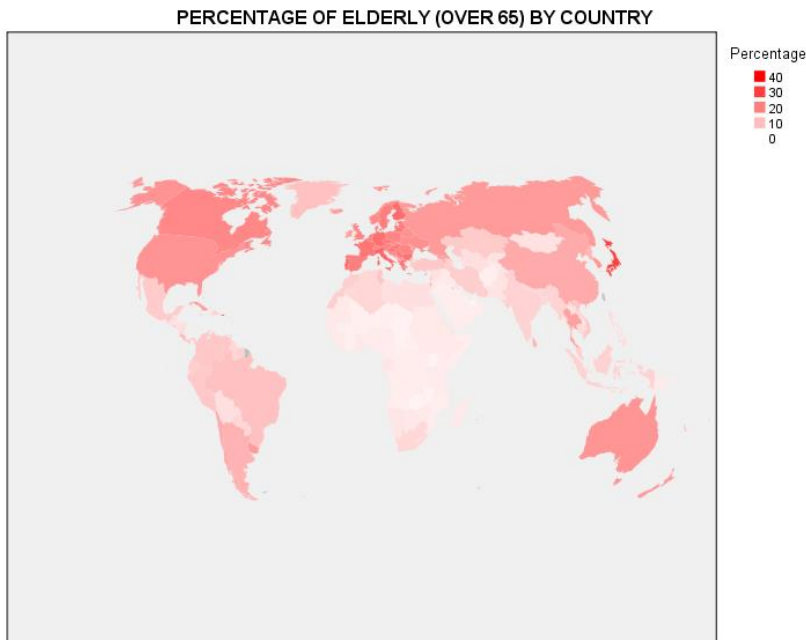


Figure 1. World choropleths of population percentages of (A) obesity and (B) elderly by country. Obesity represents body mass index of 30 or greater, and elderly constitutes individuals aged 65 or older.

Figure 2A

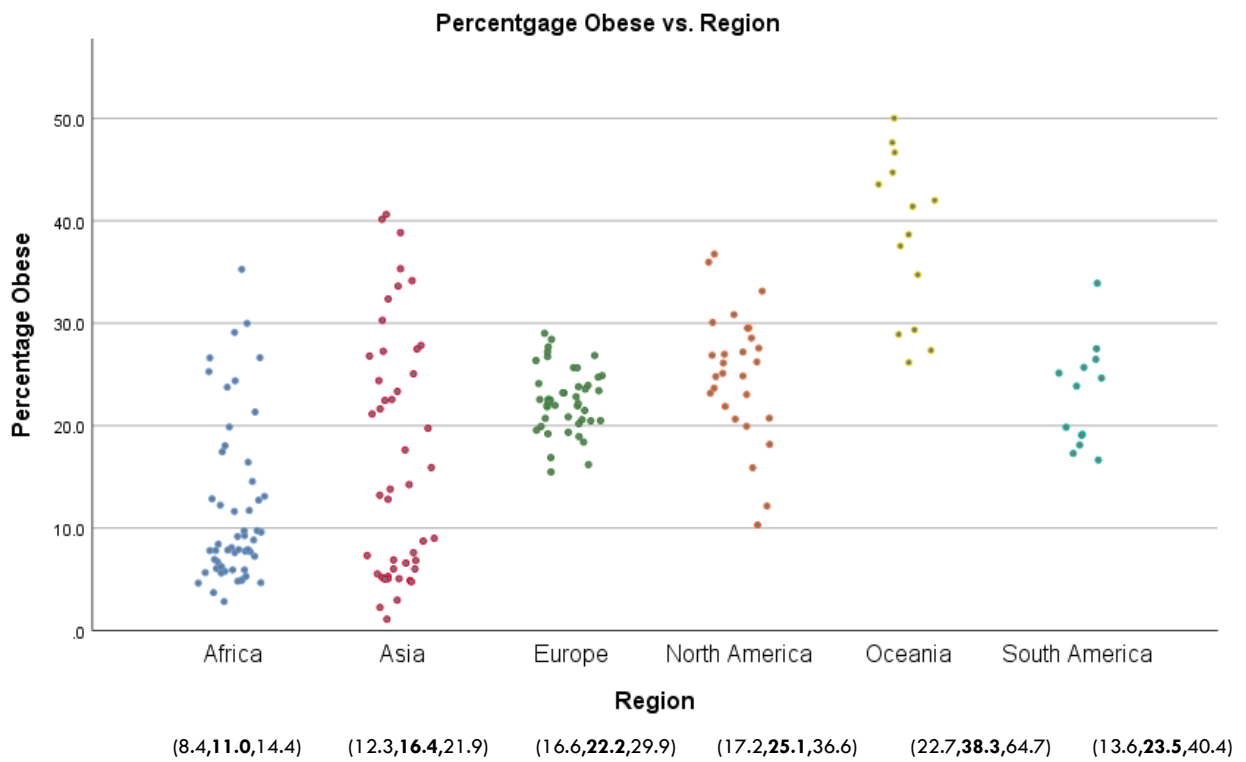


Figure 2B

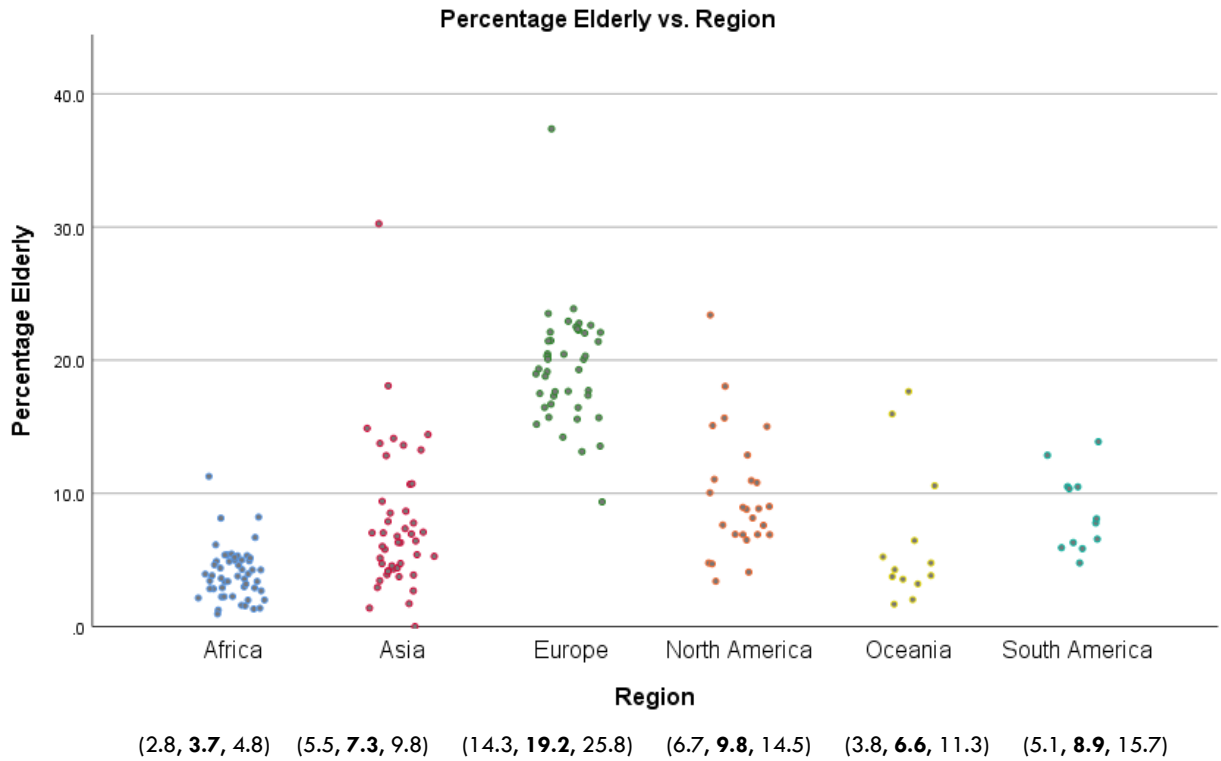
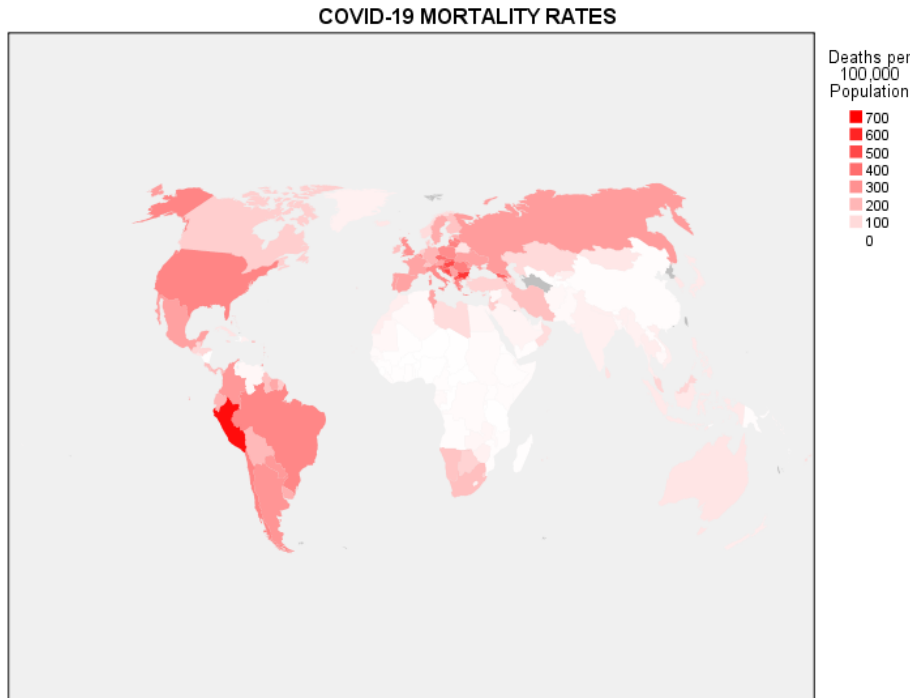


Figure 2. Percentages of (A) obesity and (B) elderly by region. Countries, from Figure 1, were classified into 6 regions: Africa, Asia, Europe, North America, Oceania, and South America. The numbers underneath the regions are the estimated marginal means of the respective percentages (middle numbers) along with associated 95% confidence limits (flanking numbers). These were obtained from negative binomial regressions per region, as explained in the text.



Mortality data were unavailable for Turkmenistan, Peoples Republic of Korea, and Taiwan (shaded gray).

Figure 3. World choropleth of COVID-19 mortality rates by country.

We next turn to COVID-19 mortality, beginning with a global choropleth in Figure 3. Differences between regions are perhaps more pronounced than found in Figure 1, with Africa in particular faring quite well on this metric. Figure 4 is analogous to Figure 2, a scatter diagram of COVID-19 mortality by region, along with estimated marginal means of mortality and

associated 95% confidence intervals. The regions comprise two relatively homogeneous subgroups: Africa, Asia, and Oceania experienced significantly less COVID-19 mortality than Europe, North America, and South America. Oceania is relatively homogeneous relative to COVID-19 mortality, but again there is substantial variability in mortality rates in the other regions.

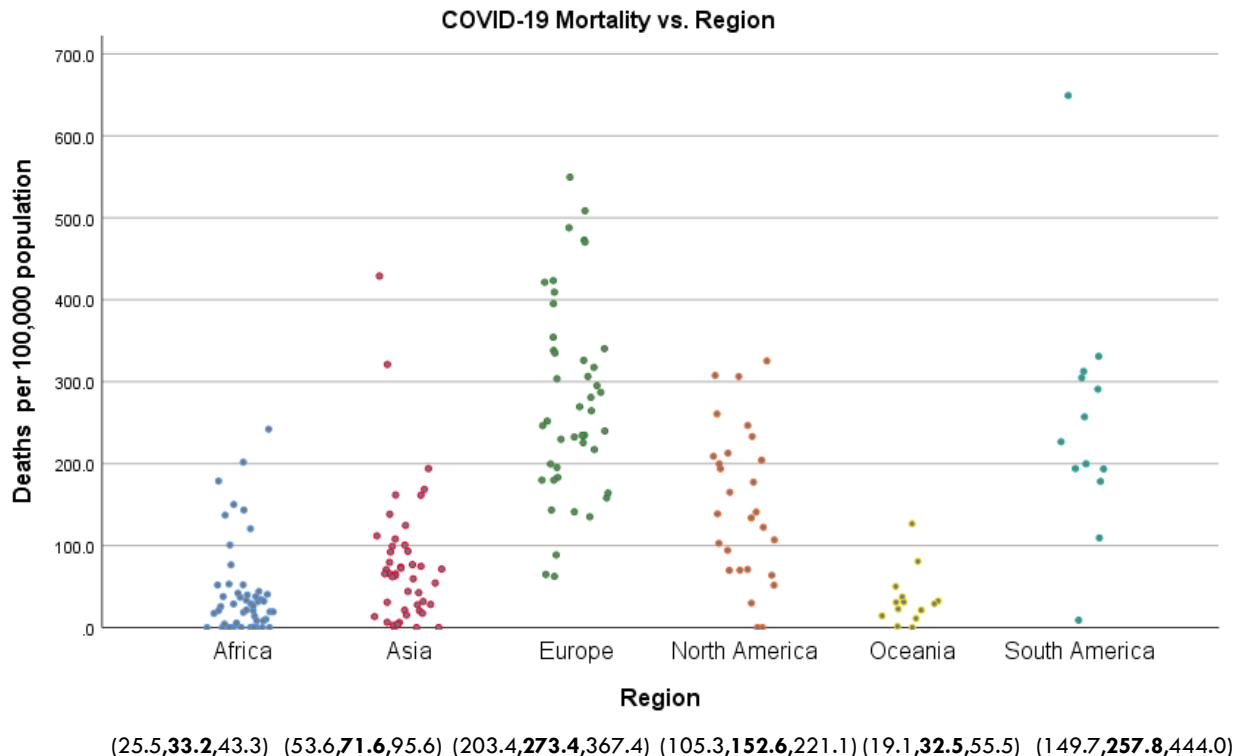


Figure 4. COVID-19 mortality rates by region (as in Figure 2), along with estimated marginal means and associated 95% confidence limits.

We further elucidate national differences in COVID-19 mortality in Figure 5, where we present graphs of percentage obesity and elderly vs. COVID-19 mortality by region, along with best fitting negative binomial regression lines. Of these graphs, there are 5 plots with significant associations, that is, slopes significantly different from zero: Africa and Asia with both obesity and elderly, and North America with obesity. The regressions in the remaining plots are characterized by slopes not significantly different from zero. Nevertheless, the plots are revelatory concerning country “extremes”, several of which we highlight: Burundi in Africa has little obesity, elderly, or COVID-19 mortality; the proportions of elderly individuals in Japan (Asia) and Monaco (Europe) vastly exceed that of the other countries in their respective regions; Haiti and Nicaragua (North America) and Venezuela (South America) experienced quite low mortality rates in their

respective regions; and the mortality rate in Peru (South America) is exceptionally high for the region.

In Figure 6, we combine the various regional regressions from Figure 5 into overall displays on the same scale, so as to better illustrate region to region differences. One might declare Africa a decisive winner in the COVID-19 mortality sweepstakes, along with Asia and Oceania (even though obesity is especially pronounced in Oceania).

Discussion

The COVID-19 pandemic has affected millions of people worldwide. Certain subpopulations, including individuals with obesity and the elderly, appear to be particularly likely to experience severe outcomes and increased mortality rates from COVID-19 infection. That obesity and elderly are considered risk factors for illness and mortality from COVID-19 infection is reasonable from a

physiological perspective. Obesity can impair lung function, leading to reduced respiratory capacity and an increased susceptibility to airborne respiratory infections as with COVID-19. In addition, excessive adipose tissue can release inflammatory cytokines that may exacerbate the inflammatory response to viral infections. Similarly, aging is associated with physiological changes to the immune system, including reduced or impaired immune responses, which in turn leads to increasing vulnerability to infections. Obesity may also be a marker of comorbidities such as cardiovascular disease, hypertension, and diabetes, the prevalence of which tends to increase with age. In short, obese and elderly subpopulations are likely

to be susceptible to adverse clinical outcomes from COVID-19 infection due to the effects of obesity-related metabolic dysregulation, age-related immune decline, and combined effects of comorbidities.

We therefore postulated that increasing prevalence of obese or elderly subpopulations in countries and territories should be associated with increasing mortality rates from COVID-19. We found wide country-to-country variations in prevalence indices and mortality rates, hence we focused on regional differences, the regions being Africa, Asia, Europe, North America, Oceania, and South America.

Figure 5A

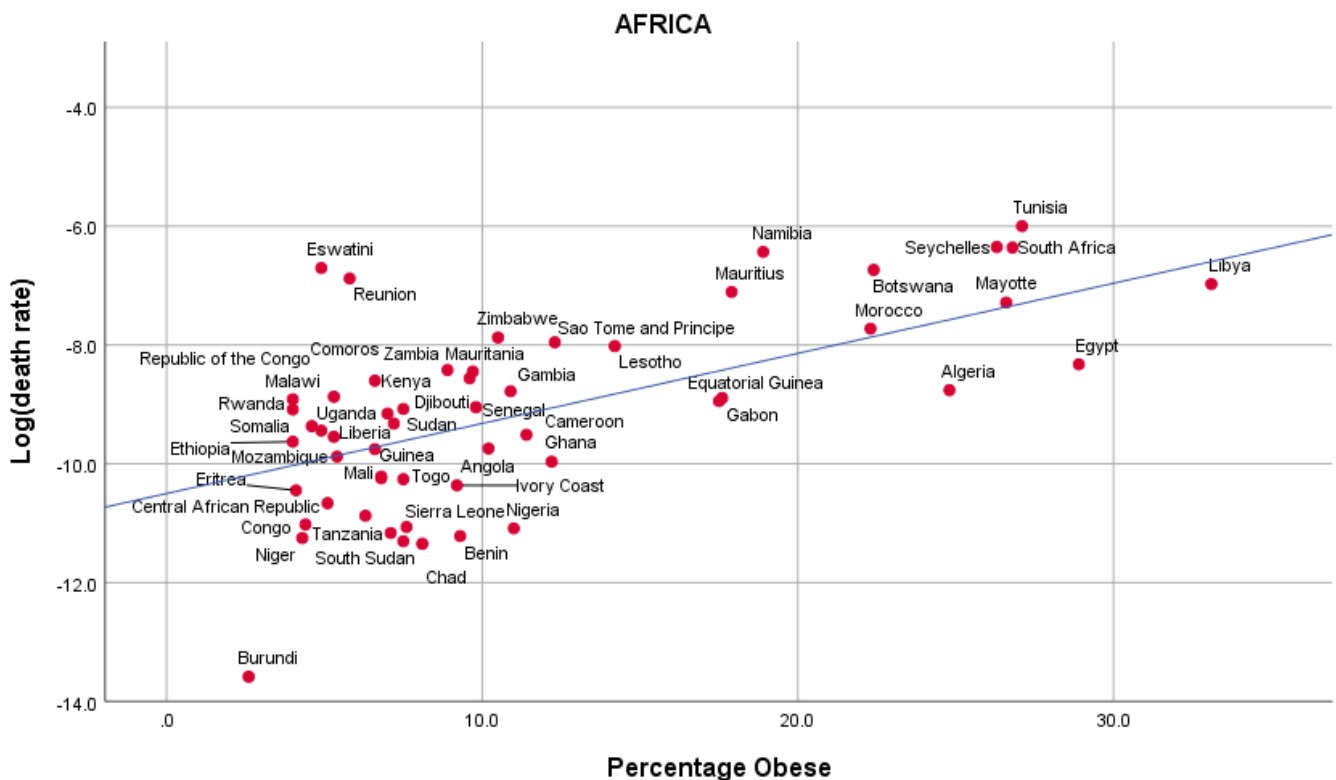


Figure 5B

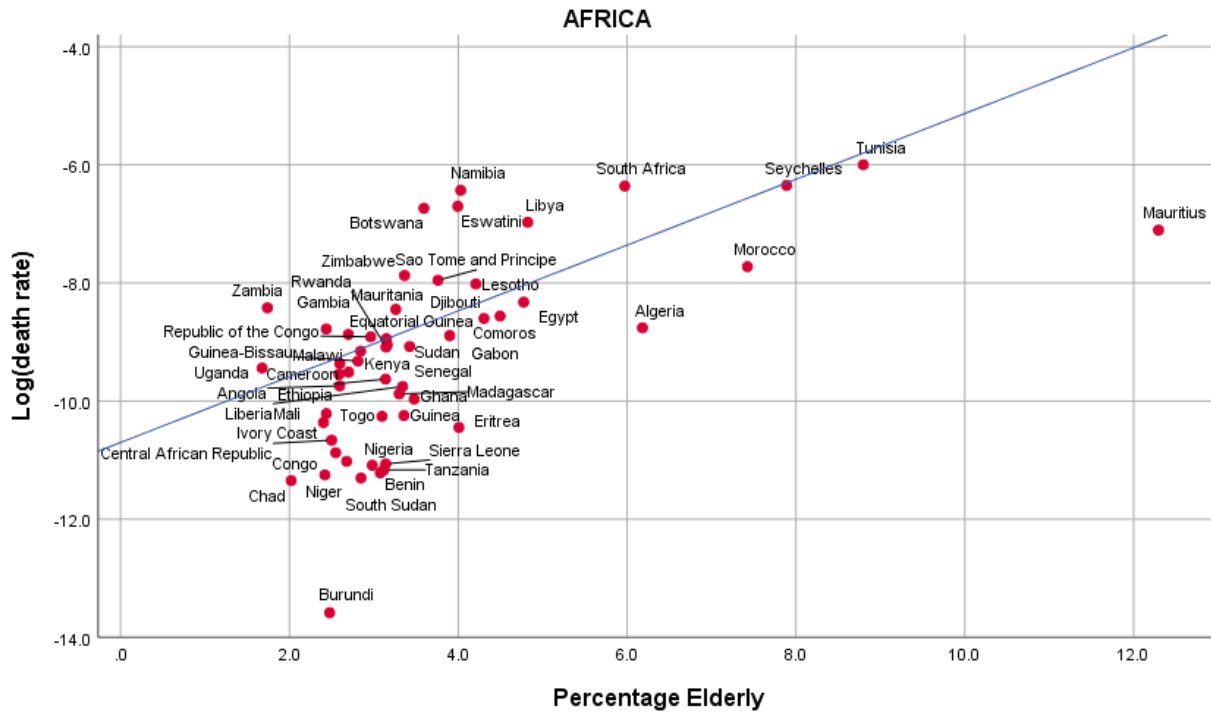


Figure 5C

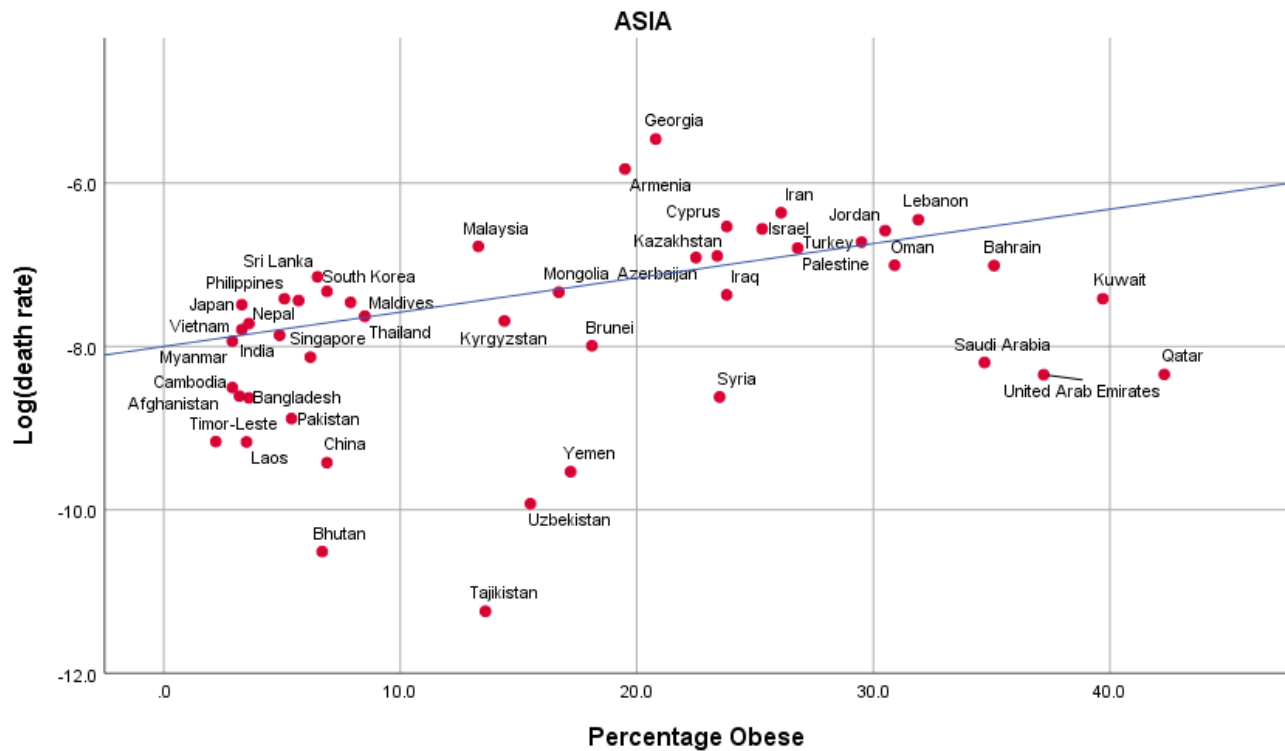


Figure 5D

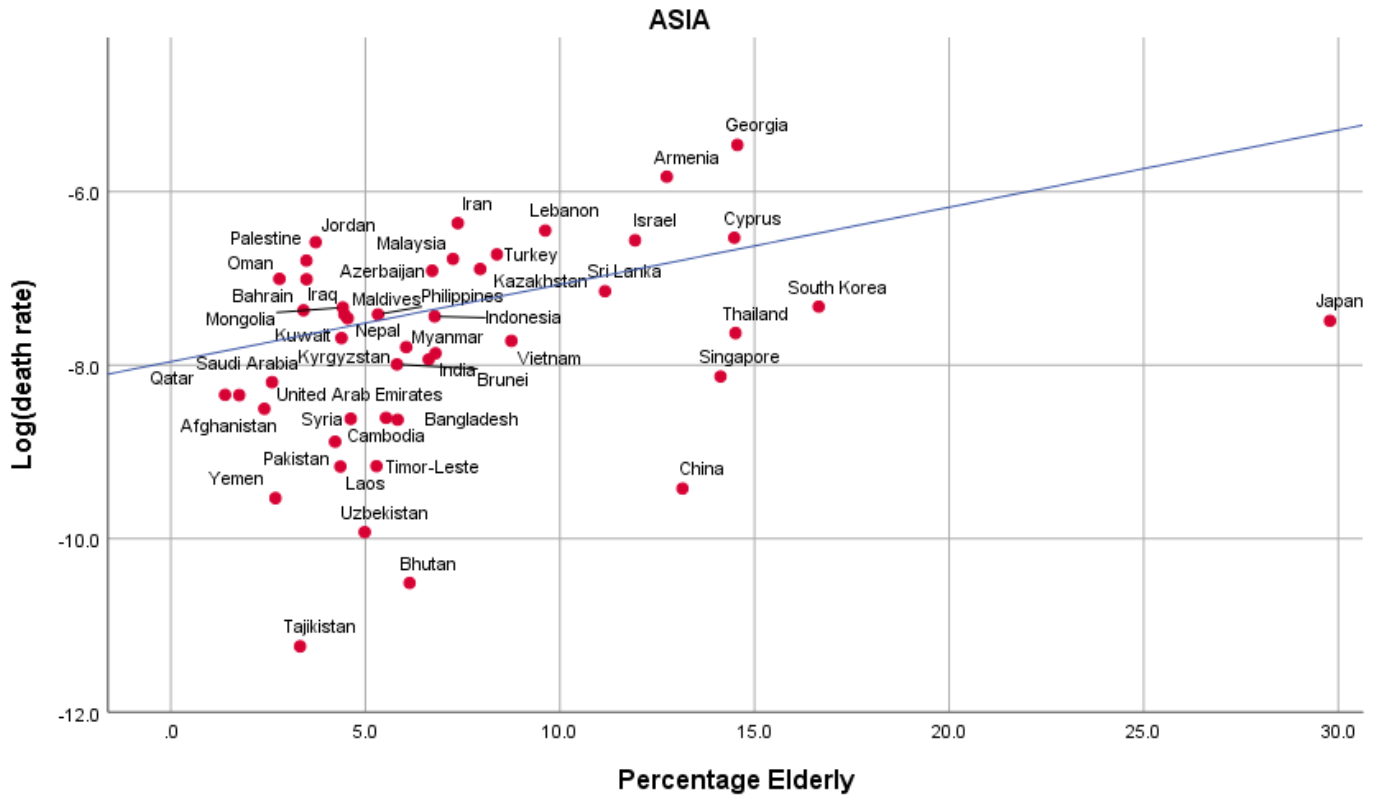


Figure 5E

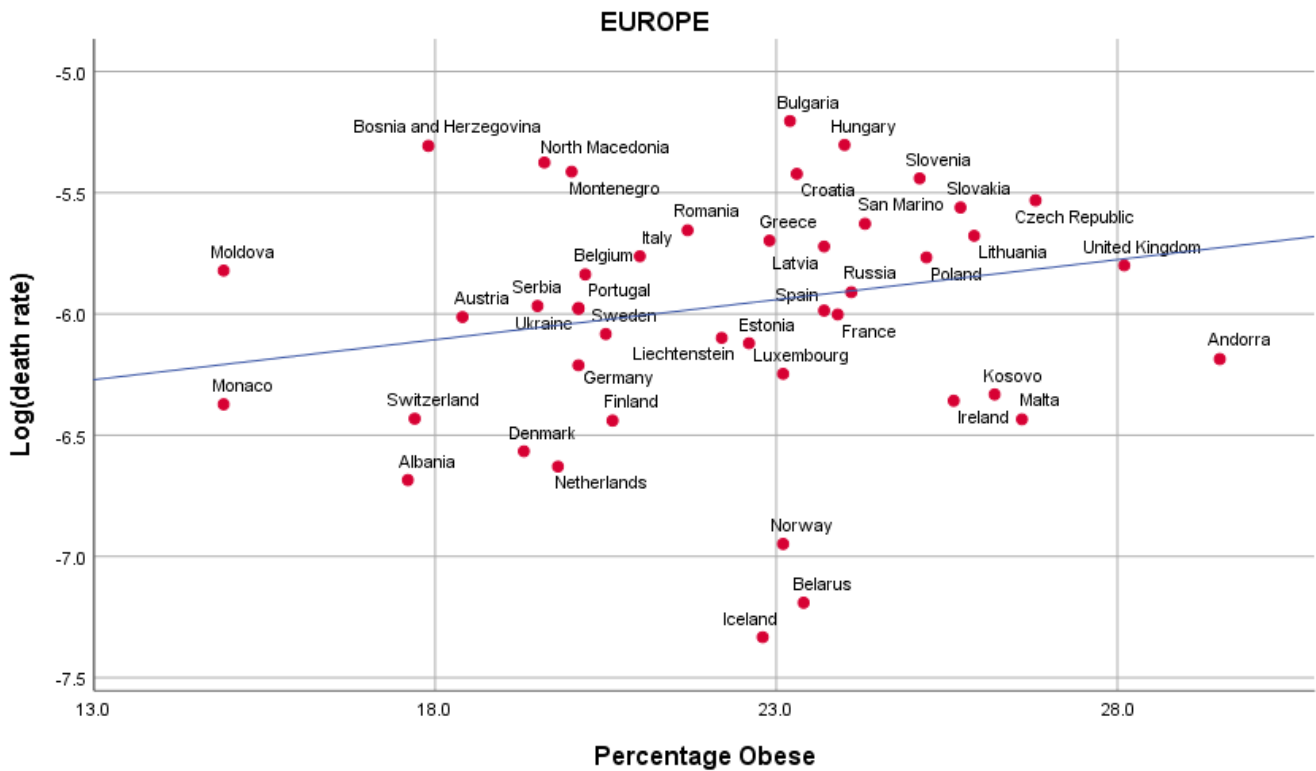


Figure 5F

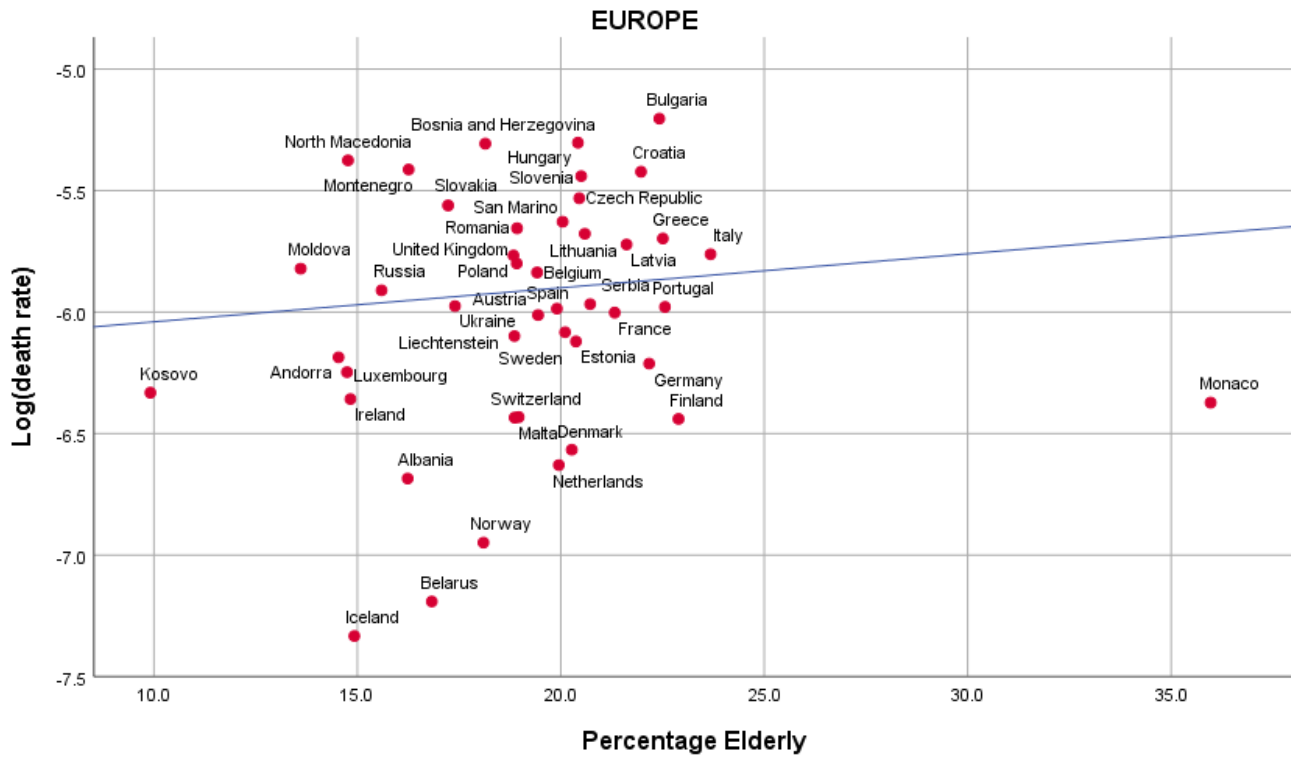


Figure 5G

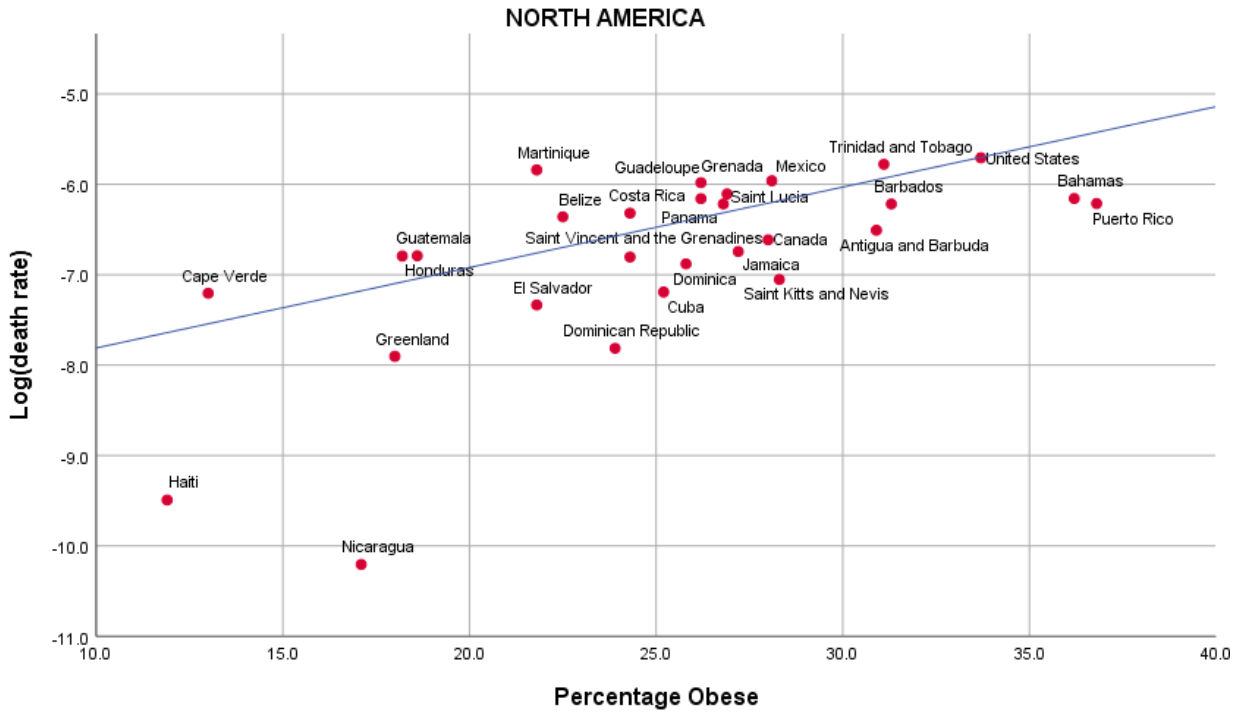


Figure 5H

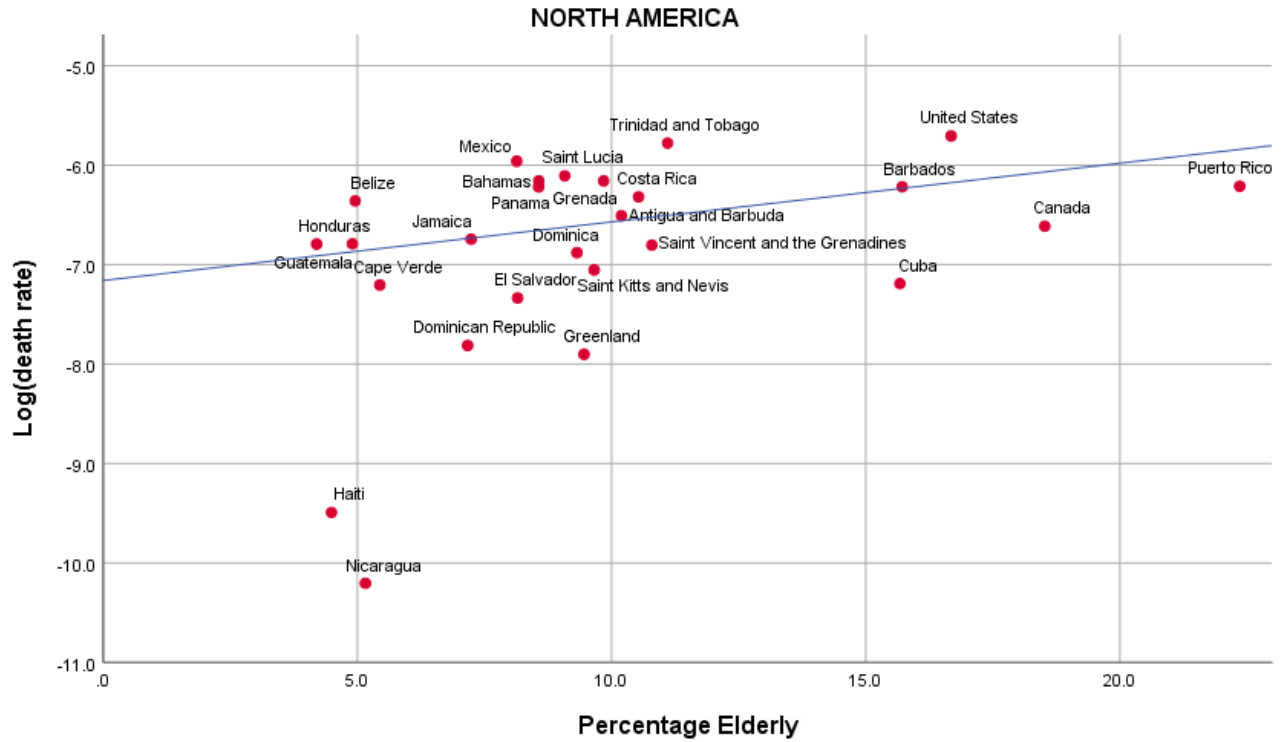


Figure 5I

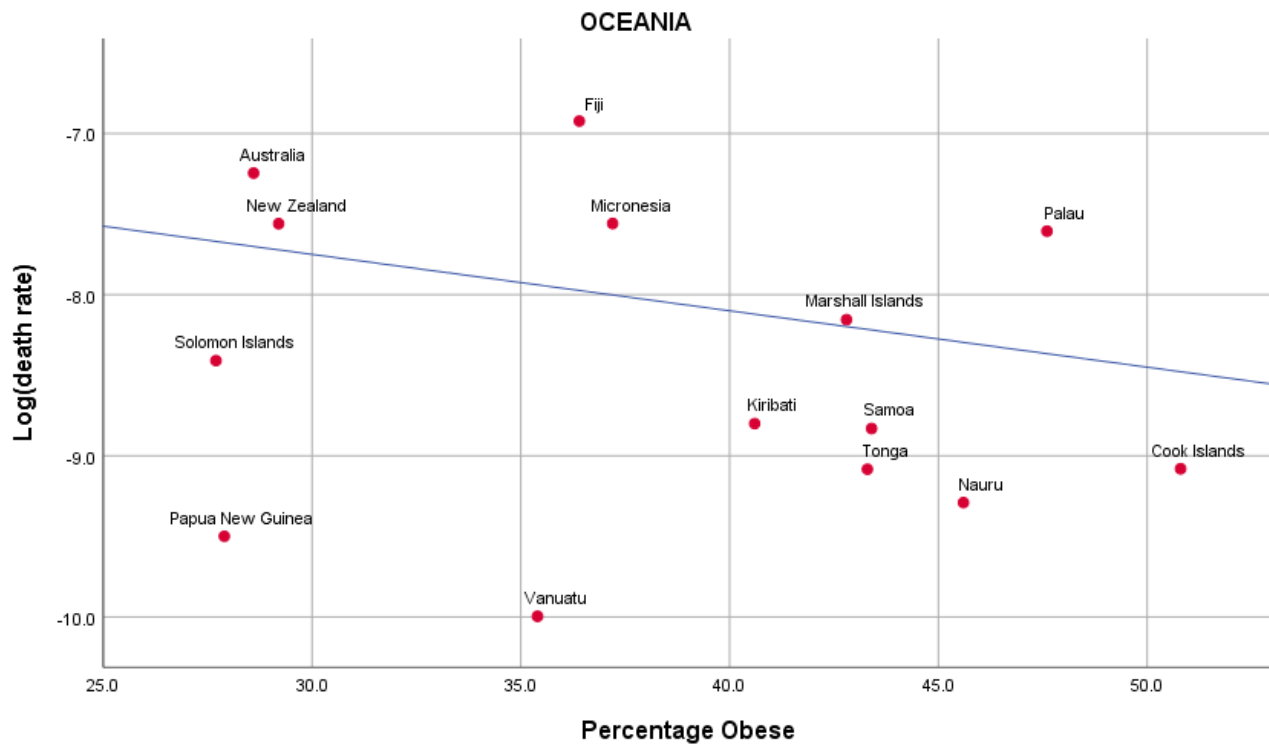


Figure 5J

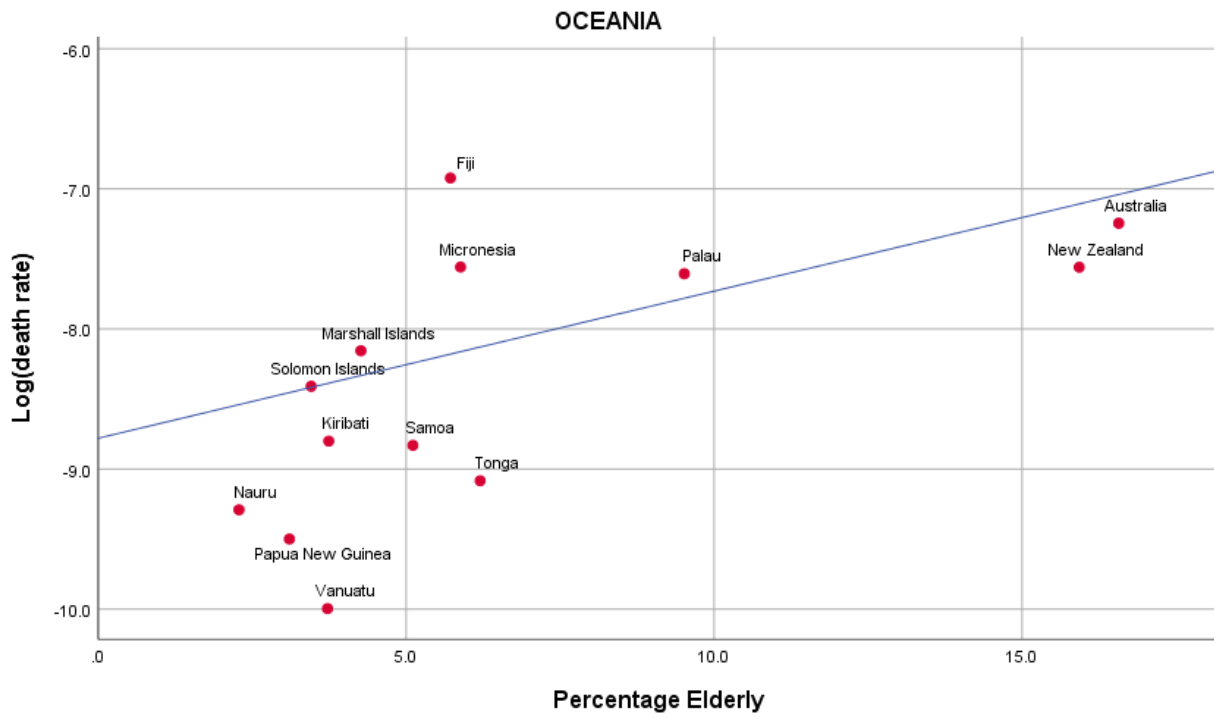


Figure 5K

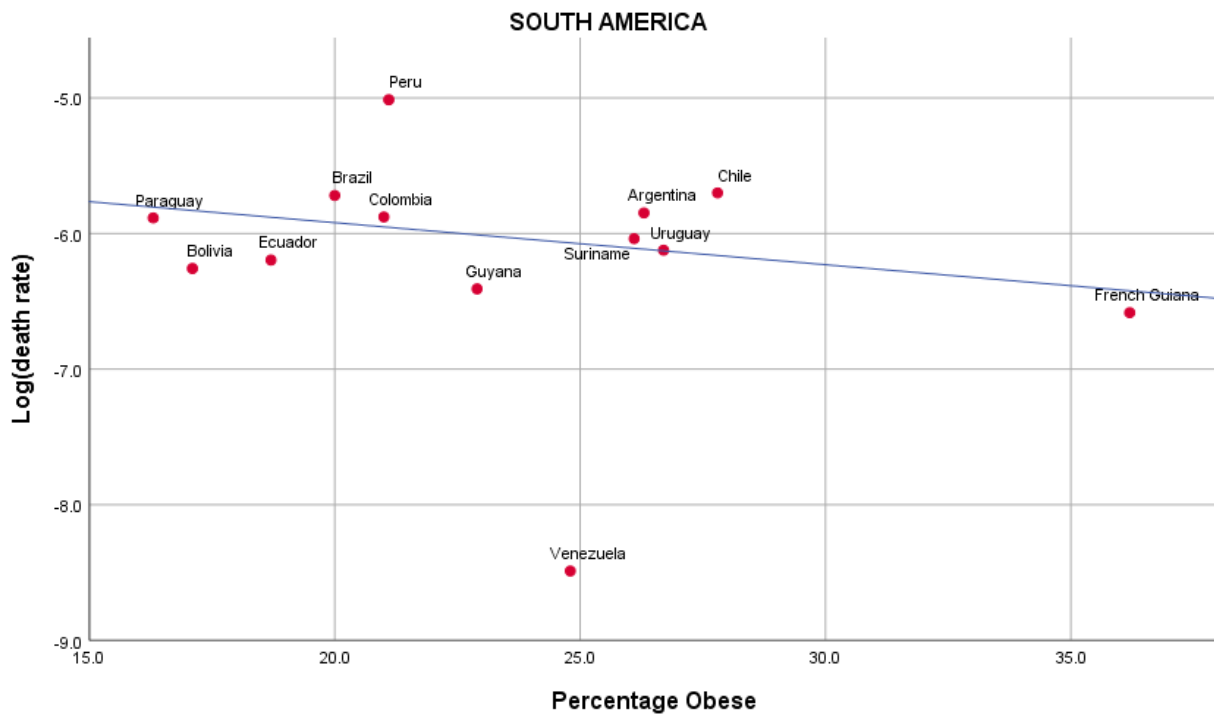


Figure 5L

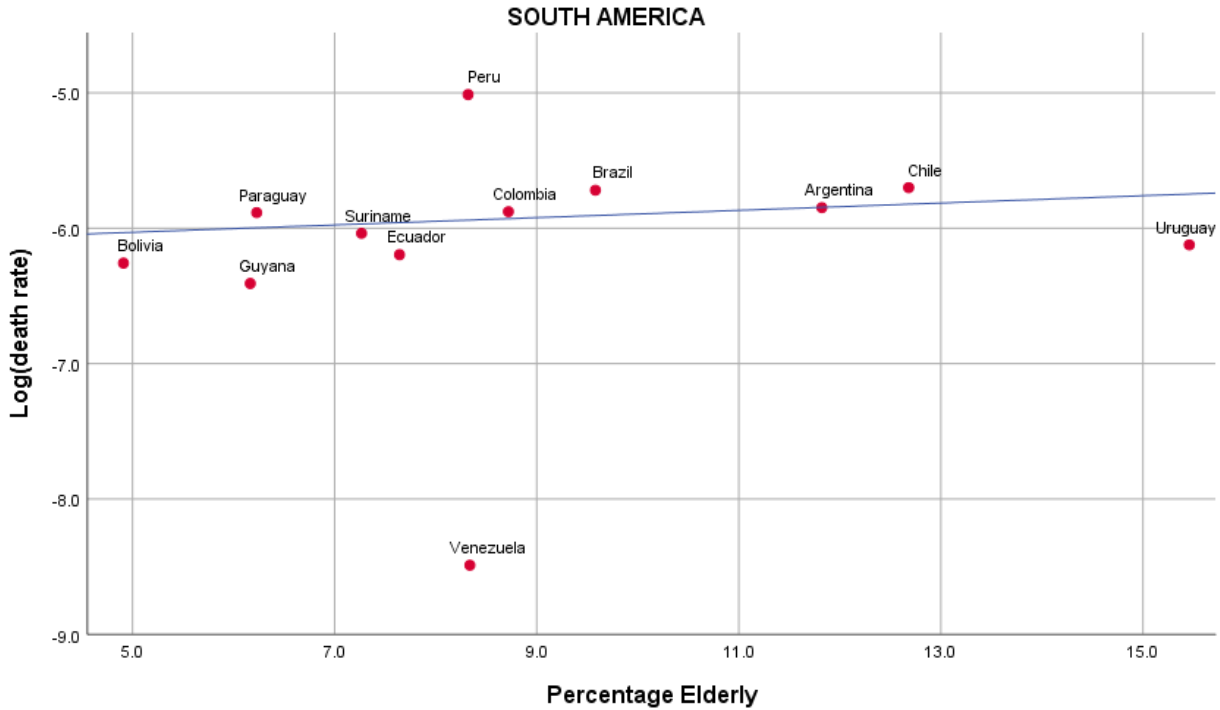


Figure 5. Population percentages of obesity and elderly vs. COVID-19 mortality rates, by region. In each region, annotations of the individual countries are given, as well as the best fitting negative binomial regression line, which is linear on a log scale.

Figure 6A

OBESITY VS COVID-19 MORTALITY

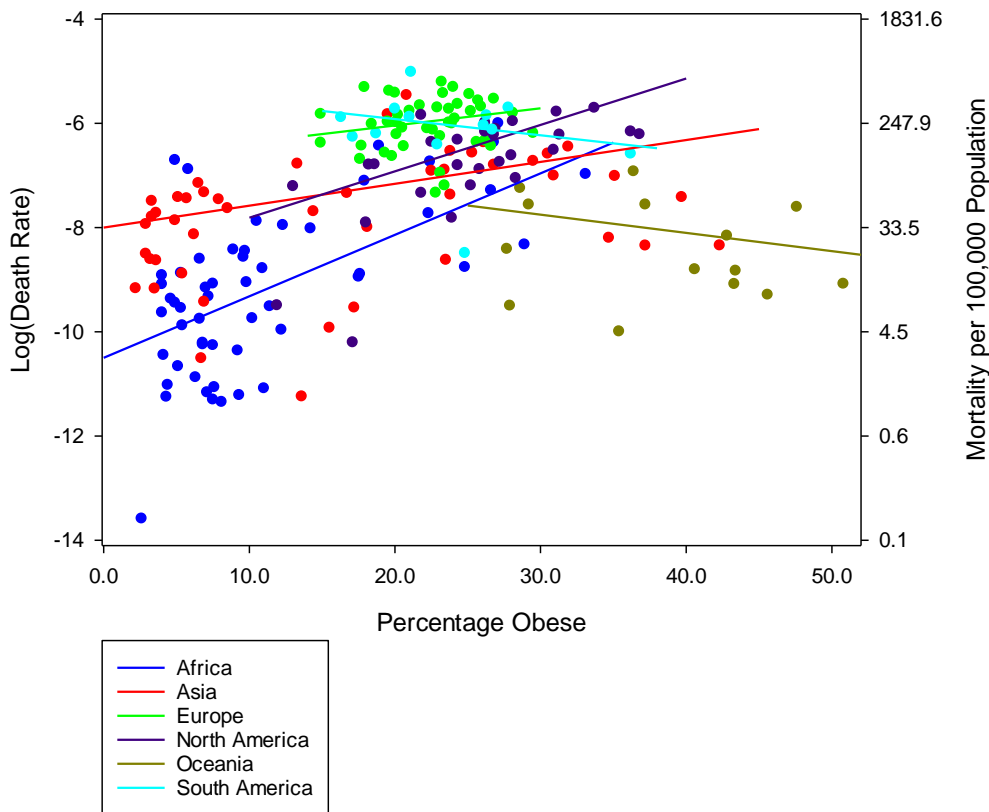


Figure 6B

ELDERLY VS COVID-19 MORTALITY

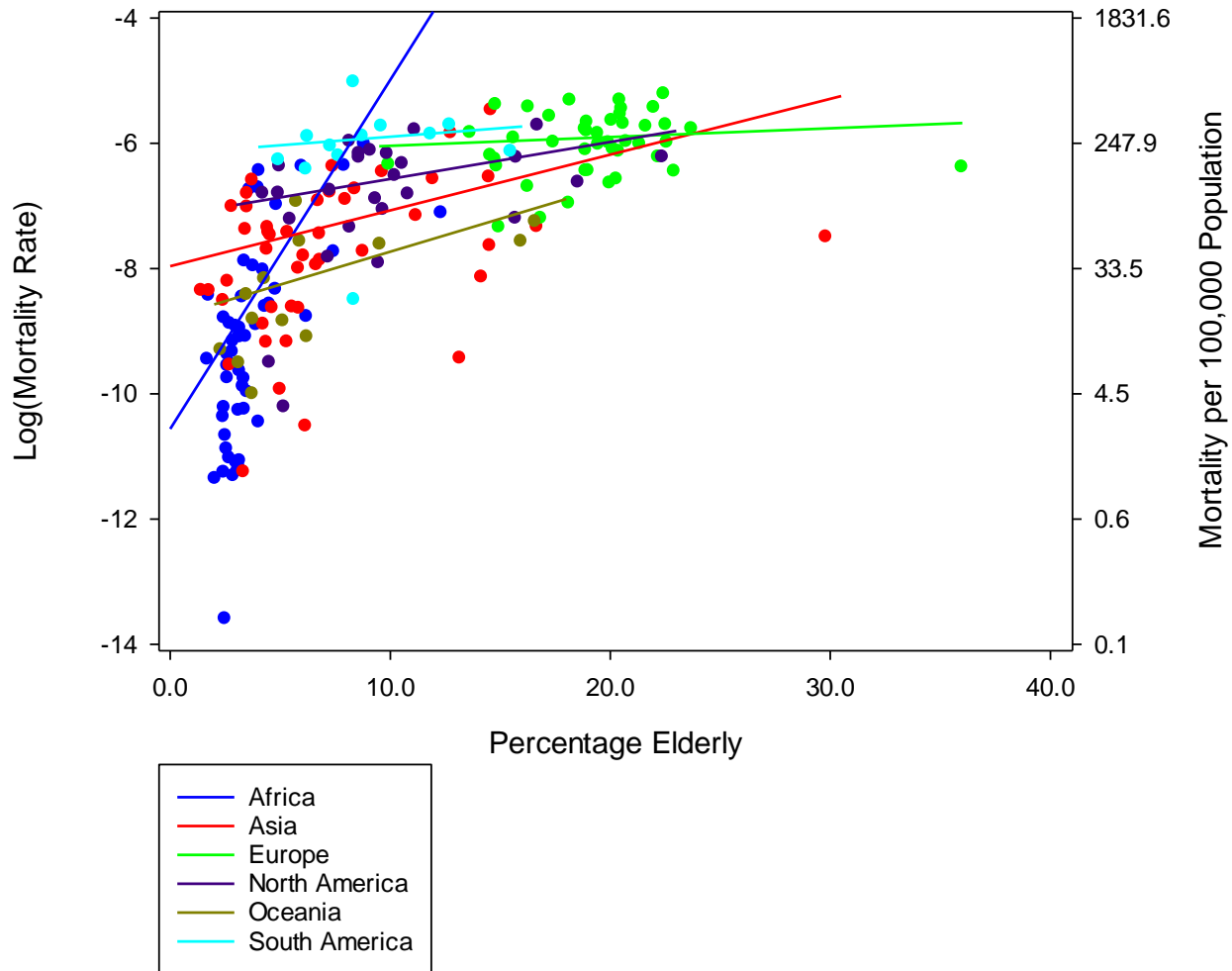


Figure 6. Overall display of percentages of (A) obesity and (B) elderly vs. COVID-19 mortality rates. The regions are color-coded, so that the individual countries as well as the best fitting negative binomial regression lines (both from Figure 5) can be identified. Unlike Figure 5, the scaling along the y-axis (COVID-19 mortality rates) is invariant, so as to afford immediate comparison of countries and regions. As in Figure 5, the left-hand y-axis displays the mortality rates on a log scale. The right-hand y-axis here displays the mortality rates on a conventional scale of deaths per 100,000 population.

Overall, Africa has lower prevalences of obesity and elderly than the other regions. But the prevalences are not homogeneous across the continent: the countries in northern and southern Africa have higher prevalences than the remainder of the continent. This is mirrored in COVID-19 mortality rates, and the significant increase in mortality with increasing prevalence of obesity or elderly is driven by this fact. The markedly low rates of COVID-19 mortality in the interior may well reflect low prevalences of obesity and elderly, but there may be other contributing factors. Pre-existing immunity to other diseases such as malaria might confer some protection against COVID-19.

Environmental factors might also play a role: the hot climate in Africa may be less conducive to the spread of an airborne virus than colder and drier environments. Interestingly, the uptake of COVID-19 vaccines in Africa has been relatively low, due to such factors as limited vaccine access and delivery infrastructure or vaccine hesitancy. On the other hand, it is possible that COVID-19 mortality in Africa has been underestimated, due to limited testing and reporting capabilities, especially in areas with relatively weak health care systems. Also, racial or ethnic differences between northern Africa and the remainder of the continent may play

a contributory role in the observed differences in the obesity and mortality metrics.

In contrast to the north-south geographic demarcation in Africa relative to obesity, elderly, and COVID-19 mortality, the geographic demarcation in Asia is an east-west differential: obesity and COVID-19 mortality are more prevalent in the west, whereas the eastern Asian countries have higher prevalences of the elderly (especially, Japan) and lower prevalences of obesity (perhaps in part a racial or ethnic divide). The countries of eastern Asia tend to have strong and robust healthcare systems with near-universal coverage and timely responses to health care emergencies. Governments imposed strict public health measures, such as widespread testing and contact tracing, and masking, social distancing and quarantine protocols. Also important are cultural norms relating to collective social responsibility leading to widespread acceptance and adherence to governmental public health directives.

Along with the United States, Europe might be considered the epicenter of the COVID-19 pandemic. Mortality rates are quite high across the continent, and the risk factors of obesity and an elderly population are prevalent. Population density might be another factor contributing to rapid virus spread. On the other hand, one might expect that the rapid individual government responses to the pandemic, and the modern healthcare systems available to the populace, would have mitigated the effects of the pandemic.

Haiti and Nicaragua might be considered outliers among the countries of North America given their impressively low mortality rates from COVID-19. Their low proportions of obesity and elderly are important mitigating factors, though these proportions are not exceptional in the region. Here, a comparison of Canada with the United States comparison is instructive: obesity is less prevalent in Canada than the United States, counterbalanced by a slightly greater percentage of the elderly. Canada's lower COVID-19 mortality rate than the US might well be due to other key factors: a more coordinated and consistent public health response to the pandemic together with greater compliance to public health directives; a government funded healthcare system that provides near universal coverage to the populace; and, lower population density.

Oceania has a high prevalence of obesity, but relatively low percentages of the elderly, and low COVID-19 mortality. The geographic isolation of

the Pacific island nations, as well as strict travel restrictions imposed in Australia and New Zealand early in the pandemic, effectively tamped down COVID-19 exposure and ultimately mortality. In addition, there may well be genetic factors contributing to the high obesity rates observed in the island nations.

The countries of South America are relatively homogeneous relative to obesity and elderly profiles, yet exhibit extreme contrasts in COVID-19 mortality. On the continent, Peru has experienced the largest COVID-19 mortality rate, and Venezuela the smallest. In this regard, note that obesity is more prevalent in Venezuela than Peru, and the elderly proportions are relatively similar. One might attribute high COVID-19 mortality to inadequate health care, but it is difficult to ascribe this circumstance solely to Peru. Perhaps high population density has played a contributory role in the spread of the virus in the urban centers of Peru and other South American cities.

It is clear from Figure 6 that overall, COVID-19 mortality rates do tend to increase with increasing prevalence of obesity or elderly populations, on a country basis. Although one might interpret this as affirmation of the orthodoxy, this overall view masks or obscures interregional differences in both risk factors and mortality, as well as intraregional differences (Figure 5). Do the exceptions prove the rule? The most glaring exception is probably Oceania, with high levels of obesity yet low COVID-19 mortality, though the low mortality rate is not altogether surprising. Some extreme country-to-country differences in mortality, e.g., Peru vs. Venezuela, might raise questions: in these cases, we might parse the differences on a finer scale, by delving into regional differences within the individual countries, as we have previously done within the United States²³. Regardless, there are a handful of countries for which reported COVID-19 mortality rates appear preternaturally low. A pronouncement on a global scale that obesity or elderly status constitute definitive risk factors for COVID-19 mortality overlooks the subtleties engendered by inter- and intraregional differences.

We recognize that our findings are far from conclusive, and are subject to various limitations. With this observational study, we are reporting associations of obesity and elderly with mortality; but stronger associations would perhaps have been obtained if the available mortality data had included detailed demographic information on an individual basis, including co-morbidities. One might

also question the accuracy and comprehensiveness of some of the mortality data, especially when arising from countries with weak public health reporting practices and networks. The negative binomial model we have used (or a Poisson model) is entirely appropriate with mortality data, and linearity of rates on a log scale is a commonly accepted metric by public health representatives; nevertheless, our analyses are not at all exhaustive, and monotonicity of rates with quantitative increases of risk factors might be more apparent under suitable transformations or other alternative analytic methodology. On the other hand, we believe our findings are informative and of practical significance, as they provide germane insights into regions' variabilities in the obesity and elderly characteristics of their populations, and concomitantly in their COVID-19 mortality rates.

Conclusions. There are significant differences both between regions and within regions relative to

COVID-19 mortality rates, as well as proportions of obese or elderly individuals. A global pronouncement that obesity and elderly constitute definitive risk factors for COVID-19 mortality masks the subtleties engendered by these intra- and inter-regional differences.

Authors' Contributions

The authors contributed equally to the conception, design, analysis, and drafting of the manuscript.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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