How many are at increased risk of severe COVID-19 disease? Global, regional and national estimates for 2020

Andrew Clark[1], Mark Jit,[2] Charlotte Warren-Gash,[3] Bruce Guthrie,[4] Harry HX Wang,[5] Stewart W Mercer,[4] Colin Sanderson,[1] Martin McKee,[1] Christopher Troeger,[6] Kanyin I Ong,[6] Francesco Checchi,[2] Pablo Perel,[3] Sarah Joseph,[7] Hamish P Gibbs,[2] Amitava Banerjee[8], CMMID COVID-19 working group,[9] Rosalind M Eggo[2]

[1]Department of Health Services Research and Policy, London School of Hygiene & Tropical Medicine, Tavistock Place, WC1H 9SH

[2]Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, Keppel Street, WC1E 7HT

[3]Department of Non-Communicable Disease Epidemiology, London School of Hygiene & Tropical Medicine, Keppel Street, WC1E 7HT

[4]Centre for Population Health Sciences, Usher Institute, University of Edinburgh, Old Medical School, Teviot Place, EH8 9AG

[5]School of Public Health, Sun Yat-Sen University, Guangzhou, 510080, PR China

[6]University of Washington, Seattle WA, USA

[7]IAVI Human Immunology Laboratory, Imperial College London

[8]Institute of Health Informatics, University College London, London

[9]Centre for Mathematical Modelling of Infectious Diseases, London School of Hygiene & Tropical Medicine, Keppel Street. WC1E 7HT UK

The LSHTM CMMID COVID-19 working group is (ordered randomly): Emily S Nightingale, Kathleen O'Reilly, Thibaut Jombart, W John Edmunds, Alicia Rosello, Fiona Yueqian Sun, Katherine E. Atkins, Nikos I Bosse, Samuel Clifford, Timothy W Russell, Arminder K Deol, Yang Liu, Simon R Procter, Quentin J Leclerc, Graham Medley, Gwen Knight, James D Munday, Adam J Kucharski, Carl A B Pearson, Petra Klepac, Kiesha Prem, Rein M G J Houben, Akira Endo, Stefan Flasche, Nicholas G. Davies, Charlie Diamond, Kevin van Zandvoort, Sebastian Funk, Megan Auzenbergs, Eleanor M Rees, Damien C Tully, Jon C Emery, Billy J Quilty, Sam Abbott, Julian Villabona-Arenas, Stéphane Hué, Joel Hellewell, Amy Gimma, Christopher I Jarvis

Correspondence to: andrew.clark@lshtm.ac.uk

Competing Interest Statement

The authors have declared no competing interest.

Funding Statement

We acknowledge the following for funding:

MM: Research Director of the European Observatory on Health Systems and Policies, a partnership of universities, international agencies, universities and foundations. RME: HDR UK (grant: MR/S003975/1), MRC (grant: MC_PC 19065); HPG: This research is funded by the Department of Health and Social Care using UK Aid funding and is managed by the NIHR. The views expressed in this publication are those of the author(s) and not necessarily those of the Department of Health and SocialCare (grant code: ITCRZ 03010); CWG: Wellcome Intermediate Clinical Fellowship (201440_Z_16_Z).

Background

The risk of severe COVID-19 disease is known to be higher in older individuals and those with underlying health conditions. Understanding the number of individuals at increased risk of severe COVID-19 illness, and how this varies between countries may inform the design of possible strategies to shield (or vaccinate) those at highest risk.

Methods

We estimated the number of individuals at increased risk (those with at least one condition listed as 'at increased risk of severe COVID-19 disease' in current guidelines) by age (5-year age groups), sex and country (n=188) based on prevalence data from the Global Burden of Disease (GBD) study for 2017 and United Nations population estimates for 2020. We also calculated the number of individuals without an underlying condition that could be considered at increased risk because of their age, using minimum ages from 50 to 70 years. The list of underlying conditions relevant to COVID-19 disease was determined by mapping across from the conditions listed in GBD to the guidelines published by WHO and public health agencies in the UK and US. We analysed data from two large multimorbidity studies to determine appropriate adjustment factors for clustering and multimorbidity. To help interpretation of the degree of risk among those at increased risk, we estimated the number of individuals at high risk (those that would require hospital admission if infected) using age-specific infection hospitalisation ratios (IHRs) recently estimated for mainland China. IHRs were adjusted to each country to account for differences in age-specific life expectancy and underlying health conditions.

Results

We estimate that 1.7 (1.0 - 2.4) billion individuals (22% [15-28%] of the global population) are at increased risk of severe COVID-19 disease, and that 350 (187-785) million (5% [3-9%] are at high risk. The share of the population at increased risk was highest in countries with older age populations, African countries with high HIV/AIDS prevalence and small island nations with high diabetes prevalence. The number of individuals at increased risk was most sensitive to the prevalence of chronic kidney disease (CKD), diabetes, cardiovascular disease (CVD) and chronic respiratory disease (CRD).

Conclusion

We estimate that one in five individuals worldwide is at increased risk of severe COVID-19 disease, and one in 22 is at high risk, but this varies considerably by age, sex and country. Our estimates have substantial uncertainty but provide a useful starting point for considering the numbers that may need to be shielded (or vaccinated) as the global pandemic unfolds.

Research in context

Evidence before this study

As the COVID-19 pandemic evolves, countries are considering policies of 'shielding' the most vulnerable, but there is currently very limited evidence on the number of individuals that might need to be shielded. Guidelines on who is currently believed to be at increased risk of severe COVID-19 illness have been published online by the WHO and public health agencies in the UK and US. We searched PubMed ("Risk factors" AND "COVID-19") without language restrictions, from database inception until April 5, 2020, and identified 62 studies published between Feb 15, 2020 and March 20, 2020. Evidence from China, Italy and the USA indicates that older individuals, males and those with underlying conditions, such as CVD, diabetes and CRD, are at greater risk of severe COVID-19 illness and death.

Added value of this study

This study combines evidence from large international databases and new analysis of large multimorbidity studies to inform policymakers about the number of individuals that may be at increased risk and at high risk of severe COVID-19 illness in different countries. We developed a tool for rapid assessments of the number and percentage of country populations that would need to be targeted under different shielding policies.

Implications of all the available evidence

Quantifying how many and who is at increased risk of severe COVID-19 illness is critical to help countries design more effective interventions to protect vulnerable individuals and reduce pressure on health systems. This information can also inform a broader assessment of the health, social and economic implications of shielding various groups.

Introduction

Emerging evidence from China, Europe and the USA has shown a consistently higher risk of severe COVID-19 disease in older individuals and those with underlying health conditions.[1-3] Severe disease is defined by WHO as "a patient with severe acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath; AND requiring hospitalization)"..[4,5] In a recent report from the USA, underlying conditions were reported in 71% (732/1037) of individuals hospitalised with COVID-19 and 94% (173/184) of deaths.[1] The World Health Organization (WHO) as well as public health agencies in countries including the UK and US, have issued guidelines on who is considered to be at increased risk of severe COVID-19 illness.[6-8] This includes individuals with cardiovascular disease (CVD), chronic kidney disease (CKD), diabetes, chronic respiratory disease (CRD) and a range of other chronic conditions. Such conditions increase the risk of needing hospital-based treatment such as oxygen supplementation or mechanical ventilation. A large proportion of the additional health care burden of COVID-19 epidemics is likely to result from infection of those with underlying conditions.

Identifying at-risk populations is important not only for making projections of the likely health burden in countries,[9,10] but also for the design of effective strategies that aim to reduce the risk of transmission to people in target groups. This is sometimes termed shielding, defined as "a measure to protect extremely vulnerable people by minimising interaction between those who are extremely vulnerable and others."[11] It has the potential to reduce mortality in vulnerable groups (direct benefits), while at the same time mitigating the expected surge in demand for hospital beds (indirect benefits).. However, trying to shield an excessive proportion of a population may strain country resources and reduce the overall effectiveness of shielding. A detailed assessment of the number of at-risk individuals can inform possible shielding strategies. If a vaccine becomes available in the future, it could also be used to inform the process of prioritising different groups, based on risk.

The aim of this analysis is to provide global, regional and national estimates of the numbers of individuals at increased risk of severe COVID-19 disease by virtue of their underlying medical conditions during 2020. The risk of severe COVID-19 disease is not binary, but unless tiered approaches are adopted, the criterion for whom to shield is, so our estimates seek to capture all those 'at increased risk' (UK terminology) or 'at higher risk' (US terminology) based on current guidelines.

Methods

Prevalence of underlying health conditions

We used the list of conditions thought to increase the risk of severe COVID-19 illness, based on current guidelines from WHO and public health agencies in the UK and US [6-8] and mapped these to eleven categories of underlying health conditions in the Global Burden of Disease Study (GBD) (supplementary appendix, p 1). The mapping was completed by a clinical epidemiologist (CWG). Prevalence estimates were extracted for the following disease categories by age, sex and country: (1) CVD, including CVD caused by hypertension; (2) CKD, including CKD caused by hypertension; (3) CRD; (4) chronic liver disease; (5) diabetes; (6) cancers with direct

immunosuppression; (7) cancers without direct immunosuppression, but with possible immunosuppression caused by treatment; (8) HIV/AIDS; (9) tuberculosis; (10) chronic neurological disorders; and (11) sickle cell disorders.

We estimate the current number of individuals with underlying conditions making them at risk of severe COVID-19 disease by age (5-year age groups), sex and country for 188 countries. Data on the prevalence of underlying conditions were extracted by age, sex and country from the GBD study for 2017[12] and combined with United Nations mid-year population estimates for 2020.[13] For this analysis, older individuals without underlying conditions were not considered to be at increased risk.

Asthma is relatively common, and mild asthma is not listed as a high risk group for shielding so we modified GBD estimates of asthma to account only for moderate-to-severe cases (defined as British Thoracic Society Steps 4, 5 and 6).[14] Based on published evidence from the UK we assumed these were 15% of total asthma cases aged <5 years, 17% aged 5-19 years, 23% aged 20-54 years, and 43% in those aged 55+ years.[15]

For HIV/AIDS, we included all populations, including those on ART. However, we carried out a sensitivity analysis to determine how estimates would change if we removed individuals using anti-retroviral therapy (ART) for instance if there is found to be no additional risk of HIV in individuals on ART. We used WHO national estimates for ART coverage among those living with HIV/AIDS.[16]

Proportion with at least one underlying condition relevant to severe COVID-19 disease

The GBD study provides prevalence estimates for each disease category separately, but not what we needed, which was the prevalence of people in at least 1 of these categories. Diseases may cluster, for example if they are causally related. To deal with this, we first calculated e, which is the expected proportion of individuals with at least one condition assuming no clustering and that various prevalences are independent (e.g. the fact that someone has diabetes does not affect their risk of getting cancer) as 1 minus the probability of not having any of the conditions c1, c2, c3….i.e. 1 – (1 – p_c1) x (1 – p_c2) x (1 – p_c3)….

We then estimated the proportion P, who have at least one underlying condition as $P = e \times r$, where r is the ratio between the observed and expected percentage of individuals with at least one condition. We based r on evidence from large cross-sectional multimorbidity studies in Scotland[17] and Southern China[18] (supplementary appendix p 2-3).

Adjustment for multimorbidity

In addition to providing estimates for r, the studies in Scotland and Southern China were used to calculate the multimorbidity fraction i.e. the proportion of individuals with multiple (two or more) underlying conditions among those with at least one, by age group and sex. All analyses were done using disease categories that matched as closely as possible to the COVID-19-relevant categories defined in our analysis. In both studies this included: CVD (defined as the presence of one or more of coronary heart disease, hypertension, cerebrovascular disease, peripheral arterial disease, heart failure, or atrial fibrillation); chronic neurological disease (defined as one or more of

dementia, multiple sclerosis and Parkinson's disease); and CRD (defined as one or both of chronic obstructive pulmonary disease and bronchiectasis). Other COVID-related conditions listed above were counted separately. The GBD provide separate estimates for hypertensive heart disease and CKD due to hypertension, but it was not possible to make this distinction in the multimorbidity datasets, so all hypertension was included in the CVD category.

Using the data from both studies, we calculated pooled estimates of the ratio r, and the multimorbidity fraction by age and sex (supplementary appendix p 2-3) and extrapolated these pooled estimates to all countries included in the analysis.

Inclusion of older individuals without underlying conditions

Some countries have also considered older age as proxy for frailty and increased risk of severe COVID-19 illness. Although frailty correlates much more closely with mortality than chronological age, there is a well-established non-linear association between increasing age and frailty.[19] We therefore calculated the number of individuals without an underlying condition that could be considered at-risk because of their age, using age thresholds ranging from 50-70 years. All age thresholds were evaluated in all regions. To calculate the total number at increased risk for different age thresholds, we added the number of older individuals without underlying conditions to our earlier estimates of the number of individuals with at least one underlying condition.

Estimating individuals at high risk

To help interpretation of the degree of risk among those at increased risk, we estimated the number of individuals at high risk (those that would require hospital admission if infected) using age-specific infection hospitalisation ratios (IHRs) recently estimated for mainland China by Verity *et al*.[20] Two adjustments were made to generate more realistic IHRs for each country (supplementary appendix p. 4). First, for each 5-year age group we divided the life expectancy in China by the life-expectancy in the country of interest, and then multiplied this ratio (adjustment for age-based frailty) by the IHR for the same age group. Second, the prevalence of each underlying condition was multiplied by its associated odds ratio (OR) for hospital admission, assuming OR=5.0 for higher risk conditions (CKD, diabetes, CVD) and OR=3.0 for all other conditions. The totals were then summed across all 11 conditions to create a risk score for each 5-year age group. The risk score for the country of interest was divided by the risk score for China, and this ratio (adjustment for underlying conditions) multiplied by the IHR for the same age group. The ORs were informed by a rapid review of what is currently known about the strength of association between different variables and COVID-19 hospital admission (supplementary appendix p. 5-7). The two adjustments and OR values were varied in sensitivity analysis (supplementary appendix p. 8-9).

Several studies have reported a higher representation of males among COVID-19 cases that were admitted to hospital so we assumed males represented 65% of all those at high risk (supplementary appendix p 6) and assumed this ratio for all age groups.[21]

Uncertainty

For estimates of numbers at increased risk, we generated low and high estimates using the lower and upper 95% confidence limits for the country population size, individual disease prevalences and age-specific multimorbidity fraction. We also varied r, the ratio between the observed and expected percentage of individuals with at least one condition, by a range informed by the multimorbidity studies. We ran a jackknife analysis to show the influence on the results by excluding each of the underlying conditions, one at a time.

For estimates of number at high risk, we generated low and high estimates using the low and high credible interval values of the IHRs reported in Verity *et al.* We also ran several scenarios to assess the influence of our country-specific adjustments for age-based frailty and underlying conditions, and the ORs associated with each condition (supplementary appendix p 8).

All analyses are provided in an Excel spreadsheet, available at https://cmmid.github.io/topics/covid19/.

Results

Individuals with at least one underlying condition at risk of severe COVID-19 disease

We estimate that 1.7 billion (1.0 - 2.4) individuals (22% [15-28%] of the global population) have at least one underlying condition that could increase their risk of severe COVID-19 disease (tables 1 and 2, supplementary appendix p 10-11). This value does not include older individuals without underlying conditions. The prevalence of one or more condition was approximately 10% by age 25 years, 33% by 50 years, and 66% by 70 years, and similar for males and females (figure 1). The most prevalent conditions in those aged 50+ years were CKD, CVD, CRD and diabetes. These were also the most influential conditions when conditions were removed from the analysis, one at time (supplementary appendix, p 12).

Based on crude proportions without age-standardisation, the share of the population at-risk ranged from 16% in Africa to 31% in Europe (table 1)(figures 2,3 and 4). The share of the population at increased risk was highest in countries with older age populations, African countries with high HIV/AIDS prevalence and small island nations with high diabetes prevalence.

In African countries with high HIV prevalence excluding those on ART reduced the at-risk proportion e.g. from 27 to 20% in Botswana, 30 to 24% in Lesotho, 27 to 23% in South Africa and 29 to 19% in Swaziland.

We estimate that 23% of the global working age population (15-64 years) have at least one underlying condition, with low and high estimates of 15 and 29%. . CKD and diabetes were the most common conditions in this age range.

Individuals with multiple conditions associated with severe COVID-19 disease

Among the 1.7 billion individuals estimated to be at increased risk, we estimate that 0.4 billion (0.2 – 0.7) individuals (6% [3-8%] of the global population) are living with two or more conditions relevant to COVID-19 outcomes in the year 2020 (table 1, supplementary appendix p 10-11, figures 2, 3 and 4). As expected, this proportion was higher in regions with an older age

profile. The prevalence of multimorbidity (two or more underlying conditions) was three times higher in Europe than in Africa (10% vs 3%) (table 1).

Inclusion of older individuals without underlying conditions

The number of individuals without an underlying condition that could be considered at-risk solely because of their age varied by region and choice of age threshold (table 1). In Africa, around 5% of individuals aged 50+ years are estimated to have no underlying conditions linked to severe COVID-19 disease. A similar proportion is estimated at age 65+ years in Europe, North America and Oceania, and at 60+ years in Asia and Latin America.

Estimating individuals at high risk

We estimate that 350 (187-785) million (5% [3-9%] of the global population) are at high risk of severe COVID-19 disease and would require hospital admission if infected (table 2, Figures 2 and 3). The percentage of each age group at high risk ranged for one in every 6 individuals aged 70+ years, to one in every 650 individuals aged <20 years (table 2).

Adjustments for age-based frailty and underlying conditions were influential. For example, in Africa, the share of the population at high risk was 2.2% (30 million) without adjustment, 2.7% (36 million) with adjustment for age-based frailty and 3.3% (44 million) with adjustment for both age-based frailty and underlying conditions. Also, the share of the population at high risk increased from 3.3% (44 million) to 3.8% (50 million) when the OR for HIV was increased from 3.0 to 10.0 (supplementary appendix, p 8).

Discussion

We calculate that one in every five individuals worldwide has a condition that is on the list of those at increased risk of severe COVID-19 disease, and one in 22 is at high risk (would require hospital admission if infected). However, there was considerable variation in these estimates by age, sex and country. Our estimates have substantial uncertainty but provide a useful starting point for considering the numbers that may need to be shielded (or vaccinated) as the global pandemic unfolds.

Recent estimates from the United Nations Economic Commission for Africa suggest that an unmitigated pandemic could lead to a substantial proportion of the African continent being infected and 23 million severe cases of COVID-19 disease requiring hospitalisation.[22] Our estimates for Africa, based on the same IHRs estimated for mainland China by Verity *et al*[20], were higher (44 versus 23 million) reflecting important adjustments for age-based frailty and underlying conditions. However, even after these adjustments, the share of the total population at high risk is still lower in Africa than in Europe (3% vs 6%). This is driven by the younger age of the population and the strength of association between age and COVID-19 severity. This evidence will need to be carefully communicated to policy makers to avoid complacency about the risk in Africa, where a high proportion of severe cases are likely to be fatal. If a safe and effective vaccine is produced, then our estimates provide an indication of the volumes that would be required for vaccination of at-risk individuals globally. In the absence of a vaccine, a key option to mitigate the pandemic is to shield at-risk individuals by more intensive physical-distancing measures than

those in the wider population. This may be especially important at times and places where health systems risk being overwhelmed by cases. Other infection control measures include provision of personal protective equipment and intensive testing of health and social care workers in maximum contact with at-risk individuals. At a minimum, timely and effective communication should be provided to communities on who within them is at increased risk. Among those who are identified, governments will rely heavily on their adherence to guidelines. This would allow practical individual-level steps to be taken, such as increased hygiene, physical isolation and home-delivered food and medical care.[6] As more evidence emerges on the risk associated with different conditions, guidelines could be refined and shielding policies tailored to different risk groups e.g. isolation for those at high risk, and less stringent measures (e.g. social distancing) for those with a lower level of increased risk. Community-level shielding approaches, including vacating houses or public buildings to physically isolate small groups of people at increased risk, may also be considered, though these will require stringent infection control arrangements, especially in crowded settings,[23] and adherence may be low if at-risk individuals are daily wage earners or people caring for children e.g. grandparents.[24]

The association between the prevalence of underlying conditions and other national characteristics, such as economic development, is complex. The prevalence of many of these conditions (HIV/AIDS may be an exception) reflect the epidemiological transition[25] but survival with these conditions may reflect the performance of the health system.[26] Hence, it is important to look at the data for each country, which goes beyond what we can report in this paper. We provide a spreadsheet tool (available at https://cmmid.github.io/topics/covid19/) that can be used for rapid assessment (and visualisation) of the estimated number and percentage of country populations targeted under different shielding policies. This allows different health conditions to be included/excluded, different age thresholds to be assessed, and different choices about key assumptions e.g. estimates of the ratio r, and the multimorbidity fraction by age. Prevalence data included in our spreadsheet can be updated as more evidence emerges on the importance (or otherwise) of specific conditions and their severities e.g. early stage CKD, simple hypertension etc.

Our analysis found that around one in five individuals in the working age range had at least one underlying condition relevant to COVID-19 severity. Strict shielding measures could cause considerable economic disruption to these individuals and their families and have a detrimental effect on the wider economy. For some at-risk individuals, particularly daily wage earners in low-income countries, it will be important to have alternative options to isolation. For example, there is growing evidence in support of face-masks as a means to prevent transmission by those wearing them.[27] If proven to be effective, or other measures emerge,[28] this could be a practical way of reducing exposure among those who are unable to avoid contact with others. Alternative shielding approaches, so that target groups are supported to reduce physical contacts (e.g. through incentives to reduce or abstain from work), can also be considered.

We based our analysis on underlying conditions listed in guidelines published by the WHO and public health agencies in the UK and US. As with seasonal influenza vaccination, these guidelines tend not to be exhaustive, and deliberately permit clinical judgement. As our understanding of this disease evolves, it should be possible to provide greater clarity on the risk of severe COVID - 19 disease associated with different underlying conditions at different severities e.g. early stage

CKD, compensated liver cirrhosis, moderately severe asthma etc.[6] A detailed multivariate analysis of risk is urgently needed because nearly all underlying conditions are likely to be at least partly confounded by age. Knowledge of the mode of action of the virus is increasing rapidly, especially in relation to its action on cells with ACE2 receptors other than in the lung, in particular in the endothelium and pancreas, which the inflammatory processes associated with diabetes may be involved in cytokine storms that can be fatal.[29]

We estimated a similar number of males and females to be at increased risk but assumed that 65% of those at high risk would be male. This is consistent with an increasing role of male gender as the severity of COVID-19 increases.[30] Earlier research in mice infected with SARS coronavirus also found an increased male susceptibility mediated by differences in oestrogen receptor signalling,[31] while others have noted the concentration of genes involved in the immune system on the x chromosome.[32] This is a clearly priority for further research.

Our estimates of the number of individuals at high risk included adjustments for the prevalence and mix of underlying conditions in different countries. This required estimates of the strength of association between each of the 11 underlying conditions and COVID-19 hospital admission. We ran scenarios with different ORs, informed by the few studies that allowed comparison with a control group that was not hospitalised. However, the true strength of association is uncertain and likely to vary across settings. Also, we focused on the list of underlying chronic causes of disease available in GBD2017 and did not include other risk factors. Obesity may be an important omission, but we chose not to selectively include some risk factors and not others e.g. ethnicity, deprivation, smoking, working in the health and social care system, living in care homes and other facilities. Also most do not yet appear in guidelines or have baseline prevalence data available for 188 countries by age (5-years age groups) and sex.

Our estimates of the number at high risk individuals in Africa were sensitive to the OR assumed for HIV/AIDS. It is not yet known whether those with HIV are at increased risk of severe disease with COVID-19.[33] Whilst it has been shown that widespread introduction of ART reduced the risk of hospitalisation and death associated with seasonal influenza,[34] a substantial proportion of those on ART remain somewhat immunocompromised.[35,36] Recent evidence from South Africa has shown that individuals living with HIV have an eight-fold higher risk of pneumonia hospitalisation associated with seasonal influenza, and a three-fold higher risk of pneumonia death.[37] Until more evidence emerges, it may be necessary to include these individuals in shielding strategies, irrespective of ART status, with priority given to those not yet receiving treatment.[38]

Our estimates of the numbers at-risk are based on prevalence estimates extracted from the GBD. The GBD study produces estimates of disease prevalence for all ages, both sexes, and for 195 territories and countries from 1990-2017.[39] Because the GBD produces internally comparable estimates for a comprehensive list of diseases, these estimates are well suited to compare prevalence of disease across locations. GBD prevalence estimates are likely to be higher than prevalence estimated from national databases because they aim to capture cases that may be undiagnosed or not severe enough to be included in EHRs. For example, over half of the CKD cases included in GBD prevalence estimates represent early stage disease (CKD stage 1 or 2) which is common and rarely has symptoms.[40] Several other underlying conditions estimated by GBD are

also likely to be undiagnosed and not recorded in national databases e.g. hypertensive heart disease, compensated chronic liver disease. In a cross-sectional study in England, more than 20% of diabetes was undiagnosed in all age groups over 25 years,[41] and in the Philippines, the undiagnosed proportion was around 50%.[42] Age thresholds could therefore play a critical role in shielding the large number of older individuals without a diagnosis. Indeed, while our analysis quantifies numbers who could benefit from shielding, in practice the low coverage of diagnosis and treatment for many chronic conditions in low-income settings means that the age threshold could largely determine the effective target group. However, older individuals without these underlying conditions could suffer adverse mental health consequences from long periods of isolation.

A recent analysis from Sweden[43] provides an opportunity to evaluate our method, and compare GBD prevalence estimates to those derived from electronic health record (EHR) data. When we applied our method, based on the calculation of e and r, to the prevalence of each condition reported in the study, we were able to reproduce the same percentage share of the population at increased risk. This provides some reassurance that our method will provide a reasonable approximation of the at-risk proportion if the same input data on disease prevalence is used.

We used data from two large studies to adjust for multimorbidity. Both studies could underestimate the prevalence of some conditions and therefore the extent of multimorbidity, although in Scotland, most of the included conditions were well recorded in routine health care, and in the Southern China study, underlying conditions were well communicated to patients, whose information was collected in a community household survey following a standard protocol. These studies cannot capture the global diversity of patterns of multimorbidity, which will differ in regions where, for example, there are high prevalences of HIV or sickle cell disorders. As multivariate analyses of the risk of serious COVID-19 become available, results that include combinations may provide more nuanced information to inform decisions about shielding.

Over the coming weeks and months, countries will need to determine mitigation strategies for the pandemic. Where feasible, shielding strategies could reduce the overall health burden by decreasing risk of infection to those most likely to experience severe disease and thus require health care. If implemented, shielding of at-risk individuals is likely to be required for several months. This may have a substantial impact on working-age people if they and their household contacts are less economically active for longer than the general population.

There is an urgent need for robust analyses of the risks associated with different underlying conditions so that countries can identify the highest risk groups and develop targeted shielding policies to mitigate the effects of the COVID-19 pandemic.

Table 1. Number of individuals in millions (% of total population) at increased risk of severe COVID-19 illness by age, number of conditions, region and age threshold

	Africa	Asia	Europe	Latin America and the Caribbean	Northern America	Oceania	**Global**
No conditions							
<15 years	519 (39)	1042 (22)	117 (16)	152 (23)	65 (18)	10 (23)	**1905 (24)**
15-49 years	534 (40)	1986 (43)	274 (37)	292 (45)	147 (40)	17 (40)	**3249 (42)**
50-54 years	25 (2)	184 (4)	33 (4)	23 (4)	14 (4)	2 (4)	**281 (4)**
55-59 years	18 (1)	137 (3)	29 (4)	18 (3)	13 (3)	1 (3)	**216 (3)**
60-64 years	12 (1)	96 (2)	23 (3)	13 (2)	10 (3)	1 (2)	**154 (2)**
65-69 years	7 (1)	69 (1)	16 (2)	8 (1)	7 (2)	1 (2)	**108 (1)**
70+ years	7 (0)	74 (2)	23 (3)	10 (2)	9 (2)	1 (2)	**123 (2)**
All ages	1121 (84)	3588 (77)	516 (69)	515 (79)	264 (72)	32 (76)	**6036 (78)**
One condition only							
<15 years	20 (1)	44 (1)	3 (0)	4 (1)	2 (0)	0 (1)	**72 (1)**
15-49 years	101 (8)	369 (8)	49 (7)	45 (7)	20 (5)	3 (7)	**588 (8)**
50-54 years	14 (1)	83 (2)	14 (2)	10 (2)	7 (2)	1 (1)	**128 (2)**
55-59 years	12 (1)	78 (2)	17 (2)	10 (2)	8 (2)	1 (2)	**127 (2)**
60-64 years	11 (1)	69 (1)	18 (2)	10 (1)	9 (3)	1 (2)	**118 (2)**
65-69 years	8 (1)	62 (1)	18 (2)	8 (1)	9 (2)	1 (2)	**105 (1)**
70+ years	11 (1)	93 (2)	40 (5)	15 (2)	17 (5)	1 (3)	**178 (2)**
All ages	178 (13)	797 (17)	159 (21)	103 (16)	72 (20)	7 (17)	**1316 (17)**
Multiple (two or more) conditions							
<15 years	1 (0)	3 (0)	0 (0)	0 (0)	0 (0)	0 (0)	**4 (0)**
15-49 years	13 (1)	53 (1)	8 (1)	7 (1)	3 (1)	0 (1)	**85 (1)**
50-54 years	4 (0)	23 (0)	4 (1)	3 (0)	2 (0)	0 (0)	**35 (0)**
55-59 years	4 (0)	27 (1)	6 (1)	4 (1)	3 (1)	0 (1)	**44 (1)**
60-64 years	4 (0)	29 (1)	8 (1)	4 (1)	4 (1)	0 (1)	**50 (1)**
65-69 years	4 (0)	33 (1)	9 (1)	4 (1)	5 (1)	0 (1)	**56 (1)**
70+ years	9 (1)	80 (2)	37 (5)	13 (2)	16 (4)	1 (3)	**156 (2)**
All ages	41 (3)	247 (5)	72 (10)	35 (5)	32 (9)	3 (7)	**430 (6)**
At increased risk of severe COVID-19 disease							
At least one condition	218 (16)	1044 (23)	231 (31)	137 (21)	104 (28)	10 (24)	**1746 (22)**
Plus others older than:							
50 years	286 (21)	1605 (35)	356 (48)	209 (32)	157 (43)	16 (37)	**2628 (34)**
55 years	261 (20)	1420 (31)	322 (43)	186 (29)	143 (39)	14 (34)	**2346 (30)**
60 years	244 (18)	1284 (28)	293 (39)	168 (26)	130 (35)	13 (30)	**2130 (27)**
65 years	238 (18)	1199 (26)	288 (39)	160 (25)	131 (35)	12 (29)	**2028 (26)**
70 years	230 (17)	1137 (25)	271 (36)	152 (23)	122 (33)	12 (28)	**1923 (25)**

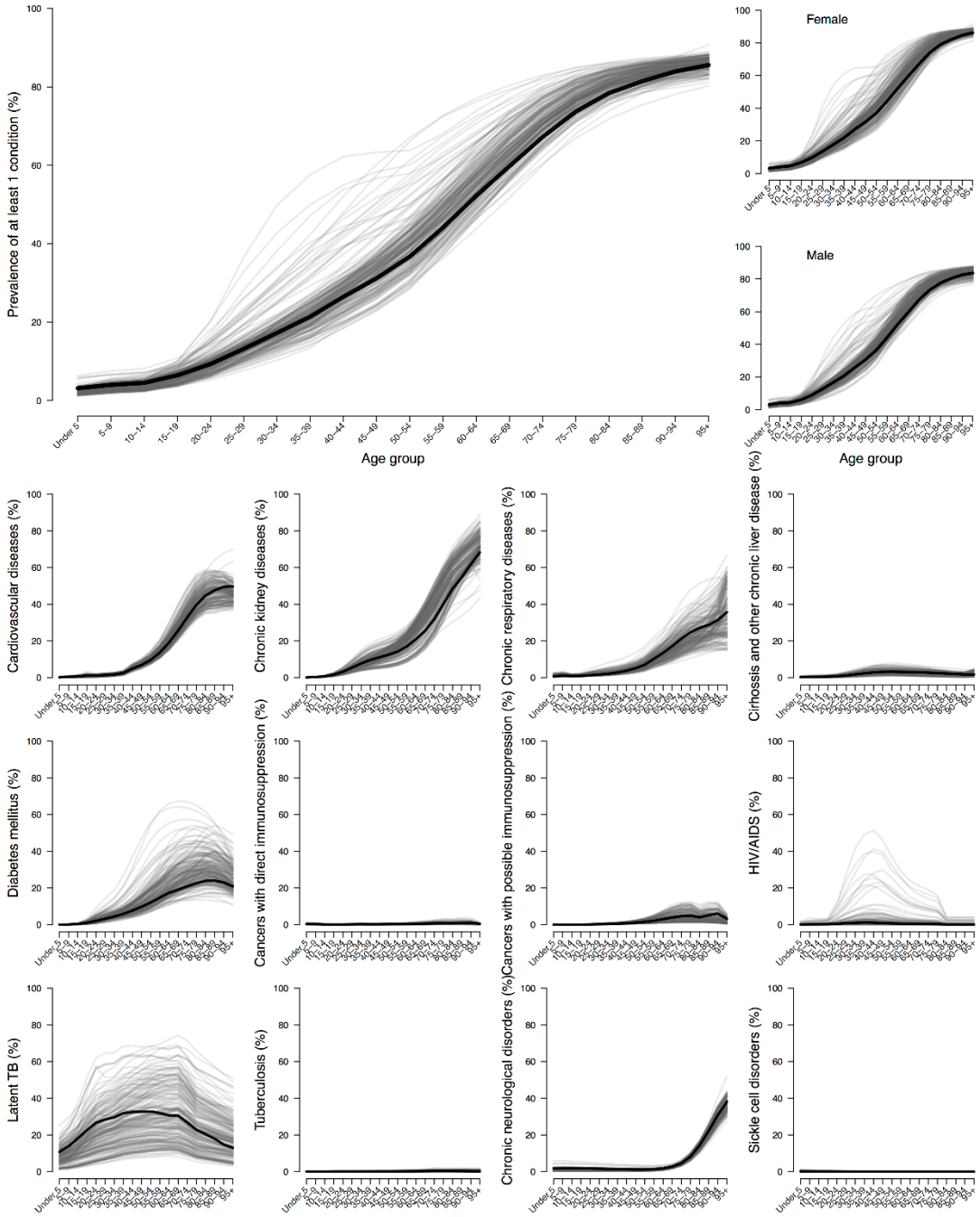
Table 2. Global number (%) of individuals at increased risk and high risk of severe COVID-19 illness by age and sex

	Increased risk *(have at least one condition listed in guidelines)*			**High risk** *(would require hospitalisation if infected)*		
	Number in millions (uncertainty interval*)	% (uncertainty interval*)	Number per population	Number in millions (uncertainty interval*)	% (uncertainty interval*)	Number per population
Total, all ages	**1746 (1032-2398)**	**22 (15-28)**	**One in 4.5**	**350 (187-785)**	**5 (3-9)**	**One in 22.2**
<20 years	116 (50-167)	4 (2-6)	One in 22.4	4 (2-10)	0 (0-0)	One in 652.4
20-29 years	134 (70-198)	11 (7-15)	One in 8.9	17 (9-38)	1 (1-3)	One in 70.3
30-39 years	220 (122-320)	19 (12-25)	One in 5.2	39 (21-87)	3 (2-7)	One in 29.5
40-49 years	279 (163-392)	29 (19-36)	One in 3.5	53 (28-119)	5 (3-11)	One in 18.4
50-54 years	163 (98-225)	37 (25-46)	One in 2.7	35 (19-79)	8 (5-16)	One in 12.7
55-59 years	171 (104-230)	44 (30-54)	One in 2.3	42 (22-94)	11 (6-22)	One in 9.2
60-64 years	168 (104-224)	52 (36-63)	One in 1.9	39 (21-88)	12 (7-25)	One in 8.2
65-69 years	161 (101-212)	60 (42-71)	One in 1.7	40 (22-90)	15 (9-30)	One in 6.7
70+ years	334 (219-429)	73 (53-85)	One in 1.4	81 (44-180)	18 (11-36)	One in 5.6
Female, all ages^	**907 (538-1242)**	**24 (16-29)**	**One in 4.3**	**123 (65-275)**	**3 (2-6)**	**One in 31.5**
<20 years	58 (26-83)	5 (2-6)	One in 21.7	1 (1-3)	0 (0-0)	One in 901.5
20-29 years	67 (35-99)	12 (7-15)	One in 8.5	6 (3-13)	1 (1-2)	One in 97.3
30-39 years	111 (62-161)	20 (12-26)	One in 5.1	14 (7-31)	2 (1-5)	One in 41.4
40-49 years	141 (82-198)	29 (19-37)	One in 3.4	18 (10-42)	4 (2-8)	One in 26.1
50-54 years	82 (49-114)	37 (25-46)	One in 2.7	12 (6-28)	5 (3-11)	One in 18.2
55-59 years	86 (52-116)	44 (30-54)	One in 2.3	15 (8-33)	8 (4-15)	One in 13.3
60-64 years	86 (53-114)	52 (36-63)	One in 1.9	14 (7-31)	8 (5-17)	One in 12.0
65-69 years	84 (53-111)	60 (42-71)	One in 1.7	14 (8-32)	10 (6-20)	One in 9.9
70+ years	191 (126-246)	74 (54-86)	One in 1.4	28 (15-63)	11 (7-22)	One in 9.1
Male, all ages^	**838 (494-1156)**	**21 (14-27)**	**One in 4.7**	**228 (121-510)**	**6 (3-12)**	**One in 17.2**
<20 years	58 (25-84)	4 (2-6)	One in 23.1	3 (1-6)	0 (0-0)	One in 518.3
20-29 years	66 (34-99)	11 (6-15)	One in 9.2	11 (6-25)	2 (1-4)	One in 55.7
30-39 years	109 (61-159)	19 (12-25)	One in 5.4	25 (13-57)	4 (3-9)	One in 23.1
40-49 years	138 (81-194)	28 (18-36)	One in 3.5	34 (18-77)	7 (4-14)	One in 14.3
50-54 years	81 (49-112)	36 (25-46)	One in 2.7	23 (12-51)	10 (6-21)	One in 9.8
55-59 years	84 (52-114)	44 (30-54)	One in 2.3	27 (14-61)	14 (8-29)	One in 7.0
60-64 years	82 (51-109)	52 (36-63)	One in 1.9	25 (14-57)	16 (10-33)	One in 6.2
65-69 years	77 (49-101)	60 (42-71)	One in 1.7	26 (14-59)	20 (12-41)	One in 4.9
70+ years	143 (93-184)	72 (53-85)	One in 1.4	53 (29-117)	27 (16-54)	One in 3.7

* For the numbers at increased risk, the low estimates were based on a scenario assuming the lower 95% CI values for the age/sex-specific population estimates, disease prevalence rates and multimorbidity fraction, and assume the r ratio = 0.7. The high estimates were based on the 95% CI values of the same parameters and assume the r ratio = 1.0. For the numbers at high risk, the low and high estimates were based on the 95% CI values published for IHRs in mainland China.

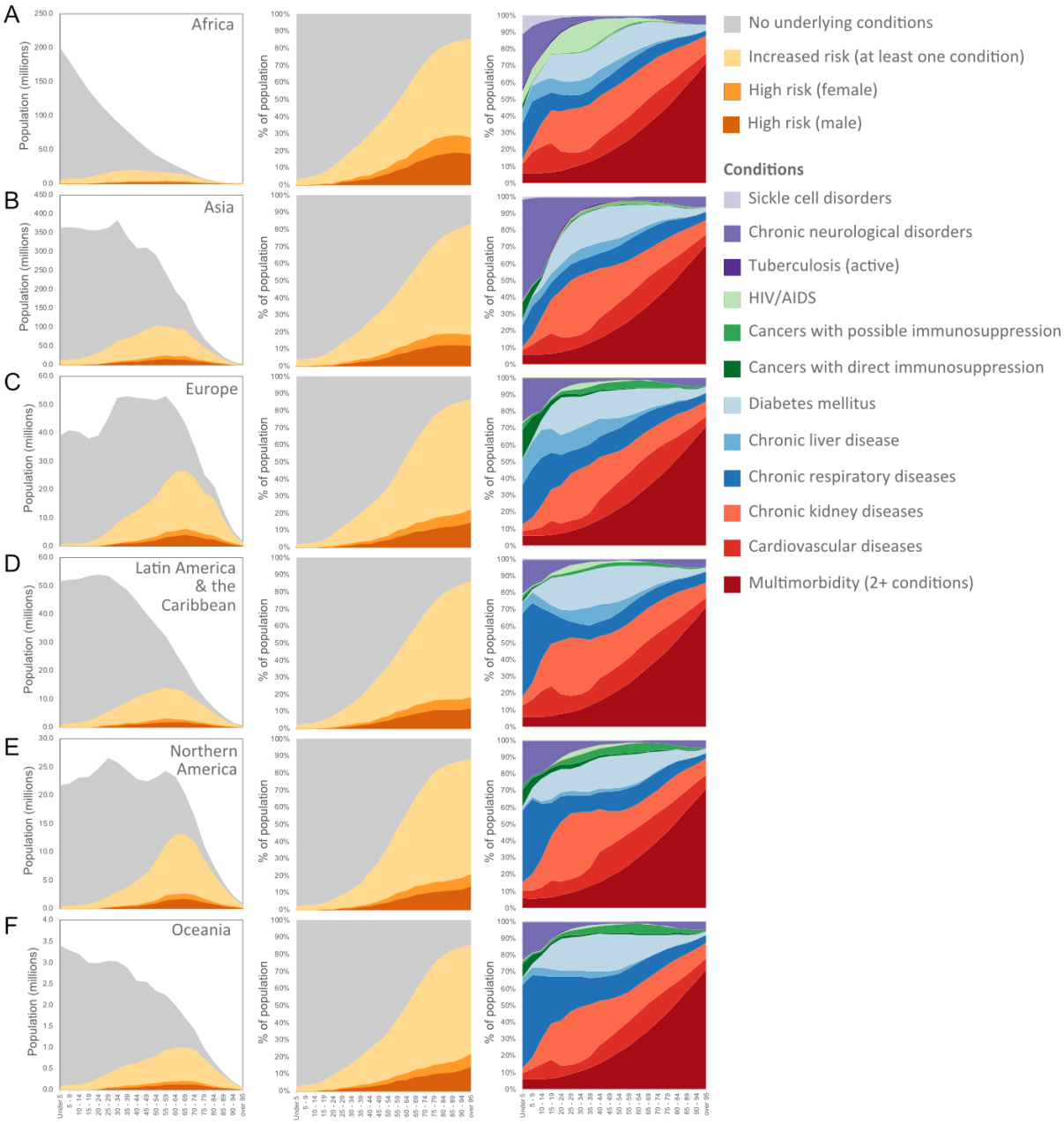
^ The prevalence of individuals at increased risk was similar for females and males due to broadly similar GBD prevalence estimates for the 11 underlying conditions by age and sex. We estimate more females than males (191 vs 143 million) with a condition listed on the current guidelines in those aged 70+ years. However, for the numbers at high risk, we assumed a 65% male percentage across all ages for consistency with the higher representation of male gender in COVID-19 hospital admissions.[21]

Figure 1. Global proportion of individuals with at least one underlying condition by age and sex (top panel); and global prevalence of each underlying condition by age (lower panel)



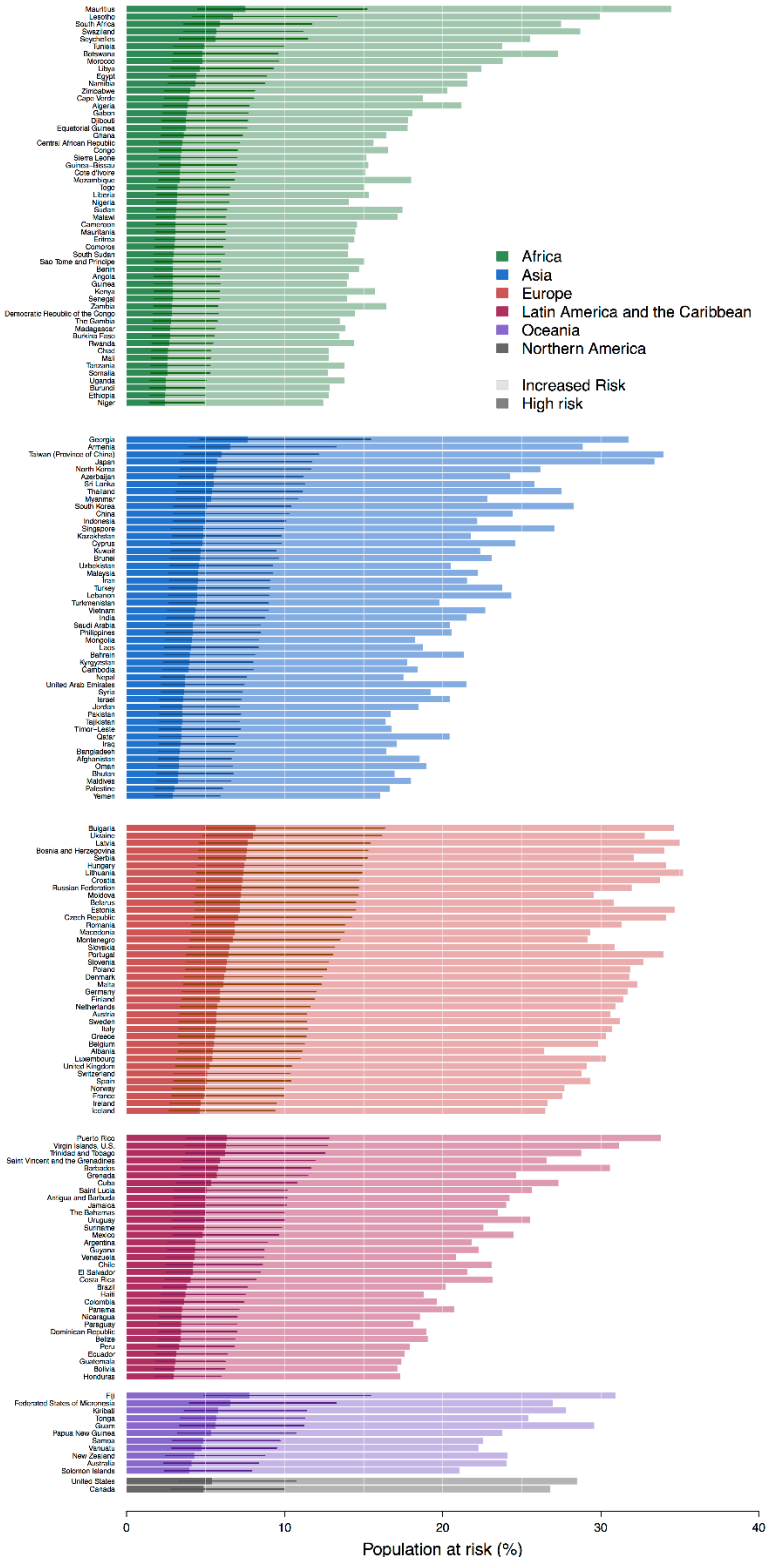
Grey lines represent individual countries and show variation around the global estimates (black lines). A similar proportion of males and females have one underlying condition by age (top right panels) based on GBD prevalence data. However, male gender has been identified as a significant independent predictor of COVID-19 severity so we assume 65% of those at high risk are male (see Figure 2). We excluded latent tuberculosis (TB) from our analysis but include it here to show the extent of overall TB that was excluded. HIV prevalence was particularly high in some African countries, and diabetes prevalence was particularly high in some small island nations.

Figure 2. Number (left panel) and percentage (centre panel) of population at increased risk and high risk of severe COVID-19 disease by age and region; and distribution of underlying conditions by age and region (right panel)



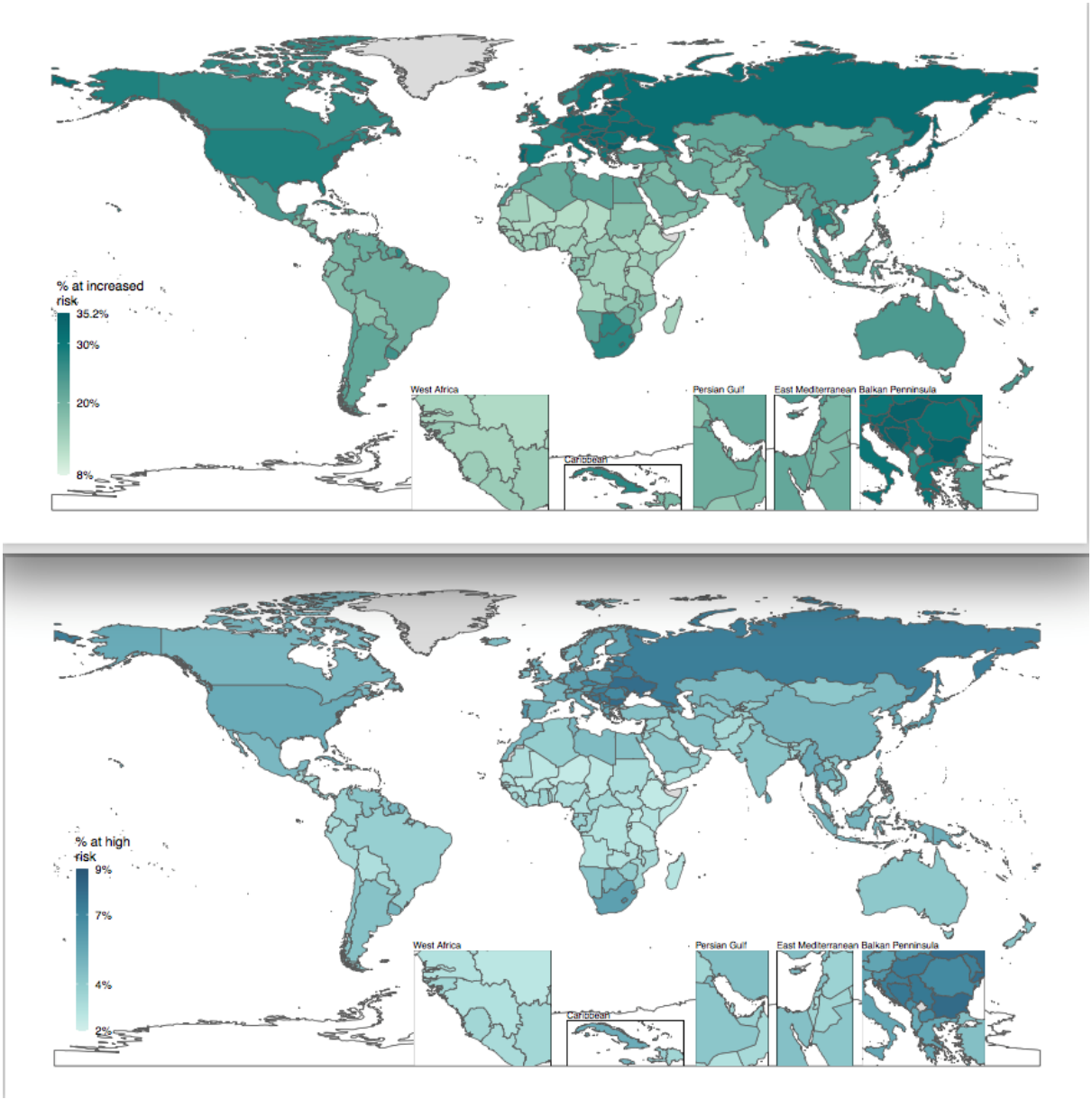
Rows A-F refer to the 6 UN regions of Africa, Asia, Europe, Latin America and the Caribbean, Northern America and Oceania. The first column shows the number of individuals with no underlying conditions (grey), those at increased risk (light orange) and the subset that are at high risk (darker orange, divided into females and males). The second column shows the same information by percentage share of the population. The third column shows the percentage distribution of the 11 underlying conditions and multimorbidity (2 or more conditions) by age.

Figure 3. Proportion of population at increased risk and high risk of severe COVID-19 illness country and region



Each country is given, grouped by UN population regions. The darker bars represent the population at high risk (those that would require hospital admission if infected), with uncertainty intervals based on the low and high 95% credible intervals reported for infection hospitalisation ratios in Verity *et al*[20]. The total length of the bars (dark and light combined) represent the total population at increased risk (those with at least one condition listed as 'at increased risk' in current guidelines).

Figure 4. Proportion of population at increased risk (top map) and high risk (bottom map) of severe COVID-19 disease by country



Countries shaded in darker green/blue have a higher proportion of their population at increased risk (top map) and high risk (bottom map). The lower proportions estimated for Africa are driven by demographics and strong association between severe COVID-19 and age (even after adjusting for age-based frailty and underlying conditions). However, many more severe cases may be fatal in Africa, and disruption to health systems could lead to substantial mortality from other non-COVID-19 diseases.

Acknowledgements

We acknowledge Jennifer Quint, Arminder Deol and Laurie Tomlinson for providing technical and clinical advice on specific diseases. We also acknowledge Ulla Griffiths and Palwasha Anwari for providing feedback on the spreadsheet.

The CMMID COVID-19 working group declare support from the following organisations: Bill and Melinda Gates Foundation (grants: OPP1183986, OPP1191821, INV-003174, OPP1180644, OPP1184344), RCUK/ESRC (grant: ES/P010873/1), UK Public Health Rapid Support Team, National Institute of Health Research (NIHR) Health Protection Research Unit (HPRU) in Modelling Methodology, European Commission (grant: 101003688), NIHR (grants: PR-OD-1017-20002, 16/137/109), NIHR EPIC grant (grant: 16/137/109), European Research Council Starting Grant (Action Numbers #757688, and #757699), Wellcome Trust (grants: 210758/Z/18/Z, 208812/Z/17/Z, 206250/Z/17/Z), Medical Research Council (MRC) London Intercollegiate Doctoral Training Program studentship (grants: MR/N013638/1), MRC (grant: MR/P014658/1), The Nakajima Foundation; The Alan Turing Institute, NIHR HPRU in Immunisation (grant: HPRU-2012-10096), Global Challenges Research Fund (GCRF) for the project "RECAP" managed through RCUK and ESRC (grant: ES/P010873/1) and Elrha's Research for Health in Humanitarian Crises (R2HC) Programme. The R2HC programme is funded by the UK Government (DFID), the Wellcome Trust, and the UK NIHR.

References

1. CDC. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 — United States, Centers for Disease Control and Prevention. February 12–March 28, 2020. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6913e2-H.pdf?deliveryName=USCDC_921-DM24524. *MMWR* 2020; **Early Release / Vol. 69**.
2. ISS. Characteristics of COVID-19 patients dying in Italy: report based on available data on March 20th, 2020. Rome, Italy: Instituto Superiore Di Sanita; 2020. COVID-19 Surveillance Group. Available at: https://www.epicentro.iss.it/coronavirus/bollettino/Report-COVID-2019_20_marzo_eng.pdf. 2020.
3. Guan WJ, Ni Z, Hu Yea. China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020.
4. CEBM. In patients of COVID-19, what are the symptoms and clinical features of mild and moderate cases? April 1, 2020. Available at: https://www.cebm.net/covid-19/in-patients-of-covid-19-what-are-the-symptoms-and-clinical-features-of-mild-and-moderate-case/. 2020.
5. WHO. Global Surveillance for human infection with coronavirus disease (COVID-19). Available at: https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov). 2020.
6. CDC. People who are at higher risk for severe illness. Coronavirus Disease 2019 (COVID-19). Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fspecific-groups%2Fhigh-risk-complications.html [accessed 1st April 2020]. 2020.
7. PHE. Guidance on social distancing for everyone in the UK. Updated 30 March 2020. Public Health England. Available at: https://www.gov.uk/government/publications/covid-19-guidance-on-social-distancing-and-for-vulnerable-people/guidance-on-social-distancing-for-everyone-in-the-uk-and-protecting-older-people-and-vulnerable-adults [Accessed 1st April 2020]. 2020.
8. WHO. COVID-19 and NCDs. Information note on COVID-19 and noncommunicable diseases. 23 March 2020. Available at: https://www.who.int/who-documents-detail/covid-19-and-ncds. 2020.
9. Banerjee A, Pasea L, Harris S, et al. RAPID COMMUNICATION 22 March 2020. Estimating excess 1- year mortality from COVID-19 according to underlying conditions and age in England: a rapid analysis using NHS health records in 3.8 million adults. DOI: 10.13140/RG.2.2.36151.27047 2020.
10. Davies N, Klepac P, Liu Y, et al. Age-dependent effects in the transmission and control of COVID-19 epidemics. Posted March 27, 2020. doi: https://doi.org/10.1101/2020.03.24.20043018. Available at: https://www.medrxiv.org/content/10.1101/2020.03.24.20043018v1. *medRxiv* 2020.
11. Public Health England. Guidance on shielding and protecting people defined on medical grounds as extremely vulnerable from COVID-19. 2020. https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19#what-is-shielding (accessed 11th April 2020).
12. GBD. Global Burden of Disease Study 2017. Available at: http://ghdx.healthdata.org/gbd-results-tool [Accessed 1st April 2020]. 2020.
13. United Nations Population Division. UNPOP (2019 Revision) estimates of population by single calendar year (2020), age, sex and country. Available at: https://population.un.org/wpp/Download/Standard/Interpolated/ [Accessed 1st April 2020]. 2020.
14. British Thoracic Society. British guideline on the management of asthma. Quick reference guide. Revised September 2016. Available at: https://www.brit-thoracic.org.uk/document-library/guidelines/asthma/btssign-asthma-guideline-quick-reference-guide-2016/.

15. Bloom CI, Nissen F, Douglas IJ, Smeeth L, Cullinan P, Quint JK. Exacerbation risk and characterisation of the UK's asthma population from infants to old age. *Thorax* 2018; **73**(4): 313-20.
16. WHO. Antiretroviral therapy coverage Estimates by country. Available at: https://apps.who.int/gho/data/node.main.626?lang=en

17. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012; **380**(9836): 37-43.
18. Wang HH, Wang JJ, Wong SY, et al. Epidemiology of multimorbidity in China and implications for the healthcare system: cross-sectional survey among 162,464 community household residents in southern China. *BMC Med* 2014; **12**: 188.
19. Romero-Ortuno R, Kenny RA. The frailty index in Europeans: association with age and mortality. *Age Ageing* 2012; **41**(5): 684-9.
20. Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis* 2020.
21. Annemarie B Docherty, Ewen M Harrison, Christopher A Green, et al. Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. medRxiv 2020.04.23.20076042; Available at: https://doi.org/10.1101/2020.04.23.20076042. 2020.
22. ECA. COVID-19 in Africa. Protecting lives and economies. Available at: https://www.uneca.org/publications/covid-19-africa-protecting-lives-and-economies. 2020.
23. Dahab M, van Zandvoort K, Flasche S, et al. COVID-19 control in low-income settings and displaced populations: what can realistically be done? 20 March 2020. Available at: https://www.lshtm.ac.uk/newsevents/news/2020/covid-19-control-low-income-settings-and-displaced-populations-what-can. 2020.
24. Lloyd-Sherlock P, Ebrahim S, Geffen L, McKee M. Bearing the brunt of covid-19: older people in low and middle income countries. *BMJ* 2020; **368**: m1052.
25. Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. *The Milbank Memorial Fund quarterly* 1971; **49**(4): 509-38.
26. GBD 2016 Healthcare Access and Quality Collaborators. Measuring performance on the Healthcare Access and Quality Index for 195 countries and territories and selected subnational locations: a systematic analysis from the Global Burden of Disease Study 2016. *Lancet* 2018; **391**(10136): 2236-71.
27. Jing Yang, Ya Zheng, Xi Gou, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. *International Journal of Infectious Diseases* 2020.
28. Susan Michie, Robert West, Amlôt R. Behavioural strategies for reducing covid-19 transmission in the general population. March 3, 2020. Available at: https://blogs.bmj.com/bmj/2020/03/03/behavioural-strategies-for-reducing-covid-19-transmission-in-the-general-population/. 2020.
29. Bornstein SR, Dalan R, Hopkins D, Mingrone G, Boehm BO. Endocrine and metabolic link to coronavirus infection. *Nature Reviews Endocrinology* 2020: https://doi.org/10.1038/s41574-020-0353-9.
30. Liu W, Tao ZW, Lei W, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chin Med J (Engl)* 2020.
31. Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. Sex-Based Differences in Susceptibility to Severe Acute Respiratory Syndrome Coronavirus Infection. *Journal of immunology (Baltimore, Md : 1950)* 2017; **198**(10): 4046-53.
32. Fischer J, Jung N, Robinson N, Lehmann C. Sex differences in immune responses to infectious diseases. *Infection* 2015; **43**(4): 399-403.
33. BHIVA E. EACS & BHIVA Statement on risk of COVID-19 for people living with HIV (PLWH). COVID-19 & HIV. Thursday 30 April, 2020. Available at: https://www.eacsociety.org/home/covid-19-and-hiv.html [Accessed 10th May 2020].

34. Cohen C, Moyes J, Tempia S, et al. Severe influenza-associated respiratory infection in high HIV prevalence setting, South Africa, 2009-2011. *Emerg Infect Dis* 2013; **19**(11): 1766-74.
35. Serrano-Villar S, Sainz T, Lee SA, et al. HIV-infected individuals with low CD4/CD8 ratio despite effective antiretroviral therapy exhibit altered T cell subsets, heightened CD8+ T cell activation, and increased risk of non-AIDS morbidity and mortality. *PLoS Pathog* 2014; **10**(5): e1004078.
36. Wilson EM, Sereti I. Immune restoration after antiretroviral therapy: the pitfalls of hasty or incomplete repairs. *Immunol Rev* 2013; **254**(1): 343-54.
37. ASSAf. ASSAf Statement on the Implications of the Novel Coronavirus (SARS-CoV-2; COVID-19) in South Africa. Available at: https://assaf.org.za/files/2020/ASSAf%20Statement%20Corona%20Virus%202%20March%202020%20web.pdf. 2020.
38. BHIVA. Comment from BHIVA and THT on UK Government Guidance on Coronavirus (COVID-19), Social Distancing to Protect Vulnerable Adults and Shielding to Protect Extremely Vulnerable Adults 23 March 2020. Available at: https://www.bhiva.org/comment-from-BHIVA-and-THT-on-UK-Government-guidance-on-Coronavirus-COVID-19. 2020.
39. Disease GBD, Injury I, Prevalence C. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392**(10159): 1789-858.
40. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2020; **395**(10225): 709-33.
41. Moody A, Cowley G, Ng Fat L, Mindell JS. Social inequalities in prevalence of diagnosed and undiagnosed diabetes and impaired glucose regulation in participants in the Health Surveys for England series. *BMJ Open* 2016; **6**(2): e010155.
42. White LV, Edwards T, Lee N, et al. Patterns and predictors of co-morbidities in Tuberculosis: A cross-sectional study in the Philippines. *Sci Rep* 2020; **10**(1): 4100.
43. Katalin Gemes, Mats Talback, Karin Modig, et al. Burden and prevalence of prognostic factors for severe covid-19 disease in Sweden. medRxiv preprint doi: https://doi.org/10.1101/2020.04.08.20057919. 2020.