Supplementary appendix

for

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

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Table 1. List of conditions included in GBD2017 with potential to increase the risk of severe COVID-19 illness

#	Category	Causes included in the Global Burden of Disease Study (GBD2017)
1	HIV/AIDS	HIV/AIDS - Drug-susceptible Tuberculosis; HIV/AIDS - Multidrug-resistant Tuberculosis without extensive drug resistance; HIV/AIDS - Extensively drug-resistant Tuberculosis; HIV/AIDS resulting in other diseases
2	Tuberculosis*	Drug-susceptible tuberculosis; Multidrug-resistant tuberculosis without extensive drug resistance; Extensively drug-resistant tuberculosis
3	Cancers with direct immune suppression	Hodgkin lymphoma; Non-Hodgkin lymphoma; Multiple myeloma; Acute lymphoid leukemia; Chronic lymphoid leukemia; Acute myeloid leukemia; Chronic myeloid leukemia; Other leukemia; Other malignant neoplasms; Myelodysplastic, myeloproliferative, and other hematopoietic neoplasms
4	Cancers with possible immune suppression (from treatment therapy)	Lip and oral cavity cancer; Nasopharynx cancer; Other pharynx cancer; Esophageal cancer; Stomach cancer; Colon and rectum cancer; Liver cancer due to hepatitis B; Liver cancer due to hepatitis B; Liver cancer due to hepatitis B; Liver cancer due to hepatitis C; Liver cancer due to alcohol use; Liver cancer due to NASH; Liver cancer due to other causes; Gallbladder and biliary tract cancer; Pancreatic cancer; Larynx cancer; Tracheal, bronchus, and lung cancer; Malignant skin melanoma; Breast cancer; Cervical cancer; Uterine cancer; Ovarian cancer; Prostate cancer; Testicular cancer; Kidney cancer; Bladder cancer; Brain and nervous system cancer; Thyroid cancer; Mesothelioma
5	Cardio-vascular diseases	Rheumatic heart disease; Ischemic heart disease; Ischemic stroke; Intracerebral haemorrhage; Subarachnoid haemorrhage; Hypertensive heart disease; Non-rheumatic calcific aortic valve disease; Non-rheumatic degenerative mitral valve disease; Other non-rheumatic valve diseases; Myocarditis; Alcoholic cardiomyopathy; Other cardiomyopathy; Atrial fibrillation and flutter; Aortic aneurysm; Peripheral artery disease; Endocarditis; Other cardiovascular and circulatory diseases; Congenital heart anomalies
6	Chronic respiratory diseases	Chronic obstructive pulmonary disease; Silicosis; Asbestosis; Coal workers pneumoconiosis; Other pneumoconiosis; Asthma*; Interstitial lung disease and pulmonary sarcoidosis
7	Cirrhosis and other chronic liver diseases	Cirrhosis and other chronic liver diseases due to hepatitis B; Cirrhosis and other chronic liver diseases due to hepatitis C; Cirrhosis and other chronic liver diseases due to alcohol use; Cirrhosis and other chronic liver diseases due to other causes
8	Diabetes mellitus	Diabetes mellitus type 1; Diabetes mellitus type 2
9	Chronic kidney diseases	Chronic kidney disease due to diabetes mellitus type 1; Chronic kidney disease due to diabetes mellitus type 2; Chronic kidney disease due to hypertension; Chronic kidney disease due to glomerulonephritis; Chronic kidney disease due to other and unspecified causes
10	Chronic neurological disorders	Alzheimer's disease and other dementias; Parkinson's disease; Multiple sclerosis; Motor neuron disease; Other neurological disorders; Idiopathic developmental intellectual disability; Down syndrome; Neural tube defects
11	Sickle cell disorders	Sickle cell disorders

* we excluded latent tuberculosis and adjusted asthma to better reflect BTS steps 4+.

Methods used to calculate the proportion of individuals with at least one underlying condition

Note: Some of the text from the main paper is repeated here for convenience.

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[1] and Southern China.[2]

The ratio r was broadly consistent by age, sex and study (see Figure 1 overleaf). For the analysis of both males and females combined, the mean of all age-specific values of r was 0.92 (range 0.86 to 0.99) in Scotland and 0.92 (range (0.75 – 1.15) in China. When extrapolating this value to other countries, we used a transparent ratio of 0.9 for all age groups and varied this this between 0.7 (low estimates) and 1.0 (high estimates). The resulting national estimates of P were constrained to be no less than each country's single most prevalent condition. We conducted sensitivity analyses to explore the impact on results of using the observed age-specific values of r rather than the same value for all ages, but this had a very small impact on the share of the population estimated to be at increased risk i.e. the share of the population at increased risk changed from 22.5% to 22.8% with adjustment for age.

Adjustment for multimorbidity

In addition to providing estimates for r, the studies in Scotland and Southern China were also 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 in the main analysis 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.

We calculated pooled estimates of the multimorbidity fraction by age and sex and extrapolated these pooled estimates to all countries included in the analysis (see Figure 1 overleaf).

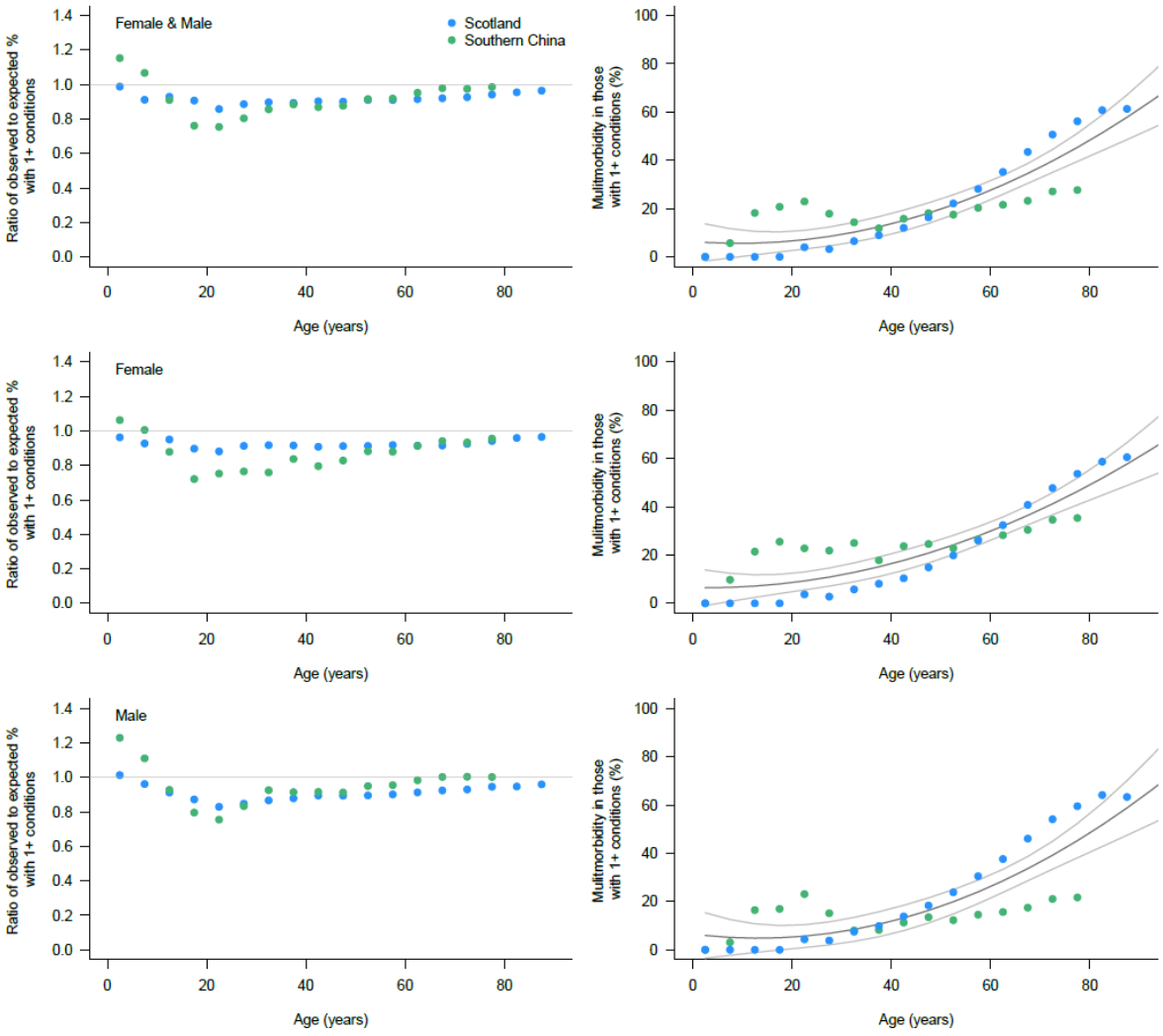
Figure 1. Empirical estimates of the ratio r (left panel) and the multimorbidity fraction among those with at least one underlying health condition relevant to COVID-19 (right panel) from cross-sectional studies in Scotland and Southern China

The top row shows results for females and males combined. The middle row shows results for females only and the bottom row shows results for males only.

The left panel/column shows the ratio between the observed and expected % of individuals with at least one condition by age. Expected estimates were calculated by assuming the prevalences of COVID-19 underling conditions 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)…. This was then compared to the observed value of the % of individuals with at least one condition based on the same dataset (either Scotland or Southern China). The ratios between expected and observed are shown on the left panel/column below. Both studies indicate that the expected value based on the assumption of independence would provide reasonable estimates of the observed value. In our main analysis we assumed the ratio was 0.9 but varied this between 0.7 and 1.0 in uncertainty analysis.

The right panel/column shows the proportion of those with at least one underlying condition relevant to COVID-19 with multimorbidity (two or more conditions). As expected, this percentage increases with age in both studies. The grey lines represent pooled estimates and 95% confidence intervals based on a 2nd order polynomial model fitted to all data points. Pooled estimates were extrapolated to all countries included in the analysis by age and sex. The lower and upper CI values were used in our low and high estimates in the main paper.

Empirical estimates of the ratio *r* by age **Empirical estimates of multimorbidity by age**



Methods to estimate who among those at increased risk (have at least one condition listed in the current guidelines) are likely to be at high risk (would require hospitalisation if infected)

Infection hospitalisation ratios

The number of individuals at high risk was assumed to be equivalent to the proportion of the population that would be hospitalised if infected, by age. We applied country-level UN estimates of the number of individuals in each 5-year age group[3] to age-specific infection hospitalisation ratios (IHRs) recently estimated for mainland China by Verity *et al.*[4] IHRs represent the proportion of people who are infected (asymptomatic or symptomatic) that will have symptoms severe enough to require hospital admission. The term 'require hospital admission' is consistent with the WHO definition for severe cases.[5]

Adjustments to IHRs

We made two adjustments to account for differences between IHRs in China and other countries:

1. *Adjusting for age-based frailty* – for each 5-year age group and sex, we divided UN estimates of age-specific life expectancy[3] for China by the equivalent estimate for the country of interest. This ratio (proxy for difference in age-based frailty) was then applied to the IHR for same age group. For example, the life expectancy for males at age 55 years is 22.8 and 19.1 years in China and Afghanistan, respectively, so the IHR for this age group was multiplied by a ratio of 1.19 (22.8/19.1) to generate a more realistic estimate for Afghanistan; and,

2. *Adjusting for underlying conditions* – for each 5-year age group and sex, the unconstrained prevalence rates for each underlying condition were multiplied by their associated ORs for hospitalisation and then summed to create a risk score. IHRs were then adjusted to account for the ratio of the risk score for China and the country of interest. For example, for males aged 55-59 years the risk score was 1.28 in China and 1.84 in Afghanistan, so the IHR for this age group was multiplied by a ratio of 1.44 (1.84/1.28). Thus, for males aged 55-59 years in Afghanistan, separate adjustments for age-based frailty and underlying conditions had the effect of increasing the IHR by 1.71 (IHR x 1.19 x 1.44), from 8% to 14%.

Odds ratios for hospital admission

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. The focus of our analysis was the risk associated with hospital admission (rather than the risk of mortality among those hospitalised) so we restricted our analysis of ORs to studies that included a control group of COVID-19 patients that were not severe enough to be admitted to hospital.

We identified one meta-analysis containing 4 studies from China that allowed comparison of patients that were non-severe and severe.[6] However, a substantial number of the non-severe cases in these studies were hospitalised, so were not eligible for inclusion. We also identified two studies from the USA. The first contained descriptive data on 6,637 COVID-19 cases reported to the CDC as of March 28, 2020.[7] The second study was a multivariate analysis of 4,103 COVID-19 cases in New York City.[8] For each variable we summarised the strength of the association (low, moderate, high) and graded our confidence in the strength of that association (low, moderate high). For the adjustment of IHRs for underlying conditions in our main analysis, we assumed OR = 5.0 for three underlying conditions (CVD, CKD, diabetes) found to have a significant independent association with hospitalisation in multivariate analyses, and assumed OR = 3.0 for other underlying conditions with insufficient data or weak evidence of an associated risk. All assumptions and ORs was varied in sensitivity analysis (p 8).

Table 2. Summary of evidence on risk factors for COVID-19 hospital admission: used in a scenario to estimate of the number of individuals at high risk of severe COVID disease

Variable	What is known about risk factors for COVID-19 hospital admission? *(evidence restricted to studies that included a control group of COVID-19 patients that were not severe enough to be admitted to hospital)*	Strength of association with hospital admission (low, moderate, high)	Confidence about strength of association (low, moderate, high)
Underlying conditions listed in guidelines with available data by age, sex and country			
Cardiovascular disease	Crude OR = 6.85 (5.75 - 8.16) based on 25% vs 5% prevalence with and without admission in the USA (n=6637).[7] Heart failure a significant independent predictor (OR = 4.29 [1-89-11.18]) in multivariate analysis in New York City (n=4103).[8]	High	Moderate
Chronic kidney disease	Crude OR = 11.23 (8.13 - 15.51) based on 10% vs 1% prevalence with and without admission in the USA (n=6637).[7] Significant independent predictor (OR =3.07 [1-78-5.52]) in multivariate analysis in New York City (n=4103).[8]	High	Moderate
Diabetes	Crude OR = 5.30 (4.51 - 6.22) based on 27% vs 6% prevalence with and without admission in the USA (n=6637).[7] Significant independent predictor (OR = 2.81 [2.14-3.72]) in multivariate analysis in New York City (n=4103).[8]	High	Moderate
Neurological disorders	Crude OR = 6.60 (3.65 - 11.92) based on 2% vs 0% prevalence with and without admission in the USA (n=6637), but the number with neurological disorders was small in this study (n=49).[7]	Moderate	Low
Chronic respiratory diseases	Crude OR = 2.60 (2.18 - 3.09) based on 16% vs 7% prevalence with and without admission in the USA (n=6637).[7] Not a significant independent predictor (OR = 1.33 [0.96-1.84]) in multivariate analysis in New York City (n=4103).[8] However, both studies include all severities of 'asthma' which is likely to deflate the true odds associated with other chronic respiratory diseases.	Moderate	Low
Tuberculosis (active)	Not data is available, so we assume the same OR assumed for chronic respiratory diseases.	Insufficient data	Low
Chronic liver disease	Crude OR = 2.31 (1.22 - 4.36) based on 1% vs 0% prevalence with and without admission in the USA (n=6637), but the number with chronic liver disease was small in this study (n=40).[7]	Moderate	Low
Cancers with possible immunosuppression	Crude OR = 2.65 (2.05 - 3.44) based on 7% vs 3% prevalence with and without admission in the USA (n=6637) based on a generic category of immunosuppressed conditions.[7] Not a significant independent predictor (OR = 1.24 [0.81-1.93]) in multivariate analysis in New York City (n=4103) based on a general malignancy category.[8]	Moderate	Low
Cancers with direct immunosuppression	Crude OR = 2.65 (2.05 - 3.44) based on 7% vs 3% prevalence with and without admission in the USA (n=6637) based on a generic category of immunosuppressed conditions.[7]	Moderate	Low
HIV / AIDS	Crude OR = 2.65 (2.05 - 3.44) based on 7% vs 3% prevalence with and without admission in the USA (n=6637) based on a generic category of immunosuppressed conditions.[7]	Moderate	Low

Sickle cell disorders	Crude OR = 2.65 (2.05 - 3.44) based on 7% vs 3% prevalence with and without admission in the USA (n=6637) based on a generic category of immunosuppressed conditions.[7]	Moderate	Low

Important variables with available data in 188 countries

Age	Current guidelines recommend protecting those aged 60+ (WHO), 65+ (US) and 70+ (UK). Compared to the reference age group (19-44 years) ORs were 2.57 (2.06 - 3.20) aged 45-54yrs, 4.17 (3.35-5.20) aged 55-64yrs, 10.91 aged 65-74yrs and 66.79 (44-73-102.62) aged 75+ years, based on multivariate analysis in New York City (n=4103).[8] The median age was 62 vs 41 years with and without admission.	High (IHRs from China have a strong age effect, and are further adjusted for age-specific frailty)	High
Male gender	Gender is not included in current guidelines. In one multivariate analysis in New York City (n=4103) male gender was a significant independent predictor of hospitalisation (OR = 2.80, 95% CI 2.38 -3.30, p <0.001).[8] In a large study of hospitalised patients in the UK, 60% of hospitalised patients were male and this effect was seen across all ages (n=16,749).[9] Males have also been identified as having worse survival after hospital admission, and in a large multivariate analysis in the UK (n=17,425,445) the hazard ratio for male gender was 1.99 (95% CI 1.88-2.10).[10]	High (for simplicity we assumed males represented 65% of those at high risk (requiring hospital admission if infected)	High

Other possible variables not included in this analysis

Pregnancy	The prevalence of pregnancy was the same among COVID-19 hospital admissions (6%) and the wider community in a large study in the UK (n=16749).	Low	Low
Current or former smoker	Included in WHO and US guidelines but not UK guidelines. Crude OR = 2.68 (2.07 - 3.48) based on 7% vs 3% prevalence with and without admission in the USA (n=6637).[7] Not a significant independent predictor (OR = 0.71, 95% CI 0.57-0.87, p=0.001) in multivariate analysis in New York City (n=4103).[8] Current and former smokers were combined into a single category and their risks may be different. It is unclear whether prevalence data for the required smoking categories would be available by 5-year age group, sex and country (n=188).	Low	Moderate
BMI 30-39	Not included in current guidelines. Significant independent predictor (OR = 4.26, 95% CI 3.50-5.20, p<0.001) in multivariate analysis in New York City (n=4103).[8] Prevalence data are available for adults aged 18+ years, but it is currently unclear if these are available by 5-year age group.	Moderate	Moderate
BMI 40+	Included in US/UK guidelines but not WHO guidelines. Significant independent predictor (OR = 6.20, 95% CI 4.21-9.25, p<0.001) in multivariate analysis in New York City (n=4103).[8] Prevalence data are available for adults aged 18+ years, but it is currently unclear if these are available by 5-year age group.	Moderate	Moderate
Hypertension (excluding hypertensive heart disease and CKD	In the GBD prevalence estimates, hypertensive heart disease is included within CVD. CKD due to hypertension is included within CKD. Other forms of hypertension are not included but could be an independent risk factor for severe COVID-19 illness. Hypertension is not included in current guidelines, and it is unclear if prevalence data are available	Low	Moderate

caused by hypertension)	for 188 countries by age and sex. In one multivariate analysis in New York City (n=4103), hypertension was not identified as a significant independent predictor (OR = 1.23, 95% CI [0.97 – 1.57], p=0.094).[8]		
Ethnicity	Not included in current guidelines. Unclear if prevalence data are available for 188 countries by sex. In one multivariate analysis in New York City (n=4103), other/multiracial race was identified as a significant independent predictor (OR = 1.99, 95% CI [1.62 – 2.45], p<0.001) compared to white race. African American and Asian race was not a significant predictor of hospital admission in this study [8]	Moderate	Low
Organ donor recipients	Included in current guidelines but unclear if prevalence data are available for 188 countries by 5-year age and sex. Studies have found an association with death among those admitted to hospital, but no studies have assessed the association with hospital admission.	Insufficient data	Insufficient data
Laboratory markers	Not included in current guidelines. Insufficient data on the prevalence of markers in a control group (e.g. C reactive protein >200 mg/L, d-dimer >500 ng/mL) so insufficient evidence for risk of hospitalisation.	Insufficient data	Insufficient data
Child malnutrition	Not included in current guidelines. Prevalence data are available but there is insufficient evidence of risk.	Insufficient data	Insufficient data
Malaria	Not included in current guidelines. Prevalence data are available but there is insufficient evidence of risk.	Insufficient data	Insufficient data
Deprivation	Not included in current guidelines. Unclear if prevalence data are available for 188 countries. Insufficient evidence of risk.	Insufficient data	Insufficient data
Crowded housing	Not included in current guidelines. Unclear if prevalence data are available for 188 countries. Insufficient evidence of risk.	Insufficient data	Insufficient data
Health and social care workers	Not included in current guidelines Unclear if prevalence data are available for 188 countries. Likely to be an important target group for a future vaccine due to increased risk of transmission.	Insufficient data	Insufficient data
Residents of care homes and other facilities	Included in some guidelines. Unclear if prevalence data are available for 188 countries. Likely to be an important target group for a future vaccine due to increased risk of transmission.	Insufficient data	Insufficient data

Sensitivity analysis for estimates of the number of individuals at high risk

Table 3 (overleaf) summarises the share of the population estimated to be at high risk (those that would require hospital admission if infected) for the base case scenario and for a range of alternative scenarios.

The following assumptions were varied:

1. *Low and high credible intervals of IHRs* – scenarios based on the low and high credible interval values of the IHRs reported in Verity *et al,*[11] were influential. The global population at high risk (4.5%) was 2.7% with low IHRs and 9.2% with high HIRs;

2. *Adjustments for age-based frailty* - as expected, removing the age-based frailty adjustment resulted in a lower population at high risk in Africa (from 3.3% to 2.7%) and a higher population at high risk in Europe and other high-income settings;

3. *Adjustments for underlying conditions* - without this adjustment the population at high risk decreased from 3.3% to 2.7% in Africa. In some countries removing this adjustment halved the population at high risk, due to very high prevalence of specific conditions relative to the same conditions in China e.g. diabetes in Fiji, HIV/AIDs in Swaziland;

4. *Altering the herd immunity ceiling value* – numbers at high risk were calculated by estimating the total number of individuals that would require hospital admission if infected in each age group. However, there may be a theoretical maximum proportion of the population that could ever become infected due to herd immunity. The global population at high risk decreased from 4.5% (no ceiling value) to 4.1%, 3.6%, 3.2% and 2.7% when assuming the total infected population could not exceed 90%, 80%, 70% and 60%, respectively; and,

5. *Altering the ORs for specific conditions* – changing the OR values for each condition one at a time (assuming low and high values of 1 and 10 respectively) had a limited impact on the total population at high risk (<5% increase/decrease). Results were most sensitive to CVD, CKD, diabetes and liver disease (due to its higher prevalence in China relative to many other settings). Increasing the OR for HIV/AIDS from 3.0 to 10.0 was influential in Africa and increased the population at high risk from 3.3% (44 million) to 3.8% (51 million).

Table 3. Population in millions (%) at high risk by region: base case and alternative scenarios

	Africa	Asia	Europe	Latin America and the Caribbean	North America	Oceania	Global
Central, low and high estimates for main analysis							
Base case scenario • IHRs based on Verity *et al*,	44 (3.3)	212 (4.6)	46 (6.2)	26 (4.0)	20 (5.3)	2 (4.5)	350 (4.5)

• IHRs adjusted for both age-based frailty • IHRs adjusted for underlying conditions • Ceiling of population infected = 100% • OR = 5.0 (CVD, CKD and diabetes) • OR = 3.0 (all other conditions)							
IHRs based on lower 95% credible intervals	26 (2.0)	126 (2.7)	28 (3.7)	16 (2.4)	12 (3.2)	1 (2.7)	208 (2.7)
IHRs based on upper 95% credible intervals	90 (6.8)	432 (9.3)	95 (12.7)	54 (8.2)	40 (10.9)	4 (9.2)	715 (9.2)
Scenarios for different IHR adjustments							
Removing adjustment for underlying conditions	36 (2.7)	193 (4.2)	42 (5.6)	24 (3.7)	17 (4.7)	2 (4.1)	315 (4.0)
Removing adjustment for age-based frailty	37 (2.7)	205 (4.4)	51 (6.8)	28 (4.3)	23 (6.3)	2 (4.9)	346 (4.4)
Removing both adjustments	30 (2.2)	188 (4.1)	46 (6.1)	26 (4.0)	20 (5.5)	2 (4.6)	312 (4.0)
Scenarios with 'herd immunity' ceiling values							
Assumes population infected cannot exceed 90%	40 (3.0)	190 (4.1)	42 (5.6)	24 (3.6)	18 (4.8)	2 (4.1)	315 (4.1)
Assumes population infected cannot exceed 80%	35 (2.6)	169 (3.7)	37 (5.0)	21 (3.2)	16 (4.3)	2 (3.6)	280 (3.6)
Assumes population infected cannot exceed 70%	31 (2.3)	148 (3.2)	33 (4.4)	18 (2.8)	14 (3.7)	1 (3.2)	245 (3.2)
Assumes population infected cannot exceed 60%	27 (2.0)	127 (2.7)	28 (3.7)	16 (2.4)	12 (3.2)	1 (2.7)	210 (2.7)
Scenarios assuming OR = 1.0 for specific conditions							
Cardiovascular diseases, OR = 1.0	46 (3.4)	218 (4.7)	47 (6.3)	27 (4.1)	20 (5.4)	2 (4.7)	359 (4.6)
Chronic kidney diseases, OR = 1.0	43 (3.2)	206 (4.4)	47 (6.2)	26 (3.9)	20 (5.4)	2 (4.5)	343 (4.4)
Chronic respiratory diseases, OR = 1.0	45 (3.4)	212 (4.6)	47 (6.2)	26 (4.1)	20 (5.4)	2 (4.5)	351 (4.5)
Chronic liver disease, OR = 1.0	45 (3.3)	215 (4.6)	47 (6.3)	26 (4.1)	20 (5.5)	2 (4.6)	355 (4.6)
Diabetes mellitus, OR = 1.0	44 (3.3)	208 (4.5)	46 (6.1)	25 (3.9)	19 (5.1)	2 (4.3)	344 (4.4)
Cancers with direct immunosuppression OR = 1.0	44 (3.3)	212 (4.6)	46 (6.2)	26 (4.0)	20 (5.3)	2 (4.5)	351 (4.5)
Cancers with possible immunosuppression, OR = 1.0	45 (3.3)	212 (4.6)	46 (6.2)	26 (4.0)	19 (5.3)	2 (4.4)	351 (4.5)
HIV/AIDS, OR = 1.0	42 (3.2)	211 (4.6)	46 (6.2)	26 (4.0)	20 (5.3)	2 (4.5)	348 (4.5)
Tuberculosis, OR = 1.0	44 (3.3)	212 (4.6)	47 (6.2)	26 (4.0)	20 (5.3)	2 (4.5)	350 (4.5)
Chronic neurological disorders, OR = 1.0	44 (3.3)	210 (4.5)	47 (6.3)	26 (4.0)	20 (5.4)	2 (4.5)	349 (4.5)
Sickle cell disorders, OR = 1.0	44 (3.3)	212 (4.6)	46 (6.2)	26 (4.0)	20 (5.3)	2 (4.5)	350 (4.5)
Scenarios assuming OR = 10.0 for specific conditions							
Cardiovascular diseases, OR = 10.0	43 (3.2)	207 (4.5)	46 (6.2)	26 (3.9)	20 (5.3)	2 (4.3)	344 (4.4)
Chronic kidney diseases, OR = 10.0	45 (3.4)	216 (4.7)	46 (6.2)	27 (4.1)	20 (5.3)	2 (4.5)	356 (4.6)
Chronic respiratory diseases, OR = 10.0	43 (3.2)	212 (4.6)	46 (6.2)	26 (3.9)	19 (5.3)	2 (4.7)	348 (4.5)
Chronic liver disease, OR = 10.0	43 (3.2)	201 (4.3)	45 (6.1)	26 (3.9)	18 (4.9)	2 (4.2)	335 (4.3)
Diabetes mellitus, OR = 10.0	44 (3.3)	215 (4.6)	47 (6.3)	27 (4.1)	20 (5.5)	2 (4.7)	356 (4.6)
Cancers with direct immunosuppression OR = 10.0	44 (3.3)	210 (4.5)	46 (6.2)	26 (4.0)	20 (5.4)	2 (4.5)	347 (4.5)
Cancers with possible immunosuppression, OR = 10.0	43 (3.2)	209 (4.5)	48 (6.4)	26 (4.0)	21 (5.6)	2 (4.7)	349 (4.5)
HIV/AIDS, OR = 10.0	51 (3.8)	212 (4.6)	47 (6.3)	27 (4.1)	20 (5.4)	2 (4.5)	358 (4.6)
Tuberculosis, OR = 10.0	44 (3.3)	212 (4.6)	46 (6.2)	26 (4.0)	20 (5.3)	2 (4.5)	350 (4.5)
Chronic neurological disorders, OR = 10.0	44 (3.3)	218 (4.7)	46 (6.1)	26 (4.0)	19 (5.2)	2 (4.4)	354 (4.6)
Sickle cell disorders, OR = 10.0	44 (3.3)	212 (4.6)	46 (6.2)	26 (4.0)	20 (5.3)	2 (4.5)	350 (4.5)

Table 4. Low estimates of the 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

Assumptions:

- Population estimates: Lower 95% CI
- Disease prevalence: Lower 95% CI
- Ratio (observed vs expected % with 1+ conditions): 0.7
- Multimorbidity among those with 1+ conditions: Lower 95% CI

	Africa	Asia	Europe	Latin America and the Caribbean	Northern America	Oceania	**Global**
No conditions							
<15 years	467 (40)	948 (23)	109 (16)	137 (24)	59 (18)	9 (23)	**1729 (25)**
15-49 years	508 (43)	1910 (46)	272 (40)	276 (48)	139 (42)	17 (43)	**3122 (45)**
50-54 years	27 (2)	195 (5)	36 (5)	24 (4)	15 (5)	2 (4)	**299 (4)**
55-59 years	20 (2)	152 (4)	34 (5)	20 (3)	15 (4)	2 (4)	**242 (3)**
60-64 years	14 (1)	113 (3)	28 (4)	15 (3)	12 (4)	1 (3)	**184 (3)**
65-69 years	9 (1)	87 (2)	22 (3)	11 (2)	9 (3)	1 (2)	**139 (2)**
70+ years	11 (1)	109 (3)	40 (6)	15 (3)	15 (5)	2 (4)	**192 (3)**
All ages	1056 (90)	3513 (85)	542 (79)	499 (86)	265 (80)	32 (85)	**5906 (85)**
One condition only							
<15 years	8 (1)	21 (1)	1 (0)	1 (0)	0 (0)	0 (0)	**31 (0)**
15-49 years	59 (5)	215 (5)	29 (4)	26 (5)	11 (3)	2 (4)	**342 (5)**
50-54 years	9 (1)	52 (1)	9 (1)	7 (1)	4 (1)	0 (1)	**81 (1)**
55-59 years	8 (1)	50 (1)	11 (2)	7 (1)	6 (2)	0 (1)	**82 (1)**
60-64 years	7 (1)	45 (1)	12 (2)	6 (1)	6 (2)	0 (1)	**77 (1)**
65-69 years	6 (0)	41 (1)	12 (2)	5 (1)	6 (2)	0 (1)	**71 (1)**
70+ years	8 (1)	67 (2)	30 (4)	11 (2)	13 (4)	1 (3)	**130 (2)**
All ages	104 (9)	491 (12)	105 (15)	63 (11)	47 (14)	4 (12)	**814 (12)**
Multiple (two or more) conditions							
<15 years	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	**0 (0)**
15-49 years	5 (0)	20 (0)	3 (0)	3 (0)	1 (0)	0 (0)	**32 (0)**
50-54 years	2 (0)	11 (0)	2 (0)	1 (0)	1 (0)	0 (0)	**17 (0)**
55-59 years	2 (0)	14 (0)	3 (0)	2 (0)	2 (0)	0 (0)	**22 (0)**
60-64 years	2 (0)	16 (0)	4 (1)	2 (0)	2 (1)	0 (0)	**27 (0)**
65-69 years	2 (0)	18 (0)	5 (1)	2 (0)	3 (1)	0 (0)	**31 (0)**
70+ years	5 (0)	45 (1)	22 (3)	7 (1)	9 (3)	1 (2)	**89 (1)**
All ages	19 (2)	124 (3)	39 (6)	18 (3)	18 (5)	1 (4)	**218 (3)**
At increased risk of severe COVID-19 illness							
At least one condition	123 (10)	614 (15)	144 (21)	81 (14)	64 (20)	6 (15)	**1032 (15)**
Plus others older than:							
50 years	204 (17)	1269 (31)	305 (44)	166 (29)	131 (40)	13 (33)	**2088 (30)**
55 years	178 (15)	1074 (26)	268 (39)	142 (24)	116 (35)	11 (29)	**1789 (26)**
60 years	157 (13)	923 (22)	234 (34)	122 (21)	101 (31)	10 (25)	**1547 (22)**
65 years	136 (12)	722 (17)	187 (27)	97 (17)	83 (25)	7 (19)	**1233 (18)**
70 years	131 (11)	681 (17)	175 (25)	92 (16)	77 (24)	7 (18)	**1163 (17)**

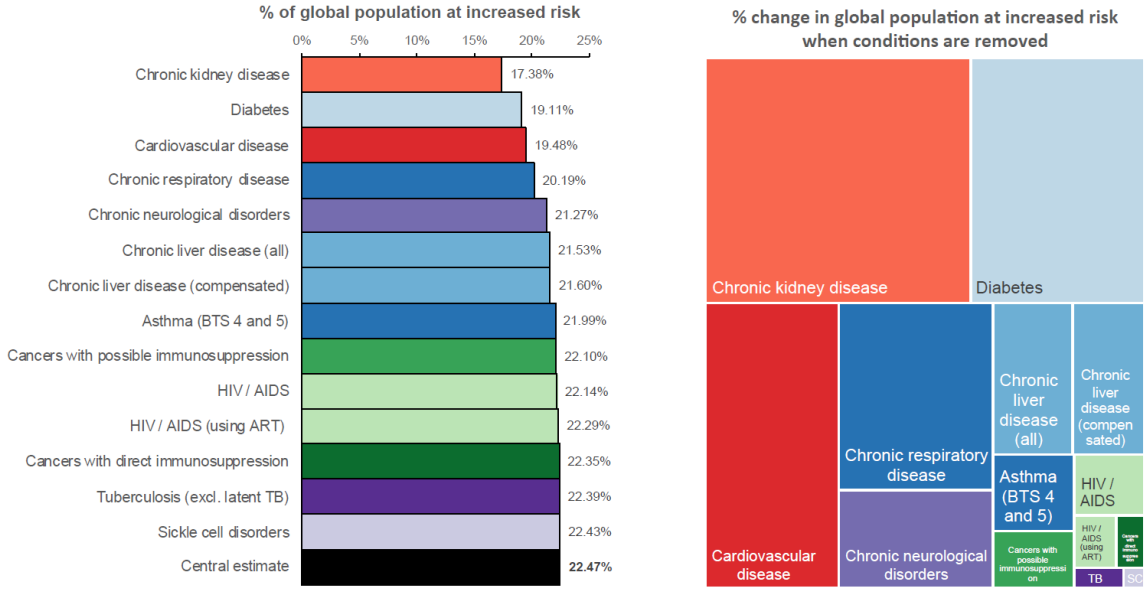
Table 5. High estimates of the number of individuals in millions (% of total population) at increased risk of severe COVID-19 illness by age, number of conditions, region and choice of age threshold

Assumptions:

- Population estimates: Upper 95% CI
- Disease prevalence: Upper 95% CI
- Ratio (observed vs expected % with 1+ conditions): 1.0
- Multimorbidity among those with 1+ conditions: Upper 95% CI

	Africa	Asia	Europe	Latin America and the Caribbean	Northern America	Oceania	**Global**
No conditions							
<15 years	577 (38)	1140 (22)	126 (16)	169 (23)	72 (18)	10 (23)	**2093 (24)**
15-49 years	560 (37)	2059 (40)	279 (34)	308 (43)	156 (38)	17 (38)	**3378 (39)**
50-54 years	23 (2)	175 (3)	31 (4)	22 (3)	14 (3)	1 (3)	**267 (3)**
55-59 years	16 (1)	126 (2)	26 (3)	16 (2)	12 (3)	1 (3)	**197 (2)**
60-64 years	10 (1)	83 (2)	18 (2)	11 (1)	8 (2)	1 (2)	**131 (2)**
65-69 years	5 (0)	56 (1)	12 (1)	6 (1)	5 (1)	1 (1)	**85 (1)**
70+ years	4 (0)	48 (1)	12 (1)	6 (1)	4 (1)	1 (1)	**73 (1)**
All ages	1193 (80)	3686 (72)	504 (62)	538 (74)	271 (66)	32 (71)	**6224 (72)**
One condition only							
<15 years	26 (2)	61 (1)	4 (0)	4 (1)	2 (0)	0 (1)	**96 (1)**
15-49 years	139 (9)	509 (10)	66 (8)	61 (8)	27 (7)	4 (8)	**807 (9)**
50-54 years	18 (1)	108 (2)	18 (2)	14 (2)	9 (2)	1 (2)	**167 (2)**
55-59 years	16 (1)	100 (2)	22 (3)	13 (2)	11 (3)	1 (2)	**162 (2)**
60-64 years	13 (1)	88 (2)	23 (3)	12 (2)	12 (3)	1 (2)	**148 (2)**
65-69 years	10 (1)	77 (1)	21 (3)	10 (1)	11 (3)	1 (2)	**130 (2)**
70+ years	13 (1)	107 (2)	43 (5)	17 (2)	20 (5)	2 (4)	**201 (2)**
All ages	236 (16)	1050 (20)	197 (24)	131 (18)	90 (22)	9 (20)	**1712 (20)**
Multiple (two or more) conditions							
<15 years	3 (0)	8 (0)	1 (0)	1 (0)	0 (0)	0 (0)	**13 (0)**
15-49 years	26 (2)	102 (2)	14 (2)	12 (2)	6 (1)	1 (2)	**161 (2)**
50-54 years	6 (0)	38 (1)	6 (1)	5 (1)	3 (1)	0 (1)	**58 (1)**
55-59 years	7 (0)	42 (1)	9 (1)	6 (1)	4 (1)	0 (1)	**68 (1)**
60-64 years	7 (0)	45 (1)	12 (1)	6 (1)	6 (1)	0 (1)	**75 (1)**
65-69 years	7 (0)	48 (1)	13 (2)	6 (1)	7 (2)	0 (1)	**82 (1)**
70+ years	14 (1)	118 (2)	52 (6)	19 (3)	23 (6)	2 (4)	**228 (3)**
All ages	69 (5)	400 (8)	107 (13)	55 (8)	49 (12)	4 (9)	**685 (8)**
At increased risk of severe COVID-19 illness							
At least one condition	305 (20)	1450 (28)	304 (38)	186 (26)	139 (34)	13 (29)	**2398 (28)**
Plus others older than:							
50 years	362 (24)	1937 (38)	404 (50)	247 (34)	182 (44)	18 (39)	**3150 (37)**
55 years	339 (23)	1762 (34)	373 (46)	225 (31)	168 (41)	16 (36)	**2884 (33)**
60 years	323 (22)	1637 (32)	346 (43)	209 (29)	156 (38)	15 (33)	**2686 (31)**
65 years	329 (22)	1634 (32)	369 (46)	213 (29)	169 (41)	16 (35)	**2729 (32)**
70 years	319 (21)	1557 (30)	348 (43)	203 (28)	158 (39)	15 (33)	**2599 (30)**

Figure 2. Percentage of global population at any increased risk of severe COVID-19 disease (left panel) and % change (right panel) when conditions are removed one at a time



The black shaded bar at the bottom represents the central estimate of the global population that are at increased risk. All other bars above show how this value changes when each of the conditions are removed one at a time. The most influential conditions are at the top of the bar chart and represent larger areas on the map shown on the right side.

References

1. 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.
2. 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.
3. 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.
4. ECA. COVID-19 in Africa. Protecting lives and economies. Available at: https://www.uneca.org/publications/covid-19-africa-protecting-lives-and-economies. 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. 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. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7194638/pdf/main.pdf. *International Journal of Infectious Diseases* 2020; **94**: 91-5.
7. 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**.
8. Petrilli C, Jones S, Yang J, et al. Factors associated with hospitalization and critical illness among 4,103 patients with COVID-19 disease in New York City. Available at: https://www.medrxiv.org/content/10.1101/2020.04.08.20057794v1. 2020.
9. Docherty A, Harrison E, Green C, 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.
10. Williamson E, Walker A, Bhaskaran K, et al. OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. The OpenSAFELY Collaborative, Available at: medRxiv 2020.05.06.20092999; Available at: https://doi.org/10.1101/2020.05.06.20092999. 2020.
11. Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis* 2020.