ASSESSMENT OF PERSONAL VULNERABILITY TO COVID-19

Sources of evidence and methods leading to adopted risk estimates

UPDATED 14 DECEMBER 2021

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Prepared on behalf of, and with guidance from, the Joint Occupational Health COVID-19 Group.

OVERVIEW

This report describes the sources of evidence underpinning the assessments of vulnerability in Table 1 of our guidance, and the methods by which adopted estimates of risk were derived. It is divided into three sections.

The first section outlines our overall approach, and summarises the main sources of evidence that have been used. The second describes the derivation of risk estimates for specific risk factors. The third sets out the methods used to translate estimates of relative risk into a more naturally interpretable measure that can be summed across risk factors to give an overall indication of personal vulnerability to Covid-19.

We aim to provide the best assessments of risk that are possible from available data, but inevitably, there are scientific uncertainties. New evidence may sometimes indicate that an earlier risk estimate was sub-optimal, and should be modified. The guidance on vulnerability is therefore periodically updated and refined as relevant new evidence become available. To make clear how this process has occurred, in each section of the report, we first describe the methods used in our initial assessments of risk (as at 20 May 2020), and then report on findings at successive updates, and any changes in adopted risk estimates that have ensued.

SECTION ONE: OVERALL APPROACH AND SOURCES OF EVIDENCE

INITIAL ASSESSMENT: 20 MAY 2020

We wished to assess and compare risks of fatality in people who contract SARSCov-2 infection, according to their age, sex, ethnicity, smoking habits, and various comorbidities. In preliminary searches of the published literature, no evidence could be found on risks of fatality in representative samples of all people infected by the virus (including those with asymptomatic infection). However, analyses of mortality from Covid-19 in the general population could be expected to provide good proxy measures of relative risk, provided the likelihood of contracting infection did not vary importantly according to the risk factors under consideration (for example because of selective shielding by people with certain comorbidities). In addition, estimates of risk might be possible by combining data on fatality rates by comorbidity in patients admitted to hospital because of Covid-19 with information about the prevalence of comorbidities in such patients as compared with the general population.

Because of the urgency to improve on earlier advice, which necessarily was based largely on consensus of expert opinion, we initially sought reports that would provide the strongest scientific evidence relevant to the UK, without attempting systematically to search for, and review, all published evidence that might bear on the risks that we were trying to characterise. In this respect, one paper stood out as particularly suited to our purpose.

That report, from the OpenSAFELY (OS) collaborative, presented first results from a cohort study of more than 17 million adults registered with English general practices and followed up from 1 February 2020 to the earlier of death or 25 April 2020 [1]. Multivariate Cox regression was used to estimate mutually adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for death in hospital with confirmed Covid-19 (ascertained by linkage to a national notification system) in relation to risk factors ascertained from pseudonymised individual primary care records. Data on other deaths in the cohort (needed for censoring of follow-up) were obtained by linkage to data held by the Office for National Statistics (ONS). A secondary analysis, which censored follow-up at 6 April 2020, allowed exploration of the possibility that HRs for some comorbidities in the main analysis underestimated vulnerability because, in response to advice from the UK government at the end of March, people with those diseases had selectively shielded themselves from exposure to infection. As well as sex, age, ethnicity, smoking habits and multiple comorbidities, analyses adjusted for deprivation (using an index graded to five levels) and for the administrative region of the patient's general practice (to allow for varying rates of infection in different parts of the country).

This study had unique strengths. It included a substantial proportion of the adult population nationally, and was based on more than 5000 deaths attributed to Covid-19. Moreover, information about risk factors came from data recorded before the onset of infection, reducing the potential for bias in relation to the outcome. Limitations included restriction of the outcome to deaths in hospital (some cohort members may have died from Covid-19 elsewhere), and incomplete data on some risk factors (although the extent of missing

information was generally small). A further limitation when applying its findings in our risk model was that some of the categories of comorbidity which it analysed were heterogeneous. For example, chronic pulmonary disease aggregated chronic obstructive pulmonary disease (COPD) of varying severity with other lung diseases such as cystic fibrosis and bronchiectasis; and there was no distinction between Type 1 and Type 2 diabetes.

These weaknesses do not detract seriously from the value of the OS study. Nevertheless, it was important to check the plausibility of its findings, using data from other studies. This was done using several independent sources of information.

The ONS has published data on mortality from Covid-19 (as the underlying cause of death) by sex and age in England and Wales during March 2020 [2]. These death rates make no allowance for effects of comorbidities, the prevalence of which may vary by age, and between men and women. However, they provide a benchmark against which more fully adjusted estimates of relative risk by sex and age can be compared.

Another useful resource was a report from the ISARIC study on outcomes, including mortality, in a cohort of 16,749 patients with Covid-19 admitted to hospitals in England, Wales and Scotland during 6 February 2020 to 18 April 2020 (28% of all such admissions nationally during that period) [3]. Within the cohort, 49% had been discharged, 33% had died, and 17% continued to receive care at the date of reporting. The prevalence of various comorbidities in the cohort was explored, and multivariate Cox regression was used to explore risk of death in relation to age, sex and selected comorbidities. An important limitation was the ascertainment of comorbidities from clinical records, which is unlikely to have been complete or uniform across the cohort.

Data were also available on the prevalence of comorbidities by sex and age in samples of people (intended to be nationally representative) from recent rounds of the Health Survey for England [4-7]. Although these data predated the ISARIC study, were only from England, and did not apply the same diagnostic criteria and methods of ascertainment, they could be used to calculate an approximate predicted prevalence of comorbidities in the ISARIC cohort. Comparison of the observed and expected prevalence then gave an indication, albeit crude, of the age- and sex-adjusted relative risk of being hospitalised with Covid-19 according to comorbidities. When combined with HRs for death following admission to hospital, this allowed approximate estimation of relative risks of mortality from Covid-19 among people with the comorbidity in the general population.

Plans for further investigation

We recognise that the checks which we have carried out on the plausibility of risk estimates from the OS study, are limited in scope, and that further reports, of varying degrees of relevance and importance, have still to be identified and reviewed. We intend to undertake this task more systematically over the next few months. In addition, further reports are expected on the OS study, and on another similar but smaller dataset. Findings from such reports will be reviewed as they become available, and risk estimates revised if the balance of evidence has changed. In particular, we hope that evidence-based risk estimates may become possible for more specific sub-divisions of some of the categories of comorbidity.

UPDATE 1: 26 MAY 2020

In the interval since this report was first compiled, an updated version of the ISARIC report has been published following peer-review [1.1]. Changes included extension of recruitment and follow-up, so that analysis was now based on 20,133 hospitalised patients. By the end of follow-up, 8,199 (41%) had been discharged alive, 5165 (26%) had died, and 6769 (34%) were still receiving care.

In addition, two important new papers have been published [1.2, 1.3], which focus principally on diabetes, but provide information also about other risk factors. They report on related population-based cohort studies, one of all patients registered with English general practices, and the second of the subset of that population with a registered diagnosis of diabetes.

In the first study (by Barron and colleagues [1.2]), a cohort of more than 61 million patients (all ages) who were registered with English general practices at 19.2.20, were followed for deaths from Covid-19 in hospital during 1 March to 11 May of that year. The main focus was risks associated with different types of diabetes, information about which was ascertained from a database (the National Diabetes Audit (NDA)), updated in 2018/19, which abstracts data from general practice and specialist records. The cohort included 263,830 patients with Type 1 diabetes, 2,864,670 with Type 2 diabetes, and 41,750 with other forms of the disease including maturity onset diabetes of the young. Information about other risk factors, and on deaths in hospital from Covid-19 (n = 23,804), was obtained by linkage to other national datasets. Multivariate logistic regression was used to estimate odds ratios for cumulative mortality from Covid-19 over the study period in relation to age, sex, ethnicity, social deprivation (five levels), region (seven categories), diabetes (broken down by type), and in some analyses, coronary heart disease, cerebrovascular disease and heart failure.

The investigation differed from the OS study in several notable ways.

- Although the cohort will have included members of the OS cohort, it was substantially larger and extended to children as well as adults
- Follow-up was for longer, and from 28 April, deaths from Covid-19 included some in which the diagnosis was made on clinical grounds, but without confirmation by testing
- Ascertainment of comorbidity was limited to diabetes and cardiovascular disease, and did not include BMI or chronic kidney disease, both of which are related to diabetes
- Ethnicity was determined from a different source (the Bridges to National Population Segmentation dataset)
- Diabetes was ascertained from the NDA

The second new paper (Holman et al. [1.3]) describes an investigation of risk factors for death related to Covid-19 (i.e. in which Covid-19, with or without confirmation by testing, was registered as the underlying or a contributing cause of death) among cohorts of patients in England with Type 1 (n = 265,090) and Type 2 (n = 2,889,210) diabetes, identified from the NDA. During follow-up to 1 May 20, there were 9,795 such deaths, including 9,341 in which Covid-19 was recorded as the underlying cause. For this analysis, which was restricted to

patients with diabetes, data were available on a wider range of risk factors, including also most recent HbA1c level as a measure of diabetic control, estimated glomerular filtration rate (eGFR) (recorded between 1.1.19 and 31.12.19), BMI (from measurements during 2017-19), smoking habits, and prescribed treatment for hypertension. Analysis used multivariate Cox proportional hazards to estimate HRs.

Despite the overlap of these new cohort studies with the OS study sample, they provide important new information. In particular, we have used them to check on several risk estimates from the OS study, to generate risk estimates for a finer classification of diabetes by type and level of control, and to explore our assumption that relative risks for diabetes multiply those from other risk factors when they occur in combination.

A description of those checks and additional risk estimates is included in the assessments of evidence on specific risk factors.

UPDATE 2: 10 JUNE 2020

In the interval since the last update, we have identified several further papers that bear consideration.

The first report describes a national analysis of hospitalisation and mortality in the first 9,159 cases of Covid-19 confirmed by PCR testing in Denmark [2.1]. Diagnoses were made during 27 February to 30 April 2020, and cohort members were followed for mortality with censoring at the earlier of May 15 or 30 days after their first positive PCR test. In a multivariate logistic regression analysis, odds ratios for mortality were estimated according to age sex and various comorbidities. For our purposes, the evidence from this investigation is not as strong as that on which our risk model currently is based – it comes from a different country; selection for PCR testing, the criteria for which changed over the study period, may have rendered the cohort unrepresentative of the wider population in some of the associations of mortality with risk factors; and risk estimates for comorbidities were not so fully adjusted. Nevertheless, it offers some support regarding the relative importance of different risk factors. Thus, risk was higher for diabetes where it was treated with insulin (OR 2.0 vs. 1.3 for other glucose-lowering drugs), higher for heart failure (OR 1.7) than for ischaemic heart disease (OR 1.2), relatively high for hospital-diagnosed kidney disease (OR 2.0), and higher for organ transplantation (OR 2.7) than for almost all of the comorbidities examined. Interestingly, the highest risk was for major psychiatric disorder treated by antipsychotic drugs (OR 3.6, 95% CI 2.5 – 5.2), a factor on which data from the UK are not yet available. For hypertension, the OR was 1.3 (95%CI 1.1-1.7), which supports the view that after adjustment for other factors (less complete in this investigation than in the OS study [1] or that by Holman and colleagues [1.3]) any risk from the disorder as a whole is likely to be fairly small (this does not preclude the possibility of a higher risk in one or more sub-categories of hypertension). On balance, we do not think the findings of this Danish study provide grounds for changing our adopted risk estimates.

Using a publicly available national dataset, Giannouchos and colleagues have used multivariate logistic regression to assess risk factors for adverse outcomes (intensive care unit admission, mechanical ventilation or death) in 89,756 people in Mexico who tested positive for Covid-19 [2.2]. Applicability of the findings to our risk model in the UK is limited for several reasons. The ethnic mix of the study population was different; the outcome was not restricted to death; indications for testing may have not have been completely standardised, raising the possibility of bias in risk estimates; and the stratification of age was crude (with only three levels, one of which was children). Therefore the results do not warrant any changes in our adopted risk estimates. They do, however, support the view that smoking is not an important determinant of vulnerability, and that any overall risk associated with hypertension is small.

A case-control study among beneficiaries of the regional Health Service in Lombardy, Italy, included a comparison of 617 cases with critical (requiring assisted ventilation) or fatal Covid-19 and 2,969 controls, matched for sex, age and community, from the general population [2.3]. After adjustment for several comorbidities and other medication, there was no significant elevation of risk in relation to prescription in the previous calendar year (2019) of angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs),

calcium-channel blockers, diuretics or beta-blockers. The highest OR (1.15, 95%CI 0.91-1. 44) was for calcium-channel blockers.

Another paper describes characteristics associated with hospitalisation in a series of 600 Covid-19 patients with rheumatic diseases from 40 countries [2.4]. The most common of the rheumatic comorbidities in the study sample were rheumatoid arthritis (38%), SLE (14%), psoriatic arthritis (12%) and axial and other spondyloarthritis (8%). Forty six percent of patients were admitted to hospital. After adjustment for age (in two strata), four types of comorbidity, smoking (ever vs. never), and rheumatic disease diagnosis, the risk of hospitalisation was elevated in patients treated with glucocorticoids equivalent to ≥10 mg/day of prednisone (OR relative to no corticosteroids 2.05, 95%CI 1.06-3.96). However, in those treated by biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs), alone or in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), risk was lower than in those receiving no DMARDs. There was a suggestion of higher risk in patients with SLE as compared with rheumatoid arthritis (OR 1.80, 95%CI 0.99-3.29).

As a source of evidence for our purposes, this report has several major limitations. The data come from multiple countries, and relationships between variables cannot necessarily be extrapolated to the UK. There is no clear statement of the criteria by which potentially eligible patients were selected for inclusion in the case series. Their high rate of hospitalisation suggests that they were not typical of all Covid-19 patients with rheumatic diseases, and it is possible that decisions to enrol them were influenced by their clinical course after Covid-19 was diagnosed. The outcome was hospitalisation rather than mortality, and because its prevalence was high, ORs will have been further from the null than corresponding relative risks. For example, with an overall 46% of patients admitted to hospital, a crude OR of 2 in the 64 patients using high doses of corticosteroids as compared with the 403 not using corticosteroids would correspond to a relative risk of only 1.4. Also, control for potentially important covariates was limited – for example, only two strata of age were distinguished. For these reasons, the data cannot be used to refine our adopted risk estimate for rheumatic diseases. They do, however, suggest that among people with inflammatory arthritis, risk may be higher in those treated by high doses of oral corticosteroids, while there is no additional risk from use of b/tsDMARDs.

Five further papers were judged to provide no evidence of note in relation to our estimates of risk [2.5-2.9].

UPDATE 3: 29 JUNE 2020

New publications identified since our last report do not provide a basis on which to change the adopted risk estimates in our model, but several provide information that is relevant to the assessment of vulnerability to Covid-19.

Most notable is a paper in which McKeigue and colleagues report a matched case-control study of 2,755 patients in Scotland with severe Covid-19 (i.e. leading to intensive care or death within 28 days of a first positive test for the disease), who were diagnosed up to 13 May 2020 [3.1]. Each case was compared with seven controls, of the same sex and age, who were selected from the population register of the same primary care practice. Previous comorbidities and treatments were ascertained from diagnostic codes for hospital admissions in the past five years and prescription records over the past 9 months. In addition, diabetes was determined by linkage to a national database. Associations with risk factors were assessed by conditional logistic regression. The mutually adjusted ORs that were estimated are not directly comparable to the HRs in the OS study because the range and specification of the variables included in the regression models differ. For example, the multivariate analyses by McKeigue and colleagues aggregated chronic kidney disease with having received a transplant, and included residence in a care home as a covariate, as well as receipt of any prescribed medicine in the past 9 months, and any hospital admission in the past five years, but not ethnicity or BMI. For this reason, and also because of the smaller sample size, we do not think that the risk estimates are sufficiently different from those that we have adopted to call them into question.

It is, however, notable that for most comorbidities, risk estimates were higher when analyses were restricted to participants aged < 60 years (Table 3.1). This may in part reflect differences in case-mix. For example, among the category “chronic kidney disease or transplant recipient”, there may have been proportionately more transplant recipients at younger ages. Nevertheless, the finding suggests that for some comorbidities there could be important interactions between age and other risk factors, and that our current model, which is based on analyses for all adults, may underestimate relative risks in people of working age. We hope that further analyses of the OS or similar cohorts, restricted to working ages, will soon become available. Meanwhile, the finding emphasises the need for caution in interpretation of our adopted risk estimates.

Table 3.1 Odds ratios from multivariate analyses of case-control study by McKeigue et al stratified by age

Risk factor	Age <60 years		All age groups	
	[a]OR	(95%CI)	[a]OR	(95%CI)
Type 1 diabetes	3.20	(1.61-6.35)	2.19	(1.41-3.42)
Type 2 diabetes	2.53	(1.79-3.57)	1.62	(1.44-1.81)
Other/unknown type diabetes	3.35	(0.75-14.99)	1.70	(0.91-3.19)
Ischaemic heart disease	0.97	(0.57-1.62)	1.10	(0.97-1.24)
Other heart disease	1.81	(1.21-2.72)	1.39	(1.24-1.55)
Asthma or chronic airway disease	1.58	(1.20-2.08)	1.54	(1.39-1.71)
Chronic kidney disease or transplant recipient	17.7	(4.3-73.6)	4.27	(2.94-6.21)
Neurological (except epilepsy) or dementia	4.04	(2.41-6.78)	1.98	(1.73-2.27)
Liver disease	4.30	(1.60-11.57)	2.17	(1.38-3.40)
Immune deficiency or suppression	0.86	(0.30-2.52)	1.30	(0.82-2.08)

[a]Risk estimates are adjusted also for residence in a care home, any prescription in past nine months and any hospital admission in past five years

In addition to the paper by McKeigue et al, other recent papers report on risks of death by ethnicity in patients admitted to British hospitals with Covid-19 [3.2,3.3], risk of hospitalisation for confirmed Covid-19 by ethnicity in the Biobank cohort [3.4], relative risks of Covid-19-related mortality among sub-cohorts of the OS study sample with COPD and asthma according to their use of inhaled corticosteroids [3.5], risk of mortality among cancer patients with test-positive Covid-19 according to recent treatment [3.6], relative frequency of severe outcomes in Covid-19 patients with different types of rheumatic disease and with no rheumatic disease [3.7], and estimated infection fatality rates in Belgium [3.8]. Relevant findings from these investigations, and the conclusions that we draw from them, are set out in the sections that follow on specific risk factors and estimation of individual vulnerability.

Two other papers were reviewed, but did not impinge on our assessment of risk [3.9,3.10].

UPDATE 4: 16 JULY 2020

The most telling new publication since our last update describes an updated analysis of the OS cohort [4.1], which differs in several ways from the analysis that was previously reported.

Most important is a substantial increase in the number of Covid-19 deaths that were analysed (10,926 as compared with 5,683). This is attributable in part to slightly longer follow-up (up to 6 May), but mainly to inclusion of all deaths in which confirmed or suspected Covid-19 was mentioned anywhere on the death certificate, irrespective of whether death occurred in hospital or elsewhere (ascertained through linkage with ONS data). The extra deaths occurred disproportionately at older ages and in women.

In addition, the cohort was slightly smaller (17,278,392), mainly because patients with missing data on social deprivation were excluded. There were also a few refinements in the specification of several risk factors. In the main analysis, chronic renal failure was graded to two levels, and a secondary analysis assessed risk in relation to a history of kidney dialysis or end-stage renal failure. Brain tumours appear no longer to have been included in "Other neurological disease", and secondary analyses examined more detailed associations with ethnicity and interactions between hypertension and age.

As a consequence of these changes and additions, there were some notable changes in the results. The increase in risk with age was a little steeper (a relative risk of approximately 2.8 for each additional 10 years in the fully adjusted analysis). The relative risk for men as compared with women was reduced (1.59, 95%CI 1.53-1.65), although interestingly, it was higher in a sensitivity analysis with follow-up censored at 6 April 2020 (HR 1.90, 95%CI 1.75-2.05). It is unlikely that this difference can be ascribed to random sampling variation, and it suggests that as the epidemic evolved, levels of exposure in men relative to women may for some reason have reduced. Some risk estimates by ethnicity were slightly lower, as were those for obesity, asthma and several other comorbidities, although this may in part reflect a greater effect of selective shielding with more prolonged follow-up. The HR for liver disease was somewhat higher.

The implications of the new findings for our adopted risk estimates are discussed in Sections 2 and 3.

A second new paper describes a case-control study in London, comparing 872 inner city residents admitted to hospital with confirmed Covid-19 and 3,488 community controls matched for sex and age [4.2]. After adjustment for deprivation and comorbidities, admission for Covid-19 was significantly associated with black but not Asian ethnicity (ORs 2.28, 95%CI 1.87-2.79, and 1.20, 95%CI 0.86-1.66 relative to white ethnicity). The paper also reports a linked cohort study of 1,827 adults consecutively admitted to hospital with Covid-19. Age, male sex, and Asian (adjusted HR 1.54, 95%CI 0.98-2.41 vs. white) but not black (adjusted HR 0.84, 95%CI 0.63-1.11) ethnicity were associated with in-hospital mortality. These results are broadly consistent with our currently adopted risk estimates for black and Asian ethnicity.

Two papers present data that bear on estimation of absolute case-fatality rates corresponding to Covid-age (see Section 3). The first, which applied a mathematical model

to data on 191,392 laboratory-confirmed Covid-19 cases and 201,141 confirmed and probable Covid-19 deaths in New York city residents during 1 March to 16 May 2020, estimated infection fatality rates (IFRs) of 0.12%, 0.94% and 4.67% at ages 25-44, 45-64 and 65-74 years respectively [4.3]. The second, based on repeated cross-sectional surveys of population-representative households in England, found that among individuals who tested positive, 61% (95% credibility interval 53% to 69%) reported no symptoms, stably over time [4.4].

In a nationally representative prevalence survey of SARS-CoV-2 virus swab positivity in England (response rate 31%), during 1 May to 1 June 2020, the test-positive rate declined from 0.17% at age 25-34 years to 0.10% at age 55-64 [4.5]. Also, people with Asian (predominantly South Asian) ethnicity were more likely to be test positive than whites (adjusted OR 1.7, 0.86-2.5). Because of the low response rate, caution is needed in interpretation of these findings, but they highlight the potential for bias in risk estimates when mortality rates in the general population are used to estimate relative vulnerability. In particular, relatively lower exposure to infection at older ages could lead to underestimation of the vulnerability associated with increasing age. The study also found that among people who had tested positive, 69% (95%CI 61% to 76%) had been symptom-free for 7 days before the test.

A large population-based cohort study in Catalonia explored risk factors for being diagnosed with Covid-19, hospitalised with the disease, and for subsequent death among those diagnosed and hospitalised [4.6]. However, many of the people who died of Covid-19 had not been admitted to hospital, many of the hospitalised patients did not have an earlier out-patient diagnosis of Covid-19, and risks of mortality in relation to risk factors in the general population are not presented. Therefore, the findings cannot be used to estimate relative risks of vulnerability.

Four other reports, all from non-UK countries, assess relative risks of mortality among patients with diagnosed Covid-19 or hospitalisation for the disease [4.7 -4.10]. However, they cannot be used to estimate vulnerability in relation to risk factors because of uncertainties about the extent of bias from differential selection for testing or criteria for hospital admission.

An analysis of mortality by ethnicity in patients with a positive COVID-19 test in England from 1 March to 21 April, was limited to deaths in hospitals, and did not adjust for comorbidities [4.11].

UPDATE 5: 27 JULY 2020

In originally developing the Covid-age tool, we made an assumption that relative risks from different risk factors multiply, which we considered reasonable in the absence of persuasive evidence to the contrary (Section 3, paragraph 3). Since then, we have noted that an analysis of Scottish data by McKeigue and colleagues [3.1], found that that for most comorbidities, risk estimates were higher when analyses were restricted to participants aged < 60 years (Update 3). And in update 4, we reported new evidence from the OS study [4.1], indicating an important interaction of hypertension with age, with higher relative risk for hypertension in young adults than at older ages. This led us to add hypertension to our table of risk estimates, for the working age population.

We have now become aware of further indications that such interactions with age may apply to a number of other comorbidities. Quantitative data on this have not yet been published, but pending any such publication, we think it is worth highlighting that the vulnerability associated with some of the comorbidities in Table Z3 may be higher at young ages.

UPDATE 6: 13 AUGUST 2020

When we first developed Covid-age as an evidence-based tool to assist health professionals in the assessment of workers' personal vulnerability to Covid-19, we identified various scientific limitations, including uncertainties about interactions between variables as markers for risk of fatality [6.1]. In the absence of persuasive evidence to the contrary, we assumed that when two or more risk factors were present in combination, their relative risks would multiply – that being the default assumption of most regression analyses, including those on which the tool was based (see paragraph 3 of Section 3). However, we recognised that relationships might depart from this frequently observed pattern.

Subsequently, in Update 1, we noted evidence suggesting that the combined effects of obesity with Type 2 (but not Type 1) diabetes might be less than multiplicative (Table D3), and in Update 3 that data from Scotland indicated that for most comorbidities, relative risk estimates were higher when analyses were restricted to participants aged < 60 years. However, at that stage, we did not have sufficiently reliable quantitative data to allow for interactions of other risk factors with age.

It was only when an updated report from the OS study included risk estimates for hypertension broken down by age [4.1], that we were able to incorporate any age-specific risk estimates into our model (in Update 4). For other risk factors, however, we remained reliant on published summary estimates of relative risk for adults of all ages.

At our request, the OS team have now published (as an online supplement to their Nature paper) further analyses: a) restricted to people aged 18-69 years; and b) exploring possible interactions with age through separate regression models (one for each risk factor) incorporating interaction terms [6.2]. This showed that for some comorbidities (e.g. CKD and haematological malignancy), there were strong interactions, with higher RRs at younger ages. In contrast, for other comorbidities (e.g. mild asthma, inflammatory arthritis), there was no clear pattern of interaction with age.

Some of the interactions with age may be attributable in part to differences in case-mix. For example, among the haematological malignancies, relative to the acute leukaemias, chronic lymphatic leukaemia is more prevalent at older ages. In addition, interactions will reflect the biological mechanisms underlying the steep rise in vulnerability to Covid-19 with increasing age, and those linking vulnerability to each comorbidity. For the most part, these mechanisms are as yet poorly understood. It should be noted, however, that although relative risks associated with some comorbidities are higher at younger ages, the absolute risks in those affected still increase with age, even if more slowly than in other people. This is because the increase in risk with age is so steep.

In response to the new evidence on interactions with age, we have substantially revised and refined our risk model, where appropriate specifying estimated relative risks (and their equivalence to added years of age) by individual year of true age. The results reported from the OS study are for age strata and not by individual year of age. However, we wished to avoid anomalies at the boundaries of age strata such that, for example, a man of 39 with CKD had a higher Covid-age than a man of 40 with similar CKD. We had no biological basis on which to predict patterns of age interaction for different comorbidities, and the published

risk estimates for age strata were liable to substantial statistical uncertainty, especially at younger ages (because there have been few deaths from Covid-19 in young adults). Therefore, we opted to estimate age-specific relative risks by a manual process that entailed interpolation between, and minor extrapolation from, the results for age strata, with minor smoothing to allow for a small proportion of apparently anomalous risk estimates. The smoothing was performed not only to trends across age strata, but also, where appropriate, to trends by level of severity of a comorbidity within individual age strata.

In the context of other uncertainties in the risk model, we believe that this simplification of methods is justified. However, Section 2, which describes the process in more detail for each risk factor, presents the reported results from the OS study as well as the modelled RRs, allowing readers to judge how well the method has worked.

As a consequence of the incorporation of age interactions, the method of calculating Covid-age becomes a little more complicated, with the need to specify the added years for many comorbidities according to a person's true age. Table Z6 can be used for that purpose, if the user first specifies a patient's true age, and then from the column of the table corresponding to that age, reads off the added (or subtracted) years of age for each risk factor that applies. However, to make the task easier for users, we plan to install an online app on the ALAMA website. This will simplify the calculation, but continue to indicate the added years for each risk factor so that clinicians can make modifications based on clinical judgement where they are deemed appropriate.

It should be noted that while the risk model now allows for differences in relative risks by age, the possibility remains that relative risks do not always multiply when other risk factors occur in combination. In particular, multiplying relative risks (adding equivalent age increases) may overestimate vulnerability for some combinations of comorbidity such as obesity and Type 2 diabetes. However, we do not currently have empirical data to address this question.

In addition to the supplementary report from the OS study, we have identified three other new papers that are worth highlighting, although they do not warrant any additional changes to our risk model.

In a cohort study of patients registered with general practices in England that contributed to the QResearch database, 8,275,949 men and women aged 20-99 were followed from 1 January 2020 to the earliest of death, leaving their general practice, admission to intensive care with Covid-19, or 27 April [6.3]. Cox regression was used to estimate HRs for admission to intensive care in relation to use of ACE inhibitors and angiotensin receptor blockers (ARBs) after adjustment for sex, age, ethnicity, region, social deprivation, body mass index (BMI) and various comorbidities. No elevation of risk was found for either category of drug, either in the full cohort, or with restriction of analysis to patients with hypertension or congestive cardiac failure. Interpretation of HRs for other risk factors is complicated by uncertainties about clinical criteria for admission to intensive care, which particularly at older ages, may not always have been provided, even when Covid-19 was severe. When this is taken into account, the findings seem reasonably consistent with our currently adopted risk estimates.

A study of 269,070 members of the UK Biobank cohort used logistic regression to examine associations of various pre-existing comorbidities with death up to 26 April 2020 following a positive test for coronavirus while a hospital in-patient in England [6.4]. Elevations of risk were found in relation to disorders such as diabetes and COPD, but the findings do not have significant implications for our risk model because: a) the study was restricted to participants aged 65 years or older; b) the total number of deaths was small (n = 141); c) the range of covariates analysed was smaller than in other studies (for example, it did not include socioeconomic deprivation or body mass index); and d) the ascertainment of comorbidities was less complete than in other investigations.

An analysis briefly reported in a letter to a journal used daily case and death incidence reports in combination with population-based seroprevalence rates to estimate age-specific infection fatality rates (IFRs) in the Swiss canton of Geneva [6.5]. Despite the possibility that mild infections were under-ascertained, the IFR at ages 50-64 years was 1.4/1000, which is lower than we have estimated (Table Z4). However, the methods are not reported in detail, and there are statistical uncertainties because of the small number of deaths (only 16) in that age band. Therefore, we do not think the findings are sufficiently strong to warrant changes to Table Z4.

UPDATE 7: 27 AUGUST 2020

Since our last update, two papers that underpin our risk assessments for diabetes have been re-published following revision in response to peer-review [7.1, 7.2]. The main analyses differ in minor ways from those previously reported [1.2, 1.3]. For example, although follow-up periods were unchanged, slightly more Covid-19 deaths were identified in the study cohort. Also, the updated report from Holman et al specifies the lowest category for level of diabetic control as <48 rather than 45-48 mmol/mol HbA1c, re-specifies the reference category for level of diabetic control as 48-53 mmol/mol HbA1c, subdivides one of the previous strata of CKD, and includes several additional factors of adjustment in Cox regression analyses (systolic blood pressure, use of anti-hypertensive drugs, use of statins, total cholesterol level, and previous myocardial infarction) [7.2]. However, the impact of these modifications is small (see Section 2). More telling is the report of new supplementary analyses restricted to people below age 70 years. These confirm important age interactions, with higher relative risks for all categories of diabetes at younger ages.

Two new reports (one based on the OS cohort [7.3], and one from the ISARIC study [7.4]) provide data on death from Covid-19 in people with HIV infection, and are described further in Section 2Y. Another paper reports an analysis of data from the OS study to assess possible vulnerability to Covid-19 from recent use of non-steroidal anti-inflammatory drugs [7.5]. No effect on mortality was found.

Of particular interest is an investigation using data from the Real-time Assessment of Coronavirus Transmission-2 (REACT-2) programme [7.6]. Early in July 2020, data on the prevalence of IgG antibodies to SARS-CoV-2 were obtained through a self-administered test in a random population sample of adults registered with general practices in England. Tests were satisfactorily completed by 99,908 of 315,000 individuals who had been invited to take part, and national estimates of prevalence according to demographic characteristics were derived with adjustment for sampling fractions, the performance of the test in comparison with in-house ELISA assays, and survival bias (from omission of people who had died from Covid-19 in the five months since the epidemic began). These were then combined with data on mortality from Covid-19 (up to 17 July) to give estimated infection fatality rates (IFRs).

The estimated prevalence of infection was higher: in younger adults (7.9% at ages 18-24 years vs. 5.9% at 55-64 and 3.2% at 65-74); among people of Asian (11.9%) or Black (17.3%) as compared with White (5.0%) ethnicity; with greater social deprivation and larger household size; and in London as compared with other regions. The higher prevalence in Black people was reduced, but persisted, after adjustment for various covariates (OR 2.0, 95%CI 1.6-2.4).

Estimated IFRs (excluding deaths in care-home residents) were 0.71% in women as compared with 1.07% in men, with values (for both sexes combined) of 0.03%, 0.52% and 3.13% at ages 15-44, 45-64 and 65-74 years.

In regard to findings for people of working age, the study has two main limitations. First, the participation rate among those invited to take part was only 32%. It may be that people who had not experienced symptoms were less inclined to take part, especially in the younger age groups. Also, some cases of infection may have been missed because of weak or waning

antibody responses. Both of these sources of bias would tend to cause overestimation of IFRs. Under-ascertainment of deaths from infections acquired only shortly before the survey was conducted should have had only a small effect, since by then, death rates from Covid-19 in England were much lower than earlier.

A similar analysis from Spain used data on the prevalence of IgG antibodies from a series of surveys conducted during 27 April to 22 June (i.e. beginning one month after the peak of the first wave of Covid-19 in that country) to estimate IFRs among people not resident in care homes [7.7]. Adjustments were made to allow for differences in sampling by province and non-response, and estimated prevalence rates by sex and age were related to stratum-specific data on deaths from Covid-19 (again in people resident outside care homes) up to 15 July. The latter were determined a) from reports of laboratory-confirmed fatal infections and b) as excess deaths from all causes. The IFR was estimated as 0.8 to 0.9 per 1000 in men aged 40-49 years (with a rate of 0.4 to 0.5 per 1000 among women of that age), and 3.3-3.8 per 1000 in men aged 50-59. The main limitation of the analysis is the possibility that some infections were not detected using IgG antibodies, which could have caused fatality rates to be overestimated.

The implications of new findings on IFR are discussed further in Sections 2 and 3.

The only changes to our adopted risk estimates as a consequence of Update 7 are minor reductions to the relative risks associated with Type 2 and other diabetes where HbA1c is unknown (Section 2 F).

UPDATE 8: 11 OCTOBER 2020

In reviewing new evidence that has been published since our last update, we have focused on findings which might challenge or confirm our currently adopted estimates of relative risk, explore vulnerability in relation to comorbidities not currently included in our risk model, or quantify infection fatality rates (IFRs) by age. Reports which support the relevance of risk factors that are already included in our model, but without adding useful new information on associated levels of relative risk, have not been summarised as part of this update.

The new evidence has not led to any changes in our adopted risk estimates, but we have identified several studies on possible markers for vulnerability which are not currently included in our model. These are described in Section 2X. Two of the investigations relate to risks associated with use of non-steroidal anti-inflammatory drugs (neither found clear associations). Our risk model currently incorporates treatment modalities only as markers for severity of disease (e.g. oral corticosteroids for asthma). However, it is possible that some treatments, such as radiotherapy and immunosuppressive medication, add to any vulnerability that is associated with the diseases for which they are used. This will be kept under review. New evidence on risks by ethnicity is summarised in Section 2C.

Further information has emerged also on infection fatality rates by age (in our reports we have used the terms infection fatality rate (IFR) and case-fatality rate (CFR) synonymously – i.e. taking CFR to refer to cases of infection rather than to cases of symptomatic disease). Although important scientific uncertainties remain, we judge that evidence on IFR by age is now sufficient to warrant the inclusion of estimated IFRs (expressed as a plausible range) in our online calculator. Further details of how this has been done are presented in Section 3.

UPDATE 9: 28 OCTOBER 2020

Since our last update, an important new record linkage study (QCovid) has been reported [9.1]. Its methods were similar to those of the OpenSAFELY study, but the investigation focused on a different population – patients registered with English general practices contributing to the QResearch database. The primary aim was to develop a risk prediction model for hospital admission and mortality outcomes from Covid-19, according to demographic variables, lifestyle and comorbidities. As part of this, HRs for death from Covid-19 were estimated in a "derivation" cohort of 6,083,102 adults aged 19-100 years, who were registered with a sample of participating practices on 24 January 2020, and followed up to 30 April. The mortality outcome was defined as confirmed or suspected death from Covid-19 recorded on a death certificate, or death occurring in an individual with confirmed SARS-CoV-2 infection at any time during the follow-up period. Risk factors (potential predictor variables) at entry to follow-up were ascertained from the general practices' electronic health records, and (for chemotherapy, radiotherapy and transplants) from linked hospital records. After imputation of missing data on ethnicity, Townsend material deprivation score, BMI and smoking, sub-distribution hazard (Fine and Gray) models were fitted separately for women and men to obtain estimated HRs. The final models included age, BMI and Townsend score (all modelled as fractional polynomials); ethnicity; residence (not in care home or homeless/residential or nursing home/homeless); various comorbidities and medical treatments; and interaction terms between age and Type 2 diabetes. However, there was no adjustment for region of residence.

Detailed findings and their implications for our risk model are discussed in Section 2. Comparisons with our currently adopted estimates of RR are limited by the omission of terms for age interactions, other than for Type 2 diabetes, in the final regression models. However, no major inconsistencies have been identified. Thus we consider that the new evidence provides some support for the validity of our current risk estimates, and does not indicate a need to change any of them. Nor is it sufficient to support the inclusion of new risk factors in our model, although it adds to the evidence that severe psychiatric illness is associated with at least a small increase in vulnerability. It also indicates that among cancer patients, after allowance for type of malignancy (haematological or other) and time since diagnosis, vulnerability to Covid 19 may be higher in those recently treated by radiotherapy or by cytotoxic drugs that carry a high risk of febrile neutropenia or lymphopenia. We suggest that this should be taken into account when applying clinical judgement in the interpretation of Covid-age and associated estimates of infection fatality rate.

UPDATE 10: 11 DECEMBER 2020

New reports published in the interval since our last update do not call into question the risk estimates currently adopted in our risk model. Nor do they provide evidence sufficient to support additions to, or refinements of, the risk factors included in the model.

A project to develop and validate a predictive model of mortality in patients testing positive for SARS-CoV-2 within the US Veterans Health Administration, confirmed that risk of fatality was higher in association with many types of comorbidity, and particularly in people with multiple health problems [10.1]. However, the report of the study does not present mutually adjusted risk estimates for specific comorbidities that can be compared directly with those in our risk model.

Other reports shed light on vulnerability associated with specific categories or sub-categories of morbidity, or use of particular classes of medication [10.2-10.9]. Although not in a form that could be used to modify or augment our model, the findings may be of value to users when they apply clinical judgement in interpretation of risk estimates derived from the model. They are described in more detail in Section 2.

Finally, three new papers are relevant to the estimation of infection fatality rates (IFRs) according to Covid-age [10.10-10.12], and are summarised in Section 3.

Shortly before this update was prepared, vaccination against Covid-19 began in the UK. We expect that as vaccination is rolled out over the next few months, with prioritisation of individuals at higher risk, personal vulnerability to the disease increasingly will be determined more by their immunity to the virus than by demographic factors and comorbidities. Thus, while we will continue to monitor the published literature for new reports that might call into question our currently adopted risk estimates, we will only produce further updates as and when there is sufficient case for changing our risk model.

UPDATE 11: 1 NOVEMBER 2021

In the interval since our last update, many new reports have been published that bear on the assessment of individuals' vulnerability to serious illness and death, should they contract Covid-19. For various reasons, these papers cannot be used to refine our risk model. Many concern the impacts of vaccination or previous infection on personal immunity, whereas our model focuses on vulnerability in people who are unvaccinated and have not previously been infected by SARS-CoV-2. Moreover, those that relate to unvaccinated populations do not account for all of the risk factors that are included in our model, or for important interactions of age with other factors. Nevertheless, the findings accord broadly with our current risk estimates, and do not suggest any serious errors in the model.

Of note is a new analysis of data from the OpenSAFELY cohort for March to September 2020 [11.1]. Using similar methods to earlier analyses, this found a small increase in the risk of death from Covid-19 among 1,163,438 people with immune-mediated inflammatory diseases (IMIDs) of the joints, bowel or skin (HR 1.23, 95%CI 1.20-1.27, after adjustment for age, sex, deprivation and smoking status). Risk was greatest for inflammatory joint disease (HR 1.47), and smaller for inflammatory bowel (HR 1.12) and skin disease (HR 1.12). Among those with IMIDs, there was no indication of important differences in risk between 19,119 individuals receiving targeted immune-modifying therapies such as TNF-inhibitors, and 181,694 who were prescribed standard systemic therapy such as methotrexate. A moderately increased risk among patients using rituximab (HR 1.68, 95%CI 1.11-2.56) may have occurred by chance. Overall, these findings support the advice on our website that "inflammatory bowel diseases and inflammatory skin diseases may have similar vulnerability to inflammatory joint diseases".

We will continue to monitor the literature going forward, but because vaccination and/or previous infection is now so prevalent in the UK and other developed countries, we do not expect new findings that would lead us to change our model (which relates to vulnerability in the absence of vaccination or previous infection) .

UPDATE 12: 14 DECEMBER 2021

Over the past 18 months, there have been important improvements in the treatment of Covid-19, including several newly licensed medicines. In addition, there are early indications that the severity of illness caused by the new omicron variant of SARSCov-2 may be lower than that associated with earlier variants. As a consequence of these developments, our previous estimates of infection fatality rates (IFRs) in unvaccinated people according to Covid-age are now less reliable. In addition, their practical utility has been reduced by high rates of vaccination and/or previous infection among people of working age in the UK. At this stage, therefore, we have withdrawn the estimates of IFR from our risk model, although we continue to use Covid-age as a measure of relative risk (see Section 3).

SECTION TWO: ASSESSMENT OF EVIDENCE ON SPECIFIC RISK FACTORS

A. Age

INITIAL ASSESSMENT: 20 MAY 2020

In the OS study, after adjustment for sex, multiple comorbidities, and various other risk factors, the risk of death from Covid-19 showed a near to exponential relationship to age among adults, such that the RR for a 10 year increase in age was approximately 2.5, and that for a single year of age 1.0945. Confidence intervals were not presented for the regression coefficient of log-transformed HR on age, but because the analysis was based on a large study sample (>17 million) and a large number of deaths (5,683), we would expect the estimated effect of age to be statistically precise, especially at ages 40-69 years.

Comparison with data from other sources
By way of comparison, Table A1 shows ONS data on mortality from Covid-19 (as an underlying cause of death) in England and Wales during March 2020 [2].

Table A1. Mortality from Covid-19 (deaths per 100,000) by sex and age, England and Wales, March 2020

Age band (years)	Male	Female
20-24	0.0	2.0
25-29	1.7	0.0
30-34	4.7	0.0
35-39	4.8	1.8
40-44	5.2	3.9
45-49	11.1	14.5
50-54	21.0	12.5
55-59	47.9	26.4
60-64	80.7	33.0
65-69	118.1	56.9

A 10-year increase in age from 50-54 to 60-64 was associated with a 3.8-fold increase in mortality in men and a 2.6-fold increase in women. For the increase in age from 55-59 to 65-69, the corresponding increases were 2.5 in men and 2.2 in women. When allowance is made for random sampling variation, and the fact that ONS data do not take account of covariates other than sex, these ratios seem compatible with those estimated from the OS study.

Conclusion
We conclude it is reasonable to assume that after allowance for other variables, risk of death from Covid-19 increases exponentially with age among people of working age, such that a one-year increase in age carries a relative risk of 1.0945.

Robustness of risk estimate
This estimate is derived from a large study and is compatible with data from an independent source. We consider it to be robust.

UPDATE 1: 26 MAY 2020

In the report by Barron et al [1.2], ORs for cumulative mortality from Covid-19 by age, adjusted for sex, ethnicity (where known), region, social deprivation and diabetes, were as in Table A2.

Table A2: Adjusted odds ratios for cumulative mortality from Covid-19 from the report by Barron et al.

Age (years)	OR	(95%CI)
40-49	0.11	(0.10-0.12)
50-59	0.35	(0.33-0.38)
60-69	1	
70-79	2.61	(2.50-2.74)

These imply a somewhat steeper increase in risk with age than in the OS study (ORs for 10 year increases 2.6 to 3.2). However, that may be, at least in part, because they are not adjusted for other comorbidities whose prevalence increases with age.

On balance, therefore, we do not think it is justified to change the adopted risk estimate for age at this stage. However, we have downgraded our confidence in the risk estimate to "moderately robust".

UPDATE 4: 16 JULY 2020

In the updated report from the OS study [4.1], the increase in risk with age among people of working age is a little steeper than in the earlier paper from which it evolved [1]. Thus, the relative risk for each additional 10 years of age was approximately 2.8. Given that this estimate is based on a larger sample of deaths than the earlier analysis, and is broadly consistent with other evidence that we have reviewed, including the study by Barron et al [1.2], we believe that it justifies a small change to our adopted risk estimate for age. We have therefore now adopted a relative risk of 1.1084 for each additional year of age. We judge this slightly amended risk estimate to be robust.

UPDATE 7: 27 AUGUST 2020

The new report from the REACT-2 programme uses only broad categories of age, and does not present IFRs for combinations of sex and age [7.6]. The estimated IFRs of 31.3 per

1000 at ages 65-74 years and 5.2 per 1000 at ages 45-64 years indicate a six-fold increase for approximately 15 additional years of age, which is rather more than our current model assumes. The difference may in part reflect lower rates of infection in older people that were not fully taken into account in our earlier estimates of vulnerability. However, it should be noted also that the REACT-2 study did not adjust for comorbidities, which will have been more prevalent at older ages.

We do not think that the data from the REACT-2 study are sufficiently detailed and robust to warrant a change in our adopted risk estimates for age, but we will review that position if and when further evidence becomes available.

UPDATE 9: 28 OCTOBER 2020

Exact numerical estimates of relative risk by age are difficult to determine from the QCovid paper [9.1] because results are presented only in a graph plotted on a linear rather than a logarithmic scale (Supplementary Figure A of the report). However, from measurements of the graph made with a ruler, it appears that the adjusted HRs at age 70 relative to age 60 were approximately 4.0 in women and 3.7 in men, whereas for ages 80 relative to 70, the corresponding ratios were 2.8 and 2.5, and for ages 90 relative to 80, 2.3 and 2.3. In comparison, our adopted age coefficient implies a relative risk of $1.1084^{10} = 2.8$ for a 10-year increase in age.

B. Sex

INITIAL ASSESSMENT: 20 MAY 2020

In the OS study, after adjustment for age, multiple comorbidities, and various other risk factors, the HR of death from Covid-19 in men relative to women was 1.99 (95%CI 1.88-2.10). We would not expect this risk estimate to be liable to any major bias.

Comparison with data from other sources
By way of comparison, in ONS statistics on mortality from Covid-19 (as the underlying cause of death) in England and Wales during March 2020 [2], the directly-standardised mortality rate per 100,000 was 97.5 in men and 46.6 in women, giving a ratio of 2.09. This ratio might change slightly if it were adjusted for comorbidities with differing prevalence by sex, but data from the Health Survey for England indicate that such differences in prevalence are generally small [4-7]. Thus, we consider that the ONS data, which relate to deaths outside as well as within hospital, support the relative risk from the OS study.

Conclusion
We conclude that after allowance for other risk factors, the relative risk of death from Covid-19 in men as compared with women should be taken as 2.0. Correspondingly, the risk in women relative to men can be taken as 0.5.

Robustness of risk estimate
Given the statistical precision of its source, and its close compatibility with other data, we judge this risk estimate to be robust.

UPDATE 1: 26 MAY 2020

In the new whole-population study by Barron et al, the OR for male vs. female sex after adjustment for age, ethnicity (where known), region, deprivation and diabetes, was 1.93 (95%CI 1.88-1.98) [1.2]. We consider this risk estimate to be compatible with, and supportive of, that which we previously adopted.

UPDATE 4: 16 JULY 2020

In the main analysis from the updated report of the OS study [4.1], the adjusted HR for male as compared with female sex (1.59, 95%CI 1.53-1.65) was substantially lower than that in the initial paper from which it evolved (1.99, 95%CI 1.88-2.10). This may be explained in part by expansion of the outcome measure to include deaths from Covid-19 outside hospital, such deaths being relatively more common among older women. However, it is of note that when analysis was censored at 6 April 2020, the risk estimate for male sex was significantly higher (HR 1.90, 95%CI 1.75-2.05). It is unclear what accounts for this difference, but it indicates that interpretation should be cautious. In response to the new evidence, we have reduced our adopted risk estimate for men relative to women to 1.8 (i.e. 0.6 for women relative to men), which is in line with the independent analysis of Scottish data by McKeigue et al [3.1]. In addition, we have downgraded the estimate to moderately robust.

UPDATE 6: 13 AUGUST 2020

The new supplementary analysis of the OS study finds adjusted HRs by age band for men relative to women as shown in Table B1 [6.2].

Table B1. Adjusted hazard ratios for men relative to women by age band in the OpenSAFELY study

Age (years)									
18-39		40-49		50-59		60-69		70-79	
HR	(95%CI)	HR	(95%CI)	HR	(95%CI)	HR	(95%CI)	HR	(95%CI)
1.10	(0.68-1.78)	1.65	(1.27-2.16)	2.11	(1.84-2.41)	1.81	(1.66-1.98)	1.60	(1.51-1.71)

In the absence of any clear trend by age, and recognising that statistical uncertainty is greater for the youngest age band, we think it is reasonable to retain our previously adopted RR of 1.8 for men relative to women (equivalent to 0.6 for women relative to men) across the spectrum of working ages.

UPDATE 7: 27 AUGUST 2020

In the new report from the REACT-2 programme [7.6], the estimated IFR in women was 0.71% as compared with 1.07% in men – a ratio of 0.66. The comparison is not broken down by age, and in the absence of further information, we do not think any change is warranted to our currently adopted RR of 0.6 for women as compared with men.

UPDATE 9: 28 OCTOBER 2020

The QCovid paper presents HRs from separate regression models for men and women, and does not give risk estimates for women relative to men that are adjusted for other risk factors [9.1]. When the HRs for ethnicity, comorbidities and medication in Figures 1 and 2 of the QCovid report are compared, none are clearly divergent between women and men. Thus, the QCovid study does not point to important effect modification by sex that should be taken into account in our risk model.

C. Ethnicity

INITIAL ASSESSMENT: 20 MAY 2020

In the OS study, data on ethnicity were available for 74% of patients in the cohort. Table C1 shows HRs adjusted for sex, age, multiple comorbidities and various other risk factors, according to ethnicity and the date at which follow-up was censored.

Table C1. Adjusted hazard ratios for ethnic groups from the OS study according to date when follow-up was censored

Ethnic group		Follow-up to 25.4.20			Follow-up to 6.4.20	
		HR	(95%CI)		HR	(95%CI)
White		1			1	
Mixed		1.64	(1.19-2.26)		1.13	(0.62-2.05)
Asian or Asian British		1.62	(1.43-1.82)		1.77	(1.48-2.13)
Black		1.71	(1.44-2.02)		1.90	(1.48-2.45)
Other		1.33	(1.03-1.73)		1.81	(1.28-2.57)

Differences between corresponding risk estimates from the two analyses, especially for the less common ethnic groups (mixed, black and other) may have arisen through random sampling variation, and we have no reason to suspect that lower relative risks for some ethnic groups in the analysis with longer follow-up reflect a tendency for those groups to have avoided infection more effectively as the epidemic evolved. Thus, we consider that the risk estimates from the analysis with later censoring, which were statistically more precise, are the most reliable.

Comparison with data from other sources

The Office for National Statistics has published data on odds ratios for death related to Covid-19 in England and Wales during 2 March to 10 April 2020 according to ethnic group, with adjustment for age, geographical region, household composition, socioeconomic status and self-reported health at the 2011 census [8]. Table C2 shows risk estimates from that report for selected ethnic groups.

Table C2. Odds ratios for death related to Covid-19 according to ethnic group, England and Wales, 2 March to 10 April 2020

(Odds ratios are adjusted for age, geographical region, rural/urban, deprivation, household composition, socioeconomic status and self-reported health at the 2011 census).

Ethnic group		Male			Female	
		OR	(95%CI)		OR	(95%CI)
White		1			1	
Bangladeshi/Pakistani		1.81	(1.55-2.11)		1.61	(1.31-1.97)
Black		1.93	(1.70-2.18)		1.89	(1.63-2.20)
Indian		1.32	(1.15-1.53)		1.43	(1.20-1.71)

The estimated odds ratios for the Bangladeshi/Pakistani and Indian groups seem broadly compatible with the HR for the Asian or Asian British group in the OS study, as do the odds ratios for black men and women with the HR for the black group in the OS study.

Conclusion

We conclude that is reasonable to adopt relative risk estimates for ethnic group from the OS study as follows: Asian or Asian British 1.6; Black 1.7; Mixed 1.6; Other non-white 1.3. All of these risk estimates are relative to white as the reference.

Robustness of risk estimate

The risk estimate for the Asian or Asian British group is fairly precise statistically, and accords with independent ONS data. We therefore judge it to be moderately robust. The other risk estimates are less precise and we regard them as provisional.

UPDATE 1: 26 MAY 2020

In the new whole population study by Barron et al, ORs for death in hospital from Covid-19, adjusted for age, sex, region, social deprivation and diabetes, and relative to white ethnic group, were 1.36 (95%CI 1.29-1.44) for Asian, 1.73 (95%CI 1.63-1.83) for black, and 1.43 (95%CI 1.23-1.67) for mixed [1.2]. These results are consistent with our adopted risk estimates for black and mixed ethnicity, but the OR for Asian ethnicity suggests a lower relative risk than that which we previously adopted (1.6). The difference may in part reflect less extensive adjustment for comorbidities in the new study, but it is an indication that the chosen value may be slightly too high.

In the light of this new evidence, we have slightly reduced the adopted relative risk for Asian ethnicity to 1.5, and upgraded the robustness of that for black ethnicity to moderately robust.

UPDATE 3: 29 JUNE 2020

A new analysis of data from the ISARIC cohort assessed outcomes among 30,693 patients with recorded (self-reported) ethnicity, who were admitted to British hospitals during 6 February to 8 May 2020, and followed to 22 May [3.2]. After adjustment for age, sex and location, HRs for fatality relative to white ethnicity were 1.19 (95%CI 1.05-1.36) for those of South Asian origin, 1.05 (95%CI 0.91-1.26) for black ethnicity, and 0.99 (95%CI 0.89-1.10) for other ethnic minorities. There was no interaction of ethnicity with sex or age. The higher risk in the South Asian group was in part explained by a higher prevalence of diabetes. Given that these risk estimates are derived from patients who had been admitted to hospital, and that ethnicity may also be associated with higher rates of hospitalisation in those contracting Covid-19, we do not think that they indicate any need to revise our currently adopted, somewhat higher, risk estimates for case-fatality by ethnicity.

A second paper, with the same first two authors, reports a similar analysis for 23,577 Covid-19 patients admitted to UK hospitals up to 25 April 2020 [3.3]. The findings on ethnicity are broadly similar, but it is unclear to what extent they are subsumed by the later report.

An analysis of risk factors for hospital admission with Covid-19 in the Biobank cohort found an increased risk for black (OR 2.66, 95%CI 1.82-3.91) and Asian (OR 1.43, 95%CI 0.91-2.26) as compared with white ethnicity [3.4]. However, these risk estimates, while adjusted for various other factors, do not allow for region, which may have been an important determinant of exposure to infection.

Overall, we do not think that the newly reported findings that we have reviewed give us reason to revise our adopted risk estimates for ethnicity.

UPDATE 4: 16 JULY 2020

In the newly reported results from the OS study, risk estimates for some ethnic groups are a little lower than in earlier analyses, and findings are presented for more detailed categories of ethnicity [4.1]. There is a suggestion that people of Bangladeshi origin may be more vulnerable than those of Indian or Pakistani origin, but confidence intervals are fairly wide, and we do not think the evidence is yet sufficiently strong to adopt separate risk estimates for these three ethnic groups in our model. However, in response to the new information, we have reduced our adopted relative risk estimate for mixed race to 1.4, keeping it as provisional.

UPDATE 6: 13 AUGUST 2020

Table C3 shows estimated HRs from the supplementary analysis of the OS study for ethnicity by age [6.2]. At working ages there are no consistent trends across the age bands. However, for South Asian, Black and Other ethnicity, the summary risk estimates for all adults aged <70 years are a little higher than those previously found across adults of all ages [4.1]. This suggests that there is a small interaction with age for these groups. In view of this, but bearing in mind also that the reported HRs may overestimate differences in vulnerability because differences in exposure to infection have not been fully taken into account by adjustment for region and social deprivation, we have revised our adopted risk estimates slightly for these groups, taking as the new values 1.7 for Asian or Asian British, 2.0 for Black, and 1.5 for other non-White ethnicity. The robustness of these estimates is unchanged.

Table C3. Adjusted hazard ratios for ethnicity by stratum of age in the OpenSAFELY study

Ethnicity	Age (years)						
	18-69		18-39	40-49	50-59	60-69	70-79
	HR	(95%CI)	HR	HR	HR	HR	HR
White	1		1	1	1	1	1
Mixed	1.47	(0.94-2.29)	1.39	4.14	2.55	0.35	1.74
South Asian	1.85	(1.57-2.18)	2.86	1.80	2.41	2.39	1.69
Black	2.25	(1.81-2.79)	3.59	2.30	3.86	2.36	1.43
Other	1.82	(1.32-2.50)	2.20	0.94	2.12	2.01	0.85

UPDATE 7: 27 AUGUST 2020

The higher estimated prevalence of infection among people with Black and Asian ethnicity in the REACT-2 study [7.6] supports the possibility that part, at least, of their higher mortality from Covid-19 has been driven by higher exposure to infection as opposed to greater vulnerability when infection occurs. As described above (Update 6), our currently adopted risk estimates for ethnicity allow for possible residual differences in exposure to infection, and we do not think that further changes are justified at this stage.

UPDATE 8: 11 OCTOBER 2020

A new analysis, based on follow-up of the OpenSAFELY cohort from 1 February to 3 August, used Cox regression to assess risks of mortality from Covid-19 (defined as the presence of ICD-10 codes U071 or U072 anywhere in the death certificate) according to self-reported ethnicity [8.1]. After adjustment for socio-demographic factors (including sex and age), clinical comorbidities, geographic region, care home residency and household size, HRs for Covid-19 mortality relative to white ethnicity were 1.27 (95%CI 1.17-1.38) in South Asians, 1.56 (95%CI 1.38-1.75) in blacks, 1.40 (95%CI 1.12-1.76) in those of mixed ethnicity, and 1.25 (95%CI 1.05-1.49) in those of other ethnicity. These risk estimates are lower than those previously reported from the OS study after shorter follow-up (Table C1). One explanation could be that ethnic differences in the risk of becoming infected have not been adequately controlled by adjustment for sociodemographic variables, and have changed over time (e.g. because of changes in the geographical distribution of infection or differential shielding). It should be noted that the new analysis summarises risk estimates across all adults, while earlier age-stratified analyses of the OS cohort, have suggested that relative risks for non-white ethnic groups are higher at working ages than in the population as a whole (Table C3). We do not think that the new evidence is sufficient to warrant a reduction in our adopted risk estimates for ethnicity, but will review our position if and when further evidence becomes available.

UPDATE 9: 28 OCTOBER 2020

The QCovid paper gives risk estimates for nine categories of ethnicity as compared with five in our model (Table C4).

Table C4. Risk estimates for ethnicity in QCovid and as currently estimated in our risk model

QCovid					Covid-age	
Ethnicity	**Female**		**Male**		**Ethnicity**	**Currently adopted RR**
	HR	**(95%CI)**	**HR**	**(95%CI)**		
White	1		1		White	1
Indian	1.89	(1.43-2.51)	1.59	(1.25-2.01)	Asian/Asian British	1.7
Pakistani	1.40	(0.91-2.14)	1.84	(1.39-2.44)		
Bangladeshi	1.41	(0.88-2.26)	2.27	(1.65-3.12)		
Other Asian	1.19	(0.72-1.97)	2.02	(1.49-2.74)		
Caribbean	1.68	(1.29-2.20)	2.06	(1.65-2.57)	Black	2.0
Black African	1.98	(1.39-2.83)	3.03	(2.42-3.80)		
Chinese	1.21	(0.51-2.90)	2.47	(1.49-4.09)		
Other ethnic group	1.73	(1.28-2.35)	2.04	(1.60-2.58)	Mixed	1.6
					Other non-white	1.5

The risk estimates for black and ethnic minority groups in QCovid are broadly in line with those currently adopted in our risk model, although some may have been inflated by the absence of adjustment for region in the QCovid analysis. During the period covered by the study, the cumulative prevalence of infection was higher than average in London, where some ethnic minority groups are relatively more common than nationally. We do not think that the findings from QCovid indicate a need to change our risk estimates for ethnicity.

D. Obesity

INITIAL ASSESSMENT: 20 MAY 2020

In the OS dataset, body mass index (BMI) was ascertained from measurements of weight in the past 10 years, when individuals were >16 years old, and was available for 78% of the cohort.

Table D1 shows HRs, adjusted for sex, age, multiple comorbidities and various other risk factors, according to levels of BMI.

Table D1. Adjusted hazard ratios for categories of body mass index from OS study according to date when follow-up was censored

BMI (Kg/m^2)		Censored at 25.4.20			Censored at 6.4.20	
		HR	(95%CI)		HR	(95%CI)
<30		1			1	
30-34.9		1.27	(1.18-1.36)		1.39	(1.25-1.54)
35-39.9		1.56	(1.41-1.73)		1.62	(1.39-1.90)
≥40		2.27	(1.99-2.58)		2.45	(2.00-3.01)

It is possible that the lower HRs with longer follow-up reflect selective shielding of people with obesity as the epidemic evolved, and for this reason, we consider that the analysis censored at 6 April provides the more reliable estimate of RR for our risk model.

Comparison with data from other sources

In the ISARIC cohort, of patients admitted to British hospitals with Covid-19, obesity "as recognised on admission by clinical staff" (not sub-divided by severity) had an adjusted HR of 1.37 (95%CI 1.16-1.63) for death in hospital. However, the prevalence of obesity in the ISARIC cohort was remarkably low (approximately 9%, as compared with prevalence rates from the 2017 Health Survey for England by sex and 10-year age band in the order of 30% [5]), suggesting serious under-ascertainment.

Conclusion

We consider that the apparently low prevalence of obesity among hospitalised Covid-19 patients in the ISARIC cohort is almost certainly an artefact of incomplete ascertainment, and we therefore accepted the risk estimates from the OS study (shorter follow-up period) for inclusion in our risk model, as set out in Table D2.

Table D2. Adopted relative risk estimates for obesity

BMI (Kg/m^2)	Relative risk
<30	1
30-34.9	1.4
35-39.9	1.6
≥40	2.4

Robustness of risk estimates

These risk estimates are derived from a single, large and nationally representative study, but with limited support from other investigations. We therefore consider them provisional.

UPDATE 1: 26 MAY 2020

In the large cohort study of diabetes patients by Holman et al [1.3], after adjustment for age, sex, ethnicity, region, social deprivation, HbA1c level, time since diagnosis of diabetes, eGFR, smoking, previous stroke and previous heart failure, HRs for death related to Covid-19 varied with BMI as shown in Table D3.

Table D3. Adjusted hazard ratios for death associated with Covid-19 by body mass index

Body mass index (Kg/m^2)	Type 1 diabetes		Type 2 diabetes	
	HR	(95%CI)	HR	(95%CI)
<20	2.11	(1.32-3.38)	2.26	(2.04-2.5)
20-24.9	1.38	(1.04-1.83))	1.31	(1.23-1.39)
25-29.9	1		1	
30-34.9	1.5	(1.13-1.99)	1.04	(0.98-1.11)
35-39.9	1.7	(1.18-2.46)	1.16	(1.08-1.26)
≥40	2.15	(1.37-3.36)	1.64	(1.5-1.79)
Missing	1.8	(1.23-2.63)	1.86	(1.73-2.01)

The risk estimates among patients with Type 1 diabetes, although they relate to a different reference (BMI 25-29.9), are broadly consistent with those that were adopted for obesity in our risk model. However, those in patients with Type 2 diabetes are lower, suggesting either that the combined effects of Type 2 diabetes and obesity on relative risk are less than multiplicative, or that our adopted risk estimates obesity are a little too high.

At this stage, we have not changed the risk estimates for obesity, but the possibility of a non-multiplicative interaction with Type 2 diabetes, or that they overestimate risk, reinforces our view that they should be classed only as provisional.

UPDATE 4: 16 JULY 2020

In the updated analysis from the OS cohort, the HR for BMI 30 to 34-9 Kg/m^2 is a little lower, being 1.30 rather than 1.39 with censoring of follow-up at 6.4.20, and even lower in the analysis with full follow-up [4.1]. In response, we have reduced our adopted estimate of relative risk from 1.4 to 1.3. The new data do not indicate a need to change the adopted risk estimates for more severe categories of obesity.

UPDATE 6: 13 AUGUST 2020

Table D4 shows estimated HRs from the supplementary analysis of the OS study for categories of BMI by age [6.2]. In each age band there is a monotonic gradient in risk with increasing BMI, and for each level of BMI there is, with only one exception (BMI 30-34.9 kg/m^2, ages 40-49 years), a monotonic rise in relative risk with reducing age. Smoothing across the two trends, we have adopted new age-specific estimates of RR in relation to BMI as shown in Table D5.

Table D4. Adjusted hazard ratios for body mass index by age stratum in the OpenSAFELY study

Body mass index (Kg/m^2)	**Age (years)**						
	18-69		**18-39**	**40-49**	**50-59**	**60-69**	**70-79**
	HR	**(95%CI)**	**HR**	**HR**	**HR**	**HR**	**HR**
<30	1		1	1	1	1	1
30-34.9	1.17	(1.04-1.32)	1.83	1.16	1.67	1.22	1.14
35-39.9	1.84	(1.60-2.12)	5.72	2.89	2.79	1.98	1.26
≥40	2.27	(1.92-2.69)	9.83	5.05	3.49	2.52	1.72

We acknowledge that the smoothing is somewhat arbitrary (there is no biological basis for applying any specific formula), but we judge the new risk estimates to be more reliable than the summary values that we used previously for all ages. As before, these estimates are provisional.

Table D5. Adopted relative risk estimates for obesity by year of true age

True age (years)	BMI 30.0-34.9 Kg/m²		BMI 35.0-39.9 Kg/m²		BMI ≥40 Kg/m²	
	Approximate RR	Equivalent added years	Approximate RR	Equivalent added years	Approximate RR	Equivalent added years
20	2.1	7	7.1	19	13	25
21	2.1	7	7.1	19	13	25
22	2.1	7	7.1	19	12	24
23	2.1	7	6.4	18	12	24
24	2.1	7	6.4	18	12	24
25	1.9	6	6.4	18	11	23
26	1.9	6	6.4	18	11	23
27	1.9	6	5.8	17	11	23
28	1.9	6	5.8	17	10	22
29	1.9	6	5.8	17	10	22
30	1.9	6	5.8	17	10	22
31	1.9	6	5.2	16	8.7	21
32	1.9	6	5.2	16	8.7	21
33	1.9	6	5.2	16	8.7	21
34	1.9	6	5.2	16	7.8	20
35	1.9	6	4.7	15	7.8	20
36	1.9	6	4.7	15	7.1	19
37	1.9	6	4.7	15	7.1	19
38	1.7	5	4.7	15	7.1	19
39	1.7	5	4.7	15	6.4	18
40	1.7	5	4.2	14	6.4	18
41	1.7	5	4.2	14	5.8	17
42	1.7	5	4.2	14	5.8	17
43	1.7	5	4.2	14	5.8	17
44	1.7	5	3.8	13	5.2	16
45	1.7	5	3.8	13	5.2	16
46	1.7	5	3.8	13	5.2	16
47	1.5	4	3.8	13	4.7	15
48	1.5	4	3.4	12	4.7	15
49	1.5	4	3.4	12	4.2	14
50	1.5	4	3.4	12	4.2	14
51	1.5	4	3.1	11	4.2	14
52	1.5	4	3.1	11	3.8	13
53	1.4	3	3.1	11	3.8	13
54	1.4	3	2.8	10	3.4	12
55	1.4	3	2.8	10	3.4	12
56	1.5	4	2.8	10	3.4	12
57	1.4	3	2.8	10	3.1	11
58	1.4	3	2.5	9	3.1	11
59	1.4	3	2.5	9	3.1	11

60	1.4	3	2.5	9	2.8	10
61	1.2	2	2.3	8	2.8	10
62	1.2	2	2.3	8	2.8	10
63	1.2	2	2.3	8	2.5	9
64	1.2	2	2.1	7	2.5	9
65	1.2	2	2.1	7	2.5	9
66	1.2	2	2.1	7	2.3	8
67	1.2	2	1.9	6	2.3	8
68	1.2	2	1.9	6	2.1	7
69	1.2	2	1.7	5	2.1	7
70	1.2	2	1.7	5	2.1	7
71	1.1	1	1.7	5	1.9	6
72	1.1	1	1.5	4	1.9	6
73	1.1	1	1.5	4	1.7	5
74	1.1	1	1.4	3	1.7	5
75	1.1	1	1.4	3	1.7	5

UPDATE 7: 27 AUGUST 2020

Table D6, which is based on the revised report by Holman et al [7.2], shows HRs by level of BMI in diabetic patients when analyses were restricted to patients aged <70 years.

Table D6. Adjusted hazard ratios for death associated with Covid-19 by body mass index in diabetic patients aged <70 years

Body mass index (Kg/m^2)	Type 1 diabetes		Type 2 diabetes	
	HR	(95%CI)	HR	(95%CI)
<20	2.12	(0.91-4.95)	1.72	(1.10-2.70)
20-24.9	1.47	(0.87-2.46)	1.22	(1.03-1.45)
25-29.9	1		1	
30-34.9	1.96	(1.20-3.21)	1.21	(1.06-1.39)
35-39.9	3.36	(1.94-5.84)	1.66	(1.43-1.93)
≥40	4.44	(2.44-8.10)	2.30	(1.97-2.68)
Missing	2.42	(1.30-4.50)	1.98	(1.63-2.40)

When statistical uncertainty (as indicated by confidence intervals) is taken into account, comparison with the summary risk estimates for ages 18-69 years in Table D4 does not indicate any clear departure from multiplication of relative risks when diabetes and obesity are present in combination.

UPDATE 9: 28 OCTOBER 2020

In the QCovid paper, BMI is treated as a continuous variable, and risks are estimated relative to a reference value of 25 kg/m^2 [9.1]. By making measurements on a graph (Supplementary Figure A in the report), it is possible to obtain approximate HRs as set out in Table D7.

Table D7. Approximate HRs by level of BMI in QCovid report

BMI (Kg/m^2)	Approximate adjusted hazard ratio	
	Women	Men
20	1.2	1.2
25	1	1
30	1.1	1.1
35	1.2	1.4
40	1.7	1.9
45	2.5	2.5

These findings are broadly compatible with the risk estimates that we adopted in our Update 4, which relative to a BMI of <30 Kg/m^2, were 1.3, 1.6 and 2.4 for BMIs of 30-34.9, 35-35.9, and ≥40 Kg/m^2 respectively. Like those risk estimates, the HRs from QCovid, are summary values across all adult ages, and do not allow for the important interaction between BMI and age that we highlighted in Update 6 (Table D4).

We conclude that QCovid gives some support to the validity of our adopted risk estimates for obesity, and does not indicate any need for change.

UPDATE 10: 11 DECEMBER 2020

In a cohort study of more than 2.5 million adults in Catalonia, including 467 who suffered a Covid-19 related death, a higher relative risk of fatality among those with high BMI, was most pronounced at younger ages, supporting an age interaction with BMI [10.2].

E. Asthma

INITIAL ASSESSMENT: 20 MAY 2020

In the OS study, asthma was sub-classified according to whether or not it had been treated with oral corticosteroids in the year before baseline (severe or mild). Table E1 shows the prevalence of these categories of asthma in the study cohort, and the associated hazard ratios for death from Covid-19, after adjustment for sex, age, multiple comorbidities and various other risk factors.

Table E1. Prevalence of asthma in OS cohort, and adjusted HRs for death from Covid-19 according to date when follow-up was censored

Severity of asthma		Prevalence (%) in cohort		Censored at 25.4.20			Censored at 6.4.20	
				HR	(95%CI)		HR	(95%CI)
No asthma		84.1		1			1	
Mild asthma		14.2		1.11	(1.02-1.20)		1.14	(1.01-1.29)
Severe asthma		1.7		1.25	(1.08-1.44)		1.39	(1.12-1.73)

It is possible that, as the epidemic evolved, patients with more severe asthma took more extreme measures to reduce their risk of contracting Covid-19, leading to a lower HR in the analysis over the longer follow-up period. Thus the HR from the analysis with shorter follow-up may be more reliable.

Comparison with data from other sources

In the ISARIC cohort of hospitalised patients, the overall prevalence of asthma (not sub-divided by severity) was 14%, which is similar to that in the OS cohort (15.9%). Moreover, prevalence rates for doctor-diagnosed asthma in the 2018 Health Survey for England were even higher [4]. The report from the ISARIC study does not present a risk estimate for death in patients with asthma, although it does for other comorbidities with clearly increased risk.

Conclusion

When viewed together, the above findings indicate that most asthma is associated with little, if any, increase in risk of mortality from Covid-19. However, a small elevation of risk seems likely in people with more severe asthma that has required use of oral corticosteroids in the past year. We therefore adopted relative risk estimates for our risk model as set out in Table E2.

Table E2. Adopted relative risk estimates for asthma

Severity of asthma	Relative risk
None	1
Mild (no requirement for oral corticosteroids in past year)	1.1
Severe (requiring oral corticosteroids in past year)	1.4

Robustness of risk estimate

Although derived from a single study, these risk estimates appear compatible with other independent data, and we regard them as moderately robust

UPDATE 3: 29 JUNE 2020

In a new analysis from the OS collaborative, based on 817,973 patients with asthma, in comparison with those using only a short-acting beta agonist, risk was elevated for use of high-dose inhaled corticosteroids (HR 1.52, 95%CI 1.08-2.14), but showed no clear relation to low/medium dose inhaled corticosteroids (HR 1.10, 95%CI 0.82-1.49) [3.5]. However, the analysis did not consider concomitant use of oral corticosteroids, and therefore we do not think that it can be used to refine our adjusted risk estimates for asthma.

UPDATE 6: 13 AUGUST 2020

For mild asthma that has not required treatment with oral corticosteroids during the past year, estimated HRs in the new supplementary report from the OS study show no consistent trend across age bands, and all values fall within the range from 1.01 to 1.33 (Table E3) [6.2]. Therefore, for this category of asthma, we conclude that our previously adopted RR of 1.1 can be applied across all working ages.

Table E3. Adjusted HRs for asthma by age band in the OpenSAFELY study

Severity of asthma	**Age (years)**						
	18-69		**18-39**	**40-49**	**50-59**	**60-69**	**70-79**
	HR	**(95%CI)**	**HR**	**HR**	**HR**	**HR**	**HR**
No treatment with oral corticosteroids in past year	1.02	(0.89-1.17)	1.12	1.07	1.33	1.06	1.01
Treated with oral corticosteroids in past year	1.33	(1.05-1.69)	1.55	3.12	2.79	1.17	1.20

In contrast, for more severe asthma, the extension to the OS study suggests a weak gradient in HRs across age bands (Table E3). The departure from monotonicity in the youngest age band may be a consequence of random sampling variation in an age group with relatively few deaths, the 95%CI for the estimated HR of 1.55 ranging from 0.22 to 11.18. When this is taken into account, we consider that our previously adopted RR estimate of 1.4, while appropriate at the upper end of the range of working age, should be increased for younger ages as shown in Table E4. We recognise that these values are approximations, based on interpolation, modest extrapolation and somewhat arbitrary smoothing, but we would expect them to improve on the summary risk estimate that we used previously.

The estimated relative risks at the top end of the age range remain moderately robust, but because of the uncertainties highlighted above, those for younger ages are classed as provisional.

Table E4. Adopted relative risk estimates for severe asthma (treated with oral corticosteroids in past year) by year of true age

True age (years)	Approximate RR	Equivalent added years	Robustness of risk estimate
20	4.7	15	Provisional
21	4.7	15	Provisional
22	4.7	15	Provisional
23	4.7	15	Provisional
24	4.7	15	Provisional
25	4.7	15	Provisional
26	4.2	14	Provisional
27	4.2	14	Provisional
28	4.2	14	Provisional
29	4.2	14	Provisional
30	4.2	14	Provisional
31	4.2	14	Provisional
32	4.2	14	Provisional
33	3.8	13	Provisional
34	3.8	13	Provisional
35	3.8	13	Provisional
36	3.8	13	Provisional
37	3.8	13	Provisional
38	3.4	12	Provisional
39	3.4	12	Provisional
40	3.4	12	Provisional
41	3.4	12	Provisional
42	3.4	12	Provisional
43	3.1	11	Provisional
44	3.1	11	Provisional
45	3.1	11	Provisional
46	3.1	11	Provisional
47	2.8	10	Provisional
48	2.8	10	Provisional
49	2.8	10	Provisional
50	2.5	9	Provisional
51	2.5	9	Provisional
52	2.5	9	Provisional
53	2.5	9	Provisional
54	2.3	8	Provisional
55	2.3	8	Provisional
56	2.3	8	Provisional
57	2.1	7	Provisional
58	2.1	7	Provisional

59	2.1	7	Provisional
60	1.9	6	Moderately robust
61	1.9	6	Moderately robust
62	1.7	5	Moderately robust
63	1.7	5	Moderately robust
64	1.5	4	Moderately robust
65	1.5	4	Moderately robust
66	1.5	4	Moderately robust
67	1.5	4	Moderately robust
68	1.4	3	Moderately robust
69	1.4	3	Moderately robust
70	1.4	3	Moderately robust
71	1.4	3	Moderately robust
72	1.2	2	Moderately robust
73	1.2	2	Moderately robust
74	1.2	2	Moderately robust
75	1.2	2	Moderately robust

UPDATE 9: 28 OCTOBER 2020

In the QCovid paper, the adjusted HRs for asthma were 0.84 in women and 1.03 in men [9.1]. In addition, the regression model included “Leukotriene or long acting β agonist 4+ scripts in past 6 months” (we assume this refers to leukotriene antagonists), which carried HRs of 1.23 in women and 1.04 in men, and “oral steroids 4+ scripts in past 6 months” which was associated with HRs of 1.83 in women and 1.44 in men. These results seem broadly compatible with our currently adopted risk estimate of 1.1 (across all working ages) for mild asthma (insufficient to require treatment by oral corticosteroids in the past year) and the risk estimate of 1.4 (summarised across all adult ages) that we were using for severe asthma (treated by oral corticosteroids in the past year) at Update 4. However, the HRs for asthma that are reported in the QCovid paper do not account for the interaction between severe asthma and age that we incorporated into our risk model at Update 6.

Overall, we do not think the new results warrant any change to our currently adopted risk estimates for asthma.

F. Diabetes

INITIAL ASSESSMENT: 20 MAY 2020

In the OS study, diabetes was classified to three mutually exclusive categories, according to whether an HbA1c measurement had been made in the last 15 months, and if so, whether the level was <58 mmol/mol (controlled diabetes) or higher (uncontrolled diabetes). Table F1 shows the prevalence of these categories of diabetes in the OS cohort, and their HRs for death from Covid-19 during follow-up.

Table F1. Prevalence of diabetes in the OS cohort, and adjusted HRs for death from Covid-19 according to date when follow-up was censored

Severity of diabetes		Prevalence (%) in cohort		Censored at 25.4.20			Censored at 6.4.20	
				HR	(95%CI)		HR	(95%CI)
No diabetes		90.9		1			1	
Controlled		6.0		1.50	(1.40-1.60)		1.48	(1.33-1.65)
Uncontrolled		2.8		2.36	(2.18-2.56)		2.57	(2.27-2.91)
No recent HbA1c measure		1.1		1.87	(1.63-2.19)		1.68	(1.33-2.12)

There was no clear indication that HRs with longer follow-up were lowered as a consequence of selective shielding by diabetic patients. Therefore, the statistically more robust HRs from the longer follow-up period were judged to be the more reliable.

Comparison with data from other sources

To check on the plausibility of the risk estimates from the OS study, we analysed data on diabetes from the ISARIC study and the 2017 Health Survey for England [5]. Table F2 shows approximate numbers of patients by sex and age in the ISARIC cohort (estimated by measuring the lengths of bars in a bar chart), the prevalence of doctor-diagnosed diabetes in the same age and sex strata in the 2017 Health Survey for England, and calculations from these data of the numbers of patients with doctor-diagnosed diabetes that might have been expected in the ISARIC cohort if diabetes had no effect on hospital admission for Covid-19. Summation of expected numbers across all of the strata indicates that the overall expected percentage prevalence of doctor-diagnosed diabetes in the ISARIC cohort would be: 100*(586+302)/(4401+2807) = 12%.

In contrast, the reported prevalence of uncomplicated diabetes in the ISARIC cohort was 19%, suggesting a relative risk for hospital admission in the order of 19/12 = 1.6.

This calculation has many limitations. Unlike the ISARIC study, the Heath Survey for England did not cover Wales or Scotland, and its case definition and method of ascertaining diabetes differed from that in the ISARIC study. Furthermore, the calculated ratio takes no account of possibly higher fatality among Covid-19 patients with diabetes once they are admitted to hospital. When these weaknesses are taken into account, the calculated ratio seems compatible with the risk estimates from the OS study, and gives them added plausibility.

Table F2. Calculation of expected numbers of patients with doctor-diagnosed diabetes in ISARIC cohort, based on prevalence in the 2017 Health Survey for England

Entries in the table are rounded to the nearest whole number, but calculations have used original unrounded numbers. Therefore numbers as presented may not sum exactly to reported totals.

Aggregated age band (years)	Approximate numbers in ISARIC cohort			Prevalence % of DDD* in 2017 Health Survey for England		Expected numbers of cases in ISARIC cohort	
	Male	Female		Male	Female	Male	Female
0-14	73	36					
16-24	36	40		1	0	0	0
25-34	84	124		1	0	1	0
35-44	233	131		3	2	8	3
45-54	459	339		9	5	42	18
55-64	674	357		11	7	72	26
65-74	901	474		19	11	170	52
75+	1940	1305		15	16	292	204
Total	4401	2807				586	302

*Doctor-diagnosed diabetes

Conclusions

We concluded that it is reasonable to adopt risk estimates for diabetes from the OS study for our risk model as set out in Table F3.

Table F3. Adopted relative risks for diabetes

Severity of diabetes	Relative risk
No diabetes	1
Controlled	1.5
Uncontrolled	2.4
No recent HbA1c measure	1.9

Robustness of risk estimates
In view of their derivation from a large and nationally representative dataset, and their consistency with data from other sources, we consider these risk estimates to be moderately robust.

UPDATE 1: 26 MAY 2020

The new study reported by Barron et al [1.2] found that in comparison with no diabetes, and after adjustment for age, sex, ethnicity (where available), region, and social deprivation, ORs for death in hospital from Covid-19 were 3.50 (95%CI 3.15-3.88) for Type 1 diabetes, 2.01 (95%CI 1.96-2.07) for Type 2 diabetes, and 2.16 (1.70-2.74) for other diabetes. With adjustment also for coronary heart disease, cerebrovascular disease and heart failure, these risk estimates reduced slightly to 2.86 for Type 1 diabetes and 1.81 for Type 2 diabetes.

Furthermore, in cohorts of almost all patients in England with Type 1 or Type 2 diabetes, after adjustment for age, sex, ethnicity, region, social deprivation, time since diagnosis of diabetes, eGFR, BMI, smoking, previous stroke and previous heart failure, HRs for death related to Covid-19 by level of diabetic control, were as shown in Table F4 [1.3].

Table F4 Adjusted hazard ratios for death associated with Covid-19 in patients with Type 1 and Type 2 diabetes according to level of diabetic control

HbA1c (mmol/mol)	Type 1 diabetes			Type 2 diabetes		
	Prevalence (%)	HR	(95%CI)	Prevalence (%)	HR	(95%CI)
45-48	6.8	1.22	(0.78-1.91)	25.1	1.11	(1.04-1.18)
49-53	8.2	1		20.6	1	
54-58	9.5	0.73	(0.44-1.20)	12.7	1.05	(0.97-1.13)
59-74	29.3	1.15	(0.79-1.67)	19.2	1.23	(1.15-1.32)
75-85	11.4	1.31	(0.85-2.03)	5.5	1.37	(1.24-1.51)
≥86	11.8	2.19	(1.46-3.29)	6.1	1.62	(1.48-1.79)
Missing	23.0	1.60	(1.05-2.43)	10.9	1.57	(1.46-1.70)

By combining the data in Table F4 with the adjusted overall HRs of 2.86 and 1.81 for Type 1 and Type 2 diabetes respectively, it is possible to derive approximate estimates of risk relative to no diabetes for subcategories of diabetes specified by type and level of control. Suppose, for example, that relative to no diabetes, the risk for Type 1 diabetes with HbA1c of 49-53 mmol/mol is R. Corresponding relative risks for the other strata of HbA1c can be calculated as the product of R and their HR in Table F4. It is then possible to calculate the overall relative risk for Type 1 diabetes as a function of R, by deriving an average of the stratum-specific relative risks, weighted according to their prevalence in the cohort. This should equate approximately to the measured overall HR of 2.86 for Type 1 diabetes, allowing calculation of R, and thereby of the relative risk for each of the other strata. The calculation is shown for Type 1 diabetes in Table F5, and for Type 2 diabetes in Table F6.

Table F5. Calculation of risks relative to no diabetes for sub-categories of Type 1 diabetes defined by level of HbA1c

HbA1c (mmol/mol)	Risk relative to no diabetes	Prevalence (%) in cohort	Product of relative risk and prevalence	Risk relative to no diabetes calculated by substituting 2.86/1.35 for R
45-48	1,22*R	6.8	8.30*R	2.6
49-53	R	8.2	8.20*R	2.1
54-58	0.73*R	9.5	6.94*R	1.5
59-74	1.15*R	29.3	33.70*R	2.4
75-85	1.31*R	11.4	14.93*R	2.8
≥86	2.19*R	11.8	25.84*R	4.6
Missing	1.60*R	23.0	36.80*R	3.4
Total			134.71*R	
Weighted average			1.35*R	

Table F6. Calculation of risks relative to no diabetes for sub-categories of Type 2 diabetes defined by level of HbA1c

HbA1c (mmol/mol)	Risk relative to no diabetes	Prevalence (%) in cohort	Product of relative risk and prevalence	Risk relative to no diabetes calculated by substituting 1.81/1.20 for R
45-48	1.11*R	25.1	27.86*R	1.7
49-53	R	20.6	20.60*R	1.5
54-58	1.05*R	12.7	13.34*R	1.6
59-74	1.23*R	19.2	23.62*R	1.9
75-85	1.37*R	5.5	7.54*R	2.1
≥86	1.62*R	6.1	9.88*R	2.4
Missing	1.57*R	10.9	17.11*R	2.4
Total			119.95*R	
Weighted average			1.20*R	

Given that Type 2 diabetes accounted for more than 90% of all diabetes in the national population, these risk estimates, seem broadly compatible with our previously adopted risk estimates of 1.5, 2.4 and 1.9 respectively for diabetes with HbA1c <58 mmol/mol, ≥58 mmol/mol and missing. However, the new data indicate a substantially higher risk in association with Type 1 diabetes, and we have therefore decided to revise our adopted relative risk estimates as indicated in Table F7. We recognise that these risk estimates are approximations, and that is why we have not attempted to distinguish too finely between levels of control. Also, we have taken into account that the overall ORs for types of diabetes in the study by Barron et al [1.2] were not adjusted for BMI or chronic kidney disease. From

the evidence in the Barron study, it seems reasonable to classify other diabetes (including maturity onset diabetes of the young) with Type 2 diabetes.

Table F7. New adopted relative risk estimates for diabetes.

Type of diabetes	Most recent HbA1c (mmol/mol)	Relative risk
Type 1	≤58	2.0
	>58	2.7
	Unknown	3.3
Type 2 and other	≤58	1.5
	>58	2.0
	Unknown	2.3

In view of their compatibility with the OS study, we class these risk estimates as moderately robust

UPDATE 6: 13 AUGUST 2020

Our previously adopted risk estimates for diabetes were derived from the two linked studies that analysed data relating to approximately 98% of the population of England [1.2,1.3]. The large size of that investigation, and the detailed information that was available about patients with diabetes, enabled it to investigate the risks associated with more sub-categories of diabetes than have been considered to date in the OS study [1,4.1]. However, the risk estimates reported, although adjusted for age, were summary measures across all ages. The new supplementary report of the OS study indicates a strong interaction between age and diabetes as risk factors for mortality from Covid-19, with substantially higher HRs for diabetes at younger ages (Table F8) [6.2]. This gradient may in part reflect a higher relative prevalence of Type 1 as compared with Type 2 diabetes at younger ages [1.2], but that effect is likely to be small since after allowance for level of diabetic control, summary relative risks for Type 1 diabetes are only about one-third higher than those for Type 2 diabetes (Table F7).

Table F8. Adjusted hazard ratios for diabetes by age in the OpenSAFELY study, and their ratios to the corresponding summary hazard ratios across all adults

Level of HbA1c (mmol/mol)	Age (years)										
	≥18*	18-39		40-49		50-59		60-69		70-79	
	HR	HR	Ratio	HR	Ratio	HR	Ratio	HR	Ratio	HR	Ratio
<58	1.3	7.2	5.5	5.7	4.3	3.5	2.6	2.0	1.5	1.4	1.1
≥58	2.0	10.6	5.4	7.7	3.9	5.2	2.7	3.2	1.7	2.1	1.1
No recent measurement	1.9	3.0	1.6	4.8	2.5	4.1	2.2	1.8	0.9	2.3	1.2

*Summary HRs for all adults are derived from reference 4.1.

We hope that in due course information will become available on age-specific relative risks associated with different types of diabetes as well as levels of control. Meanwhile, however, we think that our adopted risk estimates will be improved by making approximate allowance for differences by age. We note from Table F8 that within the OS study, the ratios of age specific risk estimates for diabetes to the summary HR for all adults are similar for well-controlled and poorly controlled diabetes (the numbers with missing data on HbA1c are smaller and more liable to random sampling error). Based on this observation, we think it is reasonable as a first approximation to apply approximate averages of these ratios to our previously adopted summary risk estimates for diabetes in the population as a whole. By doing this, we obtained estimates of RR for the central points of each age band (Table F9). We then interpolated/extrapolated from the midpoints of the age bands to other ages (Tables F10 and F11).

Table F9. Approximate relative risk estimates for diabetes at mid-points of age bands

	All ages*	Mid-point of age range (years)				
		29	45	55	65	75
Estimated ratio of RR to that for all ages	1.0	5.4	4.1	2.7	1.6	1.1
Estimated RR for Type 1 diabetes						
HbA1≤58 mmol/mol in past year	2.0	10.8	8.2	5.4	3.2	2.2
HbA1>58 mmol/mol in past year	2.7	14.6	11.1	7.3	4.3	3.0
HbA1c unknown	3.3	17.8	13.5	8.9	5.3	3.6
Estimated RR for Type 2 diabetes						
HbA1≤58 mmol/mol in past year	1.5	8.1	6.2	4.1	2.4	1.7
HbA1>58 mmol/mol in past year	2.0	10.8	8.2	5.4	3.2	2.2
HbA1c unknown	2.3	12.4	9.4	6.2	3.7	2.5

*Estimated RRs for all ages are taken from Table F7

We believe that these new risk estimates, differing by age, will be more accurate than those that we have used previously, especially for younger adults, and we have therefore adopted them in our revised risk model. However, because of the uncertainties arising from the varying relative prevalence of Type 1 and Type 2 diabetes at different ages, and from the crude method of interpolating/extrapolating across the age range, we classify these revised risk estimates as provisional.

Table F10. Adopted relative risk estimates for Type 1 diabetes by year of true age

True age (years	HbA1≤58 mmol/mol in past year		HbA1>58 mmol/mol in past year		HbA1c unknown	
	Approximate RR	Equivalent added years	Approximate RR	Equivalent add years	Approximate RR	Equivalent added years
20	12	24	16	27	20	29
21	12	24	16	27	20	29
22	12	24	16	27	20	29
23	12	24	16	27	20	29
24	12	24	16	27	20	29
25	12	24	16	27	18	28
26	11	23	15	26	18	28
27	11	23	15	26	18	28
28	11	23	15	26	18	28
29	11	23	15	26	18	28
30	11	23	15	26	18	28
31	11	23	15	26	18	28
32	10	22	13	25	18	28
33	10	22	13	25	16	27
34	10	22	13	25	16	27
35	10	22	13	25	16	27
36	10	22	13	25	16	27
37	8.7	21	13	25	16	27
38	8.7	21	12	24	15	26
39	8.7	21	12	24	15	26
40	8.7	21	12	24	15	26
41	8.7	21	12	24	15	26
42	7.8	20	12	24	13	25
43	7.8	20	11	23	13	25
44	7.8	20	11	23	13	25
45	7.8	20	11	23	13	25
46	7.8	20	11	23	12	24
47	7.1	19	10	22	12	24
48	7.1	19	10	22	12	24
49	6.4	18	10	22	11	23
50	6.4	18	8.7	21	11	23
51	6.4	18	8.7	21	11	23
52	5.8	17	7.8	20	10	22
53	5.8	17	7.8	20	10	22
54	5.2	16	7.1	19	8.7	21
55	5.2	16	7.1	19	8.7	21
56	5.2	16	7.1	19	7.8	20
57	4.7	15	6.4	18	7.8	20

58	4.7	15	6.4	18	7.1	19
59	4.2	14	5.8	17	7.1	19
60	4.2	14	5.8	17	6.4	18
61	3.8	13	5.2	16	6.4	18
62	3.8	13	5.2	16	5.8	17
63	3.4	12	4.7	15	5.8	17
64	3.4	12	4.7	15	5.2	16
65	3.1	11	4.2	14	5.2	16
66	3.1	11	4.2	14	4.7	15
67	3.1	11	4.2	14	4.7	15
68	2.8	10	3.8	13	4.2	14
69	2.8	10	3.8	13	4.2	14
70	2.8	10	3.8	13	4.2	14
71	2.5	9	3.4	12	3.8	13
72	2.5	9	3.4	12	3.8	13
73	2.3	8	3.4	12	3.4	12
74	2.3	8	3.1	11	3.4	12
75	2.3	8	3.1	11	3.4	12

Table F11. Adopted relative risk estimates for Type 2 and other diabetes by year of true age

True age (years	HbA1≤58 mmol/mol in past year		HbA1>58 mmol/mol in past year		HbA1c unknown	
	Approximate RR	Equivalent added years	Approximate RR	Equivalent added years	Approximate RR	Equivalent added years
20	8.7	21	11	23	12	24
21	8.7	21	11	23	12	24
22	8.7	21	11	23	12	24
23	8.7	21	11	23	12	24
24	8.7	21	11	23	12	24
25	7.8	20	10	22	11	23
26	7.8	20	10	22	11	23
27	7.8	20	10	22	11	23
28	7.8	20	10	22	11	23
29	7.8	20	10	22	11	23
30	7.8	20	10	22	11	23
31	7.8	20	10	22	11	23
32	7.8	20	10	22	11	23
33	7.1	19	8.7	21	11	23
34	7.1	19	8.7	21	11	23
35	7.1	19	8.7	21	11	23
36	7.1	19	8.7	21	11	23
37	7.1	19	8.7	21	11	23
38	7.1	19	8.7	21	10	22
39	7.1	19	8.7	21	10	22
40	7.1	19	8.7	21	10	22
41	6.4	18	7.8	20	10	22
42	6.4	18	7.8	20	10	22
43	6.4	18	7.8	20	10	22
44	6.4	18	7.8	20	10	22
45	6.4	18	7.8	20	10	22
46	5.8	17	7.1	19	8.7	21
47	5.8	17	7.1	19	8.7	21
48	5.8	17	7.1	19	8.7	21
49	5.2	16	6.4	18	7.8	20
50	5.2	16	6.4	18	7.8	20
51	5.2	16	6.4	18	7.8	20
52	4.7	15	5.8	17	7.1	19
53	4.7	15	5.8	17	7.1	19
54	4.2	14	5.2	16	6.4	18
55	4.2	14	5.2	16	6.4	18
56	4.2	14	5.2	16	6.4	18
57	3.8	13	4.7	15	5.8	17

58	3.8	13	4.7	15	5.8	17
59	3.4	12	4.2	14	5.2	16
60	3.4	12	4.2	14	5.2	16
61	3.1	11	3.8	13	4.7	15
62	3.1	11	3.8	13	4.7	15
63	2.8	10	3.4	12	4.2	14
64	2.8	10	3.4	12	4.2	14
65	2.5	9	3.1	11	3.8	13
66	2.5	9	3.1	11	3.8	13
67	2.3	8	3.1	11	3.8	13
68	2.3	8	2.8	10	3.4	12
69	2.1	7	2.8	10	3.4	12
70	2.1	7	2.5	9	3.1	11
71	1.9	6	2.5	9	3.1	11
72	1.9	6	2.5	9	3.1	11
73	1.9	6	2.3	8	2.8	10
74	1.7	5	2.3	8	2.8	10
75	1.7	5	2.3	8	2.5	9

UPDATE 7: 27 AUGUST 2020

Tables F12 and F13 show RRs calculated as in Tables F5 and F6, but using results from the revised reports by Barron et al [7.1] and Holman et al [7.2].

Table F12. Re-calculation of risks relative to no diabetes for sub-categories of Type 1 diabetes defined by level of HbA1c

HbA1c (mmol/mol)	Risk relative to no diabetes	Prevalence (%) in cohort	Product of relative risk and prevalence	Risk relative to no diabetes calculated by substituting 2.86/1.35 for R
<48	1.37*R	6.8	9.32*R	2.6
48-53	R	8.2	8.20*R	2.1
54-58	0.78*R	9.5	7.41*R	1.5
59-74	1.16*R	29.3	33.99*R	2.4
75-85	1.37*R	11.4	15.62*R	2.8
≥86	2.23*R	11.8	26.31*R	4.6
Missing	1.48*R	23.0	34.04*R	3.4
Total			134.89*R	
Weighted average			1.35*R	

Table F13. Re-calculation of risks relative to no diabetes for sub-categories of Type 2 diabetes defined by level of HbA1c

HbA1c (mmol/mol)	Risk relative to no diabetes	Prevalence (%) in cohort	Product of relative risk and prevalence	Risk relative to no diabetes calculated by substituting 1.80/1.15 for R
<48	1.11*R	25.1	27.86*R	1.7
48-53	R	20.6	20.60*R	1.6
54-58	1.05*R	12.7	13.34*R	1.6
59-74	1.22*R	19.2	23.42*R	1.9
75-85	1.36*R	5.5	7.48*R	2.1
≥86	1.61*R	6.1	9.82*R	2.5
Missing	1.20*R	10.8	12.96*R	1.9
Total			115.5*R	
Weighted average			1.16*R	

The risk estimates are very similar to those in Tables F5 and F6, the only difference of note being a lower value for Type 2 diabetes with missing HbA1c (1.9 vs. 2.4).

The revised reports also present new sensitivity analyses restricted to people below age 70 years [7.1, 7.2]. Within this younger age band, adjusted ORs for in-hospital death with Covid-19 relative to no diabetes were 6.39 (95%CI 5.40-7.56) for Type 1 diabetes, 3.74 (95%CI 3.50-3.99) for Type 2 diabetes, and 3.00 (95%CI 1.81-4.99) for other diabetes [7.1]. These values are clearly higher than in the analysis including people of all ages. However, within diabetic patients, HRs by level of diabetic control were not consistently or substantially different in the younger age band from those in the full study sample [7.2].

The summary ORs of 6.39 and 3.74 for Type 1 and Type 2 diabetes below age 70 years, which will be weighted towards the older end of that age range because that is where most deaths will have occurred, seem reasonably consistent with the approximate relative risks in Table F9. Therefore, at this stage, we have not made any changes to our adopted risk estimates for diabetes other than to downgrade those for Type 2 and other diabetes with unknown HbA1c by approximately 20% (equivalent to a reduction in 2 years of age). The revised risk estimates for this category of diabetes are shown in Table F14.

Table F14. Adopted relative risk estimates for Type 2 and other diabetes with unknown HbA1c by year of true age

True age (years	Approximate RR	Equivalent added years
20	9.6	22
21	9.6	22
22	9.6	22
23	9.6	22
24	9.6	22
25	8.7	21
26	8.7	21
27	8.7	21
28	8.7	21
29	8.7	21
30	8.7	21
31	8.7	21
32	8.7	21
33	8.7	21
34	8.7	21
35	8.7	21
36	8.7	21
37	8.7	21
38	7.8	20
39	7.8	20
40	7.8	20
41	7.8	20
42	7.8	20
43	7.8	20
44	7.8	20
45	7.8	20
46	7.1	19
47	7.1	19
48	7.1	19
49	6.4	18
50	6.4	18
51	6.4	18
52	5.8	17
53	5.8	17
54	5.2	16
55	5.2	16
56	5.2	16
57	4.7	15
58	4.7	15

59	4.2	14
60	4.2	14
61	3.8	13
62	3.8	13
63	3.4	12
64	3.4	12
65	3.1	11
66	3.1	11
67	3.1	11
68	2.8	10
69	2.8	10
70	2.5	9
71	2.5	9
72	2.5	9
73	2.3	8
74	2.3	8
75	2.1	7

UPDATE 9: 28 OCTOBER 2020

The analysis for the QCovid paper incorporated age interaction terms for Type 2 diabetes, but made no distinction between levels of diabetic control, despite strong evidence that vulnerability to Covid-19 in diabetics varies according to HbA1c concentration [7.2].

For Type 1 diabetes, the report gives summary adjusted HRs of 4.02 (95%CI 2.07-7.82) in women and 5.84 (95%CI 3.97-8.60) in men. These values are surprisingly high, given that the revised report by Barron et al [7.1], which was based on a much larger study sample than QCovid, gave a summary (across all ages) OR for in-hospital Covid-19-related death in people with Type 1 diabetes of 3.51 (95%CI 3.16-3.90). The reasons for the discrepancy are unclear. Our currently adopted relative risks for Type 1 diabetes range from 2.8 for well-controlled disease at age 70 to 16 or higher at age 20 where control is poor or unrecorded (Table Z7).

The QCovid report presents risk estimates for Type 2 diabetes by age in a graph (Supplementary Figure A of report), from which it is possible to derive approximate RRs for women and men respectively of 14.2 and 18.1 at age 20 and 2.6 and 2.1 at age 70. Corresponding estimates of RR in our current model (according to level of diabetic control) are 8.7 to 11 at age 20 and 2.1 to 2.5 at age 70 (Table Z7). It may be that the somewhat higher RRs for young adults in QCovid reflect the omission of an interaction term for age in its risk estimates for obesity, with the consequence that relatively more of the increased risk in young, obese Type 2 diabetics has been apportioned to diabetes as opposed to obesity.

On balance, we do not think the evidence in the QCovid report is sufficient to warrant any changes to our currently adopted risk estimates for diabetes.

G. Cardiovascular disease

INITIAL ASSESSMENT: 20 MAY 2020

In the OS study, chronic heart disease (CHD) included heart failure, ischaemic heart disease, and severe valve or congenital heart disease likely to require lifelong follow-up. Among the 6.7% of cohort members with CHD, the HR for death from Covid-19, adjusted for sex, age, multiple comorbidities and various other risk factors was 1.27 (95%CI 1.20-1.35) when follow-up was censored at 25.4.20, and 1.33 (95%CI 1.22-1.46) when it was censored at 6.4.20.

Comparison with data from other sources
No directly comparable data are available for other studies in the UK, but in the ISARIC study, the prevalence of CHD among Covid-19 patients admitted to hospitals in England Wales and Scotland was 29%, with an adjusted HR for death of 1.31 (95%CI 1.18-1.45). Unless people with CHD who contract Covid-19 have no increased risk of being admitted to hospital, which seems unlikely, this would suggest a relative risk for mortality among all Covid-19 cases in the wider community of at least 1.3.

Conclusions
Although based on a large and nationally representative dataset, the OS risk estimates for CHD seem low in comparison with what might be expected from the ISARIC study. Furthermore, the HR in models with censoring at 25.4.20 reduced substantially (from 2.01 to 1.27) when adjusted for other risk factors in addition to sex and age. It is unclear which factors of adjustment contributed most to such a large reduction in the risk estimate.

With these considerations in mind, we tentatively adopted a relative risk of 1.4 for CHD in our risk model.

Robustness of risk estimate
The relative risk for CHD seems likely to be higher than 1.4, but how much higher is currently quite uncertain. The value adopted for the risk model should therefore be classed as provisional.

UPDATE 1: 26 MAY 2020

In the updated report on the ISARIC study [1.1], the adjusted HR for death in hospitalised Covid-19 patients with CHD was lower than previously reported at 1.16 (95%CI 1.08-1.24).

In the large population-based cohort study by Barron et al [1.2], after adjustment for age, sex, ethnicity, region, social deprivation, and diabetes (classified by type), ORs for cumulative mortality from Covid-19 were 1.32 (95%CI 1.28-1.36) for coronary heart disease, 2.23 (95%CI 2.16-2.31) for cerebrovascular disease, and 2.23 (95%CI 2.14-2.31) for heart failure. Putting these results alongside those from the OS study, we think it is reasonable to adopt refined relative risk estimates for cardiovascular disease as set out in Table G1:

Table G1. Revised relative risk estimates adopted for cardiovascular disease

Comorbidity	Adopted relative risk
Heart failure	2.2
Other chronic heart disease	1.3
Cerebrovascular disease	2.2

As these risk estimates come largely from a single, albeit large, cohort study, without adjustment for the full range of other potentially relevant comorbidities, we class them as provisional.

UPDATE 4: 16 JULY 2020

The updated report from the OS study includes important new information on risks associated with hypertension (defined as diagnosed hypertension, or the most recent recording indicating systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg) [4.1]. Although hypertension was not associated with increased mortality when results were averaged across the whole study sample, there was a strong interaction with age, with elevated HRs at younger ages, and low HRs at older ages (Table G2).

Table G2 Hazard ratios for hypertension by age in the OpenSAFELY study [4.1]

Age band (years)	HR	(95%CI)
18 to <40	3.11	(1.68-5.71)
40 to <50	2.75	(1.97-3.83)
50 to <60	2.07	(1.73-2.47)
60 to <70	1.32	(1.17-1.50)
70 to <80	0.94	(0.86-1.02)
≥80	0.73	(0.69-0.78)

Across the range of working ages, this pattern of risk can be modelled approximately by assuming a linear decline in HR with age, and applying the equation HR = 0.94 + {(75 – age)*(3.11 – 0.94)/45}. Table G3 shows the estimated HRs (rounded to one decimal place) that are derived, and it can be seen that the values for the mid-points of the age categories in Table G2 agree reasonably well with the reported risk estimates for those age categories.

Table G3 Modelled hazard ratios by age

Age (years)	Modelled HR
20	3.6
21-22	3.5
23-25	3.4
26-27	3.3
28-29	3.2
30-31	3.1
32-33	3.0
34-35	2.9
36-37	2.8
38-39	2.7
40-41	2.6
42-43	2.5
44-45	2.4
46-47	2.3
48-49	2.2
50-51	2.1
52-54	2.0
55-56	1.9
57-58	1.8
59-60	1.7
61-62	1.6
63-64	1.5
65-66	1.4
67-68	1.3
69-70	1.2
71-72	1.1
73	1.0

These estimates for risk associated with hypertension at working ages are based on a large and representative study sample, and we have therefore adopted them provisionally in our risk model.

UPDATE 6: 13 AUGUST 2020

As in earlier reports from the OS study, the new supplementary analysis does not distinguish between hear failure and other CHD [6.2]. However, for CHD as a whole, it indicates a clear gradient in RRs across the range of working ages (Table G4). Table G4 also shows the ratios of these age-specific risk estimates to the summary risk estimate of 1.2 across all adults in the same study [4.1]. We think, therefore, that there is a need to refine our risk estimates for heart failure and other CHD to take account of differences by age. As a first approximation we have applied the calculated ratios from Table G4 to our previously adopted summary risk estimates for heart failure and CHD, and assigned the newly calculated RRs to the mid-points of the age ranges to which they apply. For example, the ratio of 2.5 for ages 50-59 when multiplied by the summary relative risk of 2.2 for heart failure gave an approximate relative risk of 5.5 that was assigned to age 55 years. Risk estimates for other ages have then been assigned by interpolation or extrapolation with minor smoothing (Table G5). As before, these estimates are classed as provisional.

Table G4. Adjusted hazard ratios for chronic heart disease by age in the OpenSAFELY study, and ratios to summary hazard ratio across all adults.

Age (years)	18-39	40-49	50-59	60-69	70-79
HR	6.48	3.84	3.01	1.64	1.32
Ratio to summary HR of 1.2 across all adults	5.4	3.2	2.5	1.4	1.1

Table G5. Adopted relative risk estimates for heart failure and other chronic heart disease by year of true age

True age (years)	Heart failure		Other chronic heart disease	
	Approximate RR	Equivalent added years	Approximate RR	Equivalent added years
20	13	25	7.8	20
21	13	25	7.8	20
22	13	25	7.8	20
23	13	25	7.8	20
24	13	25	7.8	20
25	13	25	7.8	20
26	12	24	7.1	19
27	12	24	7.1	19
28	12	24	7.1	19
29	12	24	7.1	19
30	12	24	7.1	19
31	11	23	6.4	18
32	11	23	6.4	18
33	11	23	6.4	18
34	10	22	5.8	17
35	10	22	5.8	17
36	10	22	5.8	17
37	10	22	5.8	17
38	8.7	21	5.2	16
39	8.7	21	5.2	16
40	8.7	21	5.2	16
41	7.8	20	4.7	15
42	7.8	20	4.7	15
43	7.8	20	4.7	15
44	7.1	19	4.2	14
45	7.1	19	4.2	14
46	7.1	19	4.2	14
47	6.4	18	3.8	13
48	6.4	18	3.8	13
49	6.4	18	3.8	13
50	5.8	17	3.8	13
51	5.8	17	3.4	12
52	5.8	17	3.4	12
53	5.2	16	3.4	12
54	5.2	16	3.4	12
55	5.2	16	3.1	11
56	4.7	15	3.1	11
57	4.7	15	2.8	10

58	4.2	14	2.8	10
59	4.2	14	2.5	9
60	3.8	13	2.5	9
61	3.8	13	2.3	8
62	3.4	12	2.3	8
63	3.4	12	2.1	7
64	3.1	11	2.1	7
65	3.1	11	1.9	6
66	3.1	11	1.9	6
67	2.8	10	1.7	5
68	2.8	10	1.7	5
69	2.8	10	1.7	5
70	2.5	9	1.5	4
71	2.5	9	1.5	4
72	2.5	9	1.5	4
73	2.3	8	1.4	3
74	2.3	8	1.4	3
75	2.3	8	1.4	3

The new supplement to the OS report also gives age-specific risk estimates for the diagnostic category “stroke/dementia”, which we would expect at working ages to be dominated by stroke (Table G6) [6.2]. The HR at ages 70-79 years (2.52) is similar to the summary risk estimate of 2.2 that we previously adopted for cerebrovascular disease. However, HRs are higher at younger ages, and we think that this should be taken into account in our risk model. With interpolation, extrapolation and some smoothing, we have therefore adopted RRs by age for cerebrovascular disease as set out in Table G7. As before, these estimates are provisional.

Table G6. Adjusted hazard ratios for stroke/dementia by age from OpenSAFELY study

18-69		18-49	50-59	60-69	70-79
HR	**(95%CI)**	**HR**	**HR**	**HR**	**HR**
1.96	(1.65-2.33)	4.93	4.42	2.70	2.52

Table G7. Adopted relative risk estimates for cerebrovascular disease by year of true age

True age (years)	Approximate RR	Equivalent added years
20	5.8	17
21	5.8	17
22	5.8	17
23	5.2	16
24	5.2	16
25	5.2	16
26	5.2	16
27	5.2	16
28	5.2	16
29	5.2	16
30	5.2	16
31	5.2	16
32	5.2	16
33	5.2	16
34	5.2	16
35	5.2	16
36	5.2	16
37	4.7	15
38	4.7	15
39	4.7	15
40	4.7	15
41	4.7	15
42	4.7	15
43	4.7	15
44	4.7	15
45	4.7	15
46	4.7	15
47	4.2	14
48	4.2	14
49	4.2	14
50	4.2	14
51	4.2	14
52	4.2	14
53	3.8	13
54	3.8	13
55	3.8	13
56	3.8	13
57	3.8	13
58	3.4	12

59	3.4	12
60	3.4	12
61	3.4	12
62	3.4	12
63	3.1	11
64	3.1	11
65	3.1	11
66	3.1	11
67	3.1	11
68	2.8	10
69	2.8	10
70	2.8	10
71	2.8	10
72	2.5	9
73	2.5	9
74	2.5	9
75	2.5	9

UPDATE 9: 28 OCTOBER 2020

The QCovid report provides summary estimates of relative risk for six categories of cardiovascular disease (Table G8). The final QCovid models did not include hypertension as a risk factor, although there is now strong evidence that it is associated with greater vulnerability to Covid-19, especially in younger adults [4.1].

Table G8. Summary adjusted HRs for categories of cardiovascular disease in QCovid report

Risk factor	**Women**		**Men**	
	HR	**(95%CI)**	**HR**	**(95%CI)**
Coronary heart disease	1.24	(1.10-1.40)	1.13	(1.02-1.24)
Stroke	1.34	(1.19-1.51)	1.24	(1.11-1.38)
Atrial fibrillation	1.18	(1.04-1.34)	1.11	(1.00-1.24)
Congestive cardiac failure	1.37	(1.18-1.60)	1.40	(1.24-1.59)
Thrombo-embolism	1.18	(1.01-1.38)	1.36	(1.18-1.57)
Peripheral vascular disease	1.42	(1.15-1.76)	1.38	(1.19-1.61)
Congenital heart disease	1.23	(0.75-2.03)	1.03	(0.72-1.47)

By way of comparison, Table G9 shows our currently adopted RRs for categories of cardiovascular disease, and also the summary RRs that we previously adopted at Update 4 before evidence emerged of important age interactions.

Table G9. Currently adopted RRs for categories of cardiovascular disease

Risk factor	Currently adopted RR		Previously adopted RR at Update 4
	Age 20 years	Age 70 years	
Heart failure	13	2.5	2.2
Other chronic heart disease	7.8	1.5	1.3
Cerebrovascular disease	5.8	2.8	2.2
Hypertension	3.4	1.2	

While our currently adopted RRs are substantially higher than those in QCovid, that is in large measure because they allow for age interactions. The previously adopted summary RRs across all ages are also higher than those in QCovid, but much less so. In part this may reflect the inclusion of residence in a nursing or care home in the QCovid regression model (adjusted HRs 3.61 in women and 4.28 in men). Within the QCovid regression model, there was no major heterogeneity in the HRs for subcategories of chronic heart disease other than heart failure.

On balance, we do not think the new evidence in the QCovid report indicates a need to modify our currently adopted RRs for cardiovascular disease.

H. Chronic respiratory disease other than asthma

INITIAL ASSESSMENT: 20 MAY 2020

In the OS study, this category of comorbidity included chronic obstructive pulmonary disease (COPD), fibrosing lung disease, bronchiectasis and cystic fibrosis. After adjustment for sex, age, multiple comorbidities and various other risk factors, it carried HRs of 1.78 (95%CI 1.67-1.90) when follow-up was censored at 25.4.20, and 1.97 (95%CI 1.77-2.18) with censoring at 6.4.20. The lower HR after longer follow-up may in part reflect selective shielding of people with chronic respiratory disease as the epidemic evolved.

Comparison with data from other sources

In the ISARIC study of patients admitted to hospital with Covid-19 in England, Wales and Scotland, chronic pulmonary disease other than asthma was reported in approximately 17% of cohort members, and carried an adjusted HR for death of 1.19. Table H1 shows approximate numbers of patients by sex and age in the ISARIC cohort (estimated by measuring the lengths of bars in a bar chart), the prevalence of doctor-diagnosed COPD (including chronic bronchitis and emphysema) in the same age and sex strata in the 2010 Health Survey for England [7], and calculations from these data of the numbers of patients with doctor-diagnosed COPD that might have been expected in the ISARIC cohort if COPD had no effect on hospital admission for Covid-19, and its prevalence in the general population was at similar levels in 2020. Summation across all of the strata indicates that the overall expected percentage prevalence of doctor-diagnosed COPD in the ISARIC cohort would be: 100*(339+205)/(4401+2807) = 8%. In addition, a smaller prevalence of other types of chronic pulmonary disease might be expected. When the 17% observed prevalence of chronic pulmonary disease is set alongside findings from this rough analysis of expected numbers, and also the HR of 1.2 for death in patients with chronic pulmonary disease, the OS relative risk estimates look highly plausible.

Table H1. Calculation of expected numbers of patients with doctor-diagnosed COPD in ISARIC cohort, based on prevalence in the 2010 Health Survey for England

Aggregated age band (years)	Approximate numbers in ISARIC cohort			Prevalence % of DDCOPD* in 2010 Health Survey for England		Expected numbers of cases in ISARIC cohort	
	Male	Female		Male	Female	Male	Female
0-14	73	36					
16-24	36	40		1	0	0	0
25-34	84	124		2	2	2	2
35-44	233	131		2	4	5	5
45-54	459	339		4	5	18	17
55-64	674	357		6	8	40	29
65-74	901	474		11	10	99	47
75+	1940	1305		9	8	175	104
Total	4401	2807				339	205

*Doctor-diagnosed COPD

Conclusions

Based on these considerations, we assigned a relative risk of 1.9 to chronic respiratory disease other than asthma.

Robustness of risk estimate

The adopted relative risk estimate is derived from a large and nationally representative cohort, and supported by data from an independent source. We consider it to be moderately robust.

UPDATE 1: 26 MAY 2020

In the updated report of the ISARIC study, there was no major change in the adjusted HR for death from Covid-19 in relation to chronic pulmonary disease (updated value = 1.17) [1.1].

UPDATE 3: 29 JUNE 2020

A new analysis from the OS collaborative, which focused on 148,588 patients with COPD, found that after adjustment for sex, age and multiple comorbidities, risk of Covid-19-related death was modestly elevated in relation to use of inhaled corticosteroids as compared with use of a long-acting beta-agonist or muscarinic antagonist (HR 1.38, 95%CI 1.08-1.75) [3.5]. However, the report did not provide information on the overall relative risk of death among people with COPD, and did not consider use of oral corticosteroids. For these reasons, we do not think that it can be used to modify our currently adopted risk estimates for chronic respiratory disease.

UPDATE 6: 13 AUGUST 2020

For respiratory disease other than asthma, the supplementary report from the OS study suggests that the currently adopted RR of 1.9 can reasonably be applied at the upper end of the range of working ages (Table H2) [6.2]. However, at younger ages, RRs may be as high as 4.0. We have therefore applied interpolation, extrapolation and a degree of smoothing to the HRs in Table H2 to give new adopted risk estimates by age as shown in Table H3. Like the previous summary estimate across all ages, the values at older ages are classified as moderately robust, but those at younger ages, which are based on less robust data, are considered provisional.

Table H2. Adjusted hazard ratios for respiratory disease other than asthma by age from the OpenSAFELY study

Age (years)						
18-69		18-39	40-49	50-59	60-69	70-79
HR	(95%CI)	HR	HR	HR	HR	HR
2.22	(1.93-2.55)	3.65	5.40	3.56	2.13	1.87

Table H3. Adopted relative risk estimates for respiratory disease other than asthma by year of true age

True age (years)	Approximate RR	Equivalent added years	Robustness of risk estimate
20	5.8	17	Provisional
21	5.8	17	Provisional
22	5.8	17	Provisional
23	5.8	17	Provisional
24	5.8	17	Provisional
25	5.2	16	Provisional
26	5.2	16	Provisional
27	5.2	16	Provisional
28	5.2	16	Provisional
29	5.2	16	Provisional
30	5.2	16	Provisional
31	4.7	15	Provisional
32	4.7	15	Provisional
33	4.7	15	Provisional
34	4.7	15	Provisional
35	4.7	15	Provisional
36	4.2	14	Provisional
37	4.2	14	Provisional
38	4.2	14	Provisional
39	4.2	14	Provisional
40	4.2	14	Provisional
41	3.8	13	Provisional
42	3.8	13	Provisional
43	3.8	13	Provisional
44	3.8	13	Provisional
45	3.8	13	Provisional
46	3.8	13	Provisional
47	3.4	12	Provisional
48	3.4	12	Provisional
49	3.4	12	Provisional
50	3.4	12	Provisional
51	3.4	12	Provisional
52	3.1	11	Provisional
53	3.1	11	Provisional
54	3.1	11	Provisional
55	3.1	11	Provisional
56	2.8	10	Provisional
57	2.8	10	Provisional
58	2.8	10	Provisional
59	2.5	9	Provisional

60	2.5	9	Provisional
61	2.5	9	Provisional
62	2.3	8	Moderately robust
63	2.3	8	Moderately robust
64	2.3	8	Moderately robust
65	2.1	7	Moderately robust
66	2.1	7	Moderately robust
67	2.1	7	Moderately robust
68	2.1	7	Moderately robust
69	2.1	7	Moderately robust
70	1.9	6	Moderately robust
71	1.9	6	Moderately robust
72	1.9	6	Moderately robust
73	1.9	6	Moderately robust
74	1.9	6	Moderately robust
75	1.9	6	Moderately robust

UPDATE 9: 28 OCTOBER 2020

The QCovid analysis distinguishes three categories of respiratory disease other than asthma (Table H4) [9.1].

Table H4. Adjusted HRs for respiratory disease other than asthma in QCovid report

Risk factor	**Women**		**Men**	
	HR	**(95%CI)**	**HR**	**(95%CI)**
COPD	1.50	(1.29-1.74)	1.25	(1.11-1.42)
Rare lung conditions	0.85	(0.60-1.19)	1.20	(0.93-1.56)
Pulmonary hypertension/fibrosis	1.55	(1.00-2.40)	1.47	(0.93-2.32)

It is apparent from Table 2 of the QCovid report that within the cohort that was used to derive risk estimates, COPD accounted for almost 80% of chronic respiratory disease other than asthma. Our currently adopted RRs for chronic respiratory disease other than asthma range from 1.9 at age 70 years to 5.8 at age 20 years, and the earlier summary RR across all adult ages from Update 4 was 1.9. That this last value is somewhat higher than those in QCovid, may reflect the inclusion of residence in a care home or nursing home in the QCovid regression model.

We do not think that the QCovid findings indicate a need to modify our risk estimates for chronic respiratory disease other than asthma, which have the advantage of taking into account age interactions. However, they provide reassurance that vulnerability associated with rarer lung conditions is not markedly higher than that for other non-asthmatic chronic respiratory disease.

I. Chronic kidney disease

INITIAL ASSESSMENT: 20 MAY 2020

In the OS study, chronic kidney disease (CKD) was defined as a glomerular filtration rate <60mL/min/1.73m^2, as estimated from the most recent serum creatinine measurement, where available. It was present in 6.3% of cohort members. In analyses that adjusted for sex, age, multiple comorbidities and various other risk factors, it carried HRs for mortality from Covid-19 of 1.72 (95%CI 1.62-1.83) when follow-up continued to 25.4.20, and 1.75 (95%CI 1.58-1.92) when it was censored at 6.4.20. There was no indication of any major attenuation of risk with longer follow-up because of selective shielding of patients with CKD.

Comparison with data from other studies

In the ISARIC cohort of patients hospitalised with Covid-19, the reported prevalence of CKD was approximately 14%, and it carried an adjusted HR of 1.25 for death. Table I1 shows approximate numbers of patients by sex and age in the ISARIC cohort (estimated by measuring the lengths of bars in a bar chart), the prevalence of doctor-diagnosed CKD in the same age and sex strata in the 2016 Health Survey for England [6], and calculations from these data of the numbers of patients with doctor-diagnosed CKD that might have been expected in the ISARIC cohort if CKD had no effect on hospital admission for Covid-19. Summation across all of the strata indicates that the overall expected percentage prevalence of doctor-diagnosed CKD in the ISARIC cohort would be: 100*(185+89)/(4401+2807) = 4%. This implies a ratio of observed to expected prevalence of 14%/4% = 3.5. It is possible, however, that doctor-diagnosed CKD, which after allowance for sex and age, had a lower prevalence in the 2016 Health Survey for England than CKD as determined in the OS study, represented a more severe spectrum of disease. When this is taken into account, the findings from this further analysis of ISARIC data do not call into question the relative risk estimates from the OS study.

Table I1. Calculation of expected numbers of patients with doctor-diagnosed CKD in ISARIC cohort, based on prevalence in the 2016 Health Survey for England

Entries in the table are rounded to the nearest whole number, but calculations have used original unrounded numbers. Therefore numbers as presented may not sum exactly to reported totals.

Aggregated age band (years)	Approximate numbers in ISARIC cohort			Prevalence % of DDCKD* in 2016 Health Survey for England		Expected numbers of cases in ISARIC cohort	
	Male	Female		Male	Female	Male	Female
0-14	73	36					
16-24	36	40		0	1	0	0
25-34	84	124		1	1	1	1
35-44	233	131		1	1	3	1
45-54	459	339		2	2	9	5
55-64	674	357		4	2	24	6
65-74	901	474		5	3	44	16
75+	1940	1305		5	5	104	60
Total	4401	2807				185	89

*Doctor-diagnosed CKD

Conclusions

Based on the above considerations, we adopted a relative risk of 1.7 for CKD defined as a glomerular filtration rate <60mL/min/1.73m^2, as estimated from the most recent serum creatinine measurement.

Robustness of risk estimate

This risk estimate is based on findings in a large and nationally representative cohort, and is broadly consistent with independent data from other sources. As such, we judge it to be moderately robust.

UPDATE 1: 26 MAY 2020

The large cohort study of patients with diabetes by Holman et al [1.3] provides estimated HRs for death related to Covid-19 by level of eGFR. Results were presented separately for people with Type I and Type 2 diabetes, with adjustment for age, sex, ethnicity, social deprivation, region, most recent HbA1c, time since diagnosis of diabetes, BMI, smoking, previous stroke and previous heart failure (Table I2).

Table I2. Adjusted hazard ratios for death related to Covid-19 in diabetic patients according to estimated glomerular filtration rate

Estimated glomerular filtration rate (mL/min/1.73m^2)	Type 1 diabetes		Type 2 diabetes	
	HR	(95%CI)	HR	(95%CI)
≥60	1		1	
45-59	1.92	(1.46-2.53)	1.37	(1.30-1.45)
30-44	2.16	(1.59-2.93)	1.75	(1.64-1.86)
15-29	2.98	(2.04-4.35)	2.24	(2.04-2.45)
<15	6.85	(4.65-10.09)	4.83	(4.28-5.46)
Missing	1.45	(0.83-2.55)	0.82	(0.70-0.97)

The large majority of patients with eGFR <60 mL/min/1.73m^2 had values in the range from 30 to 59, for which the HRs for Covid-19-related death ranged from 1.37 to 2.16. When compared with our previously adopted relative risk of 1.7 for CKD in the general population, these results do not suggest any major departure from multiplication of relative risks when diabetes and CKD are present in combination.

UPDATE 4: 16 JULY 2020

The updated analysis from the OS study [4.1] provides separate risk estimates for two levels of kidney function. When follow-up was censored at 6.4.20, HRs were 1.49 (95%CI 1.36-1.63) for an eGFR of 30-60 mL/min and 2.98 (95%CI 2.57-3.46) for an eGFR of <30 mL/min. With full follow-up, both HRs were lower (1.33 and 2.52 respectively), possibly reflecting an effect of selective shielding. A secondary analysis suggested a particularly high risk associated with a history of dialysis or end-stage renal failure (HR 3.69, 95%CI 3.10-4.39). It is unclear what proportion of those with eGFR <30 mL/min fell into this category, but it is likely to have been small.

Given that this gradient of risk is compatible with findings in diabetic patients (Table I2), we think the estimates can be used to refine the assessment of risk for chronic kidney disease.

We have therefore revised our adopted relative risk estimates for CKD as set out in Table I3.

Table I3 Revised relative risk estimates adopted for chronic kidney disease

Category of chronic kidney disease	Adopted relative risk
Estimated GFR 30-60 mL/min	1.5
Estimated GFR < 30 mL/min	3.0
History of dialysis or end-stage renal failure	3.7

As before, we consider the estimates for CKD to be moderately robust.

UPDATE 6: 13 AUGUST 2020

For CKD, the supplement to the OS report shows extremely steep gradients in HRs across age bands (Table I4) [6.2]. By interpolation, extrapolation and smoothing across the age bands and two severities of CKD, we obtained approximate age-specific RRs as set out in Table I5. We have removed the separate risk estimate for history of dialysis or end-stage renal failure because of the lack of age-specific risk estimates for the category and uncertainties about the extent to which it overlaps with “Estimated GFR <30 mL/min” (which carried only a slightly lower summary relative risk) and organ transplant. The new risk estimates for “Estimated GFR 30-60 mL/min” at ages older than 70 years are considered moderately robust, but the other RRs are classed as provisional.

Table I5. Adjusted hazard ratios for chronic kidney disease by age in the OpenSAFELY study

Estimated GFR (mL/min)	Age (years)						
	18-69		18-39	40-49	50-59	60-69	70-79
	HR	(95%CI)	HR	HR	HR	HR	HR
30-60	2.19	(1.89-2.54)	32.13	8.17	4.48	2.18	1.35
<30	7.87	(6.33-9.78)	114.97	21.27	24.39	8.59	4.49

Table I6. Adopted relative risk estimates for chronic kidney disease by year of true age

True age (years)	Estimated GFR 30-60 mL/min		Estimated GFR < 30 mL/min	
	Approximate RR	Equivalent added years	Approximate RR	Equivalent added years
20	75	42	234	53
21	68	41	211	52
22	61	40	190	51
23	55	39	172	50
24	50	38	172	50
25	45	37	155	49
26	45	37	140	48
27	41	36	126	47
28	37	35	114	46
29	33	34	114	46
30	30	33	103	45
31	27	32	93	44
32	27	32	93	44
33	24	31	84	43
34	22	30	75	42
35	20	29	68	41
36	18	28	61	40
37	16	27	55	39
38	15	26	50	38
39	15	26	45	37
40	13	25	41	36
41	12	24	37	35
42	11	23	37	35
43	10	22	33	34
44	8.7	21	30	33
45	7.8	20	30	33
46	7.1	19	27	32
47	7.1	19	27	32
48	6.4	18	24	31
49	6.4	18	22	30
50	5.8	17	22	30
51	5.2	16	20	29
52	5.2	16	18	28
53	4.7	15	18	28
54	4.2	14	16	27
55	4.2	14	15	26
56	3.8	13	15	26
57	3.8	13	13	25
58	3.4	12	12	24

59	3.1	11	11	23
60	3.1	11	11	23
61	2.8	10	10	22
62	2.5	9	10	22
63	2.5	9	8.7	21
64	2.3	8	7.8	20
65	2.3	8	7.8	20
66	2.1	7	7.1	19
67	2.1	7	7.1	19
68	1.9	6	6.4	18
69	1.9	6	6.4	18
70	1.7	5	5.8	17
71	1.7	5	5.8	17
72	1.5	4	5.2	16
73	1.5	4	5.2	16
74	1.4	3	4.7	15
75	1.4	3	4.7	15

UPDATE 7: 27 AUGUST 2020

Table I7, which is based on the revised report by Holman et al [7.2], shows adjusted HRs for death related to Covid-19 in diabetic patients aged <70 years, according to estimated GFR.

Table I7. Adjusted hazard ratios for death related to Covid-19 in diabetic patients aged <70 years according to estimated glomerular filtration rate

Estimated glomerular filtration rate (mL/min/1.73m^2)	Type 1 diabetes		Type 2 diabetes	
	HR	(95%CI)	HR	(95%CI)
≥90	1		1	
60-89	1.25	(0.79-1.96)	1.26	(1.13-1.41)
45-59	2.68	(1.47-4.89)	2.16	(1.82-2.57)
30-44	5.22	(2.92-9.35)	3.61	(2.94-4.43)
15-29	7.01	(3.66-13.39)	4.99	(3.87-6.44)
<15	11.46	(6.31-20.81)	8.44	(6.64-10.73)
Missing	1.91	(0.87-4.19)	0.94	(0.67-1.33)

When compared with the summary adjusted HRs for ages 18-69 years in the OS study (Table I5), these results do not point to any major departure from multiplication of relative risks when CKD is present in combination with diabetes, but conclusions must be guarded because the RRs associated with CKD vary so much with age.

UPDATE 9: 28 OCTOBER 2020

Table I8 shows adjusted HRs for CKD in the QCovid paper [9.1].

Table I8. Adjusted hazard ratios for chronic kidney disease in QCovid

Category of chronic kidney disease	Women		Men	
	HR	(95%CI)	HR	(95%CI)
CKD stage 3	1.30	(1.17-1.45)	1.18	(1.06-1.30)
CKD stage 4	1.37	(1.05-1.80)	1.83	(1.46-2.29)
CKD stage 5 only	3.00	(2.19-4.12)	2.40	(1.83-3.15)
CKD 5 with dialysis	2.68	(0.86-8.36)	3.67	(2.02-6.66)

These risk estimates are reasonably consistent with those which we adopted at Update 4 as summary values across all adult ages (1.5 for estimated GFR 30-60 mL/min, 3.0 for estimated GFR < 30 mL/min, and 3.7 for history of dialysis or end-stage renal failure). However, they make no allowance for the very strong interaction with age [6.2], which we have since incorporated into our adopted risk model, with relative risks in excess of 200 for severe renal failure at young ages.

We do not think that the findings from the QCovid report point to a need to change our currently adopted risk estimates for CKD.

X. Risk factors not included in risk model

INITIAL ASSESSMENT: 20 MAY 2020

Two potential determinants of vulnerability carried no apparent increase in the risk of death from Covid-19 in the OS study, after account had been taken of sex, age and comorbidities. These were smoking and hypertension. Adjusted HRs with follow-up to 25.4.20 were 0.88 (95%CI 0.79-0.99) for current vs. never smokers, and 0.95 (95% CI 0.89-1.01) for high blood pressure or diagnosed hypertension.

These risk factors were therefore excluded from the risk model.

UPDATE 1: 26 MAY 2020

In the large cohort study of patients with diabetes by Holman and colleagues [1.3], after adjustment for age, sex, ethnicity, social deprivation, region, HbA1c, eGFR, BMI, previous stroke and previous heart failure (but not for asthma or other respiratory disease), HRs for current smokers relative to never smokers were <1, both in people with Type 1 and Type 2 disease. Moreover, HRs in ex-smokers were barely elevated (1.10 and 1.12). Also, there was reported to be no statistically significant increase in risk in association with having been prescribed anti-hypertensive drugs. These new data support the decision not to include smoking or hypertension in our risk model.

UPDATE 2: 14 JUNE 2020

Further studies reported since the last update support the assessment that after account is taken of other risk factors, any vulnerability from smoking [2.2] or hypertension is small [2.1-2.3]. However, this does not preclude the possibility of a larger elevation of risk in association with some, as yet unidentified, sub-categories of hypertension.

UPDATE 4: 16 JULY 2020

The updated report from the OS study [4.1] indicates that although there was no overall elevation of risk for hypertension, there was an important interaction between hypertension and age, with increased risks at younger ages. In response to this observation, we have now added hypertension to our risk model (see Section G).

UPDATE 8: 11 OCTOBER 2020

Limited data have now become available on vulnerability in relation to several other risk factors not currently included in our risk model.

Inflammatory bowel disease
A Danish study analysed all individuals tested for SARSCov-2 in the Capital and Zealand geographical regions [8.2]. Between January 28, 2020 and June 2, 2020, a total of 231,601 individuals were screened for SARSCov-2, of whom 8,476 individuals (3.7%) tested positive. The prevalence of 2.5% in the subset of 2,486 people with inflammatory bowel disease (IBD) was significantly lower than among those who did not have IBD (3.7%; $p<0.01$). Within the test-positive cases with IBD, four patients (6.5%) died as compared with 5.8% of those without immune-mediated diseases. This result does not suggest any major increase in vulnerability to Covid-19 in association with IBD, but the analysis was based on small numbers and did not allow for age or other risk factors.

Rare autoimmune rheumatic diseases
A newly reported study examined age-standardised mortality from all causes during March and April 2020 (i.e. at the beginning of the Covid-19 epidemic) among 168,691 people in the UK with rare autoimmune rheumatic diseases (including systemic lupus erythematosus, scleroderma, idiopathic inflammatory myositis, Behcet's disease, giant cell arteritis and juvenile idiopathic arthritis) [8.3]. The death rate was 1.44 (95%CI 1.42-1.45) times higher than during the same months in the previous five years, whereas the corresponding ratio for the general population of England was 1.38. While mortality was standardised for sex and age, this comparison did not allow for other risk factors, and cannot be used to add rare autoimmune rheumatic diseases to our risk model. It suggests, however, that they are associated with a level of vulnerability broadly similar to that which we have estimated for rheumatoid arthritis/lupus/psoriasis.

Hypothyroidism
A cohort study in New York focused on 3,703 adult patients with laboratory-confirmed Covid-19 during March 2020 [8.4]. Among 251 (6.8%) with pre-existing hypothyroidism, after adjustment for age, sex, race, BMI, smoking and a number of comorbidities, there was no clearly increased risk of hospitalisation (OR 1.23, 95%CI 0.88-1.70), and among those hospitalised, there was no clearly increased risk of death (adjusted OR 1.07, 95%CI 0.75-1.54). These findings suggest that hypothyroidism is not a major determinant of vulnerability to Covid-19.

Psychiatric disorders
In Update 2, we noted that a cohort study in Denmark had indicated a high relative risk of mortality in Covid-19 cases who had a major psychiatric disorder treated by antipsychotic drugs (OR 3.6, 95% CI 2.5 – 5.2) [2.1]. Several further studies have now examined vulnerability to Covid-19 among people with mental illness.

In a cohort study of 48,058 patients with a broad spectrum of psychotic and non-psychotic mental illness in South Korea and 47,058 controls without a mental illness (propensity matched for age, sex, region of residence, history of diabetes, cardiovascular disease, cerebrovascular disease, COPD, asthma, hypertension or chronic kidney disease, and a comorbidity index), the prevalence of a positive test for SARSCov2 during January 1 to May 15 2020, was similar in the two groups (adjusted OR 1.00, 95%CI 0.93-1.08) [8.5]. However, among 1,383 patients with mental illness who tested positive, the risk of severe

clinical outcomes (death, admission to intensive care or invasive ventilation) was somewhat higher than in 1,391 test-positive, propensity-matched controls (adjusted OR 1.27, 95%CI 1.01-1.66).

A cohort study in Yale, USA, focused on 1,685 patients with confirmed Covid-19 who were hospitalised during 15 February to 25 April 2020, and followed to 27 May 2020 [8.6]. After control for demographic characteristics, medical comorbidities and hospital location, mortality was higher in the 473 (28%) with a previous psychiatric diagnosis (HR 1.5, 95%CI 1.1-1.9).

In a large US study based on the electronic health records of 61.8 million adults, patients with a recent diagnosis of a mental disorder (attention deficit hyperactivity disorder, bipolar disorder, depression or schizophrenia) and Covid-19 infection had a higher death rate (8.5%) than those with Covid-19 but no mental disorder (4.7%) [8.7]. However, the comparison did not adjust for potentially important covariates.

Together, these new studies add to the weight of evidence for greater vulnerability to Covid-19 among people with psychiatric disorders. However, they do not provide quantitative estimates of relative risk that allow for other factors in our risk model and that could confidently be extrapolated to the UK.

Pregnancy

A systematic review of Covid-19 in pregnant and recently pregnant women, based on four studies, found that in comparison with non-pregnant women of reproductive age with Covid-19, there was no increase in all-cause mortality (OR 0.81, 95%CI 0.49-1.33), although risk of ICU admission (OR 1.62, 95%CI 1.33-1.96) and invasive ventilation (OR 1.88, 95%CI 1.36-2.60) was higher [8.8]. It is unclear to what extent these risk estimates were adjusted for other determinants of vulnerability to Covid-19.

An investigation in New Jersey, USA, compared the prevalence of adverse maternal and neonatal outcomes in 61 mothers who had suffered from confirmed Covid-19 during pregnancy and 122 controls matched for delivery date [8.9]. After allowance for the matching (by conditional logistic regression), and for advanced maternal age, obesity and comorbid medical problems, the ORs for adverse maternal and neonatal outcomes in association with Covid-19 during pregnancy were 3.4 (95% CI 1.2-13.4) and 1.7 (95% CI 0.8-4.8), respectively.

As yet, there is still insufficient evidence for inclusion of pregnancy in our risk model. However, it is important to note that adverse effects of Covid-19 during pregnancy may extend to the foetus as well as the mother.

Medication

A population based-cohort study in Denmark explored 30-day mortality in 9,236 people who tested positive for SARS-CoV-2 during 27 February 2020 to 29 April 2020 [8.10]. Among 248 recent users of non-steroidal anti-inflammatory drugs, after allowance for calendar week of the test, and propensity scores based on age, sex, relevant comorbidities and use of

selected prescription drugs, mortality was similar to that in non-users (RR 1.02, 95%CI 0.57-1.82).

In another register-based cohort study of people in Denmark with confirmed infection by SARS-CoV-2, there was no association between recent prescription of ibuprofen and severe outcomes (acute respiratory syndrome, admission to intensive care or death) after allowance for sex, age and various comorbidities [8.11].

A systematic review and meta-analysis of clinical outcomes in patients with autoimmune diseases found lower death rates in patients treated by anti-TNF monotherapy than in those treated in other ways, but it is unclear to what extent the comparison controlled for known determinants of vulnerability to Covid-19 [8.12].

UPDATE 9: 28 OCTOBER 2020

Severe mental illness

The QCovid analysis found adjusted HRs for severe mental illness of 1.29 (95%CI 1.15-1.45) in women and 1.26 (1.13-1.42) in men. These relative risks are fairly small, and may not be representative of those associated with severe mental illness as it occurs in the workforce (which could be lower because people with the most severe forms of psychotic illness tend not to be in employment). A further complication is that the QCovid regression analyses included a separate term for being in residential care or homeless.

When the findings from QCovid are set alongside those from earlier studies, we consider that there is now convincing evidence that severe mental illness is associated with at least a small increase in vulnerability to Covid-19. However, available data are not yet sufficiently detailed and robust to allow its inclusion in our risk model.

Osteoporotic fracture

The QCovid study found small elevations of risk in association with osteoporotic fracture of the hip, spine, wrist and humerus (HRs 1.12 in women, and 1.41 in men). However, it is unclear what level of association might apply at working ages, and we do not think the evidence is sufficient to warrant the addition of osteoporotic fracture to our risk model.

UPDATE 10: 11 DECEMBER 2020

Inflammatory bowel disease

A meta-analysis of five studies found that among patients with inflammatory bowel disease and SARS-CoV-2 infection, risk of mortality was higher in those with ulcerative colitis than Crohn's disease (RR 1.94, 95%CI 1.22-3.10) [10.3]. In addition, synthesis of data from four studies indicated higher fatality in those using steroids (RR vs. non-use 2.70, 95%CI 1.61-4.55) or 5-aminosalicylate (RR 2.62, 95%CI 1.67-4.11), and lower fatality in those treated

with biological agents (RR 0.22, 95%CI 0.13-0.38). Because of differences in adjustment for covariates, these results cannot be used to add numerical estimates of risk for inflammatory bowel disease to our risk model. However, they suggest that Crohn's disease, in particular, is associated with increased vulnerability to Covid-19, which is somewhat higher on average than that associated with inflammatory arthritis. In addition, they provide some reassurance that treatment of inflammatory bowel disease with biological agents does not lead to even higher vulnerability.

Pregnancy

A retrospective cohort study of women in Mexico aged 13 to 49 years with laboratory-confirmed Covid-19, found similar fatality rates in 448 who were pregnant (2.2%) and 17,942 who were not (2.7%) [10.4]. However, no risk estimate was presented that adjusted for age and other potentially relevant covariates.

Medication

In a Danish national cohort study of 4,842 patients diagnosed with Covid-19 during 22 February to 17 May 2020, after adjustment for age, sex, ethnicity, socioeconomic status and various comorbidities, use of statins in the previous six months was not associated with significantly different risk of mortality from all causes (HR 0.96, 95% CI 0.78 to 1.18) [10.5].

A record linkage study using data on approximately 25,000 adult patients with osteoarthritis from The Health Improvement Network (THIN) database in the UK found that after adjustment by propensity matching for multiple covariates, risk of mortality subsequent to suspected/confirmed Covid-19 was no higher in patients using non-steroidal anti-inflammatory drugs than in those prescribed combinations of paracetamol with codeine or dihydrocodeine [10.6].

Y. Rarer comorbidities

INITIAL ASSESSMENT: 20 MAY 2020

The OS study also provides adjusted risk estimates for a number of other rarer comorbidities, for which we have not as yet identified any independent corroborating data. HRs for these comorbidities, adjusted for sex, age, multiple other comorbidities and various other risk factors are summarised in Table Y1, together with the relative risks that we have carried forward to our risk model. The choice of the values taken forward weighed the greater statistical precision of the estimates based on longer follow-up against the possibility that they may in some cases have been biased downwards because of selective shielding by people with the comorbidity. All adopted values are considered provisional.

Table Y1. Adjusted hazard ratios for other comorbidities from the OS cohort, and relative risk estimates taken forward to risk model

Comorbidity		Follow-up censored at 25.4.20			Follow-up censored at 6.4.20			RR adopted for risk model
		HR	(95%CI)		HR	(95%CI)		
Non-haematological cancer								
None		1			1			
Diagnosed <1 year ago		1.56	(1.29-1.89)		1.51	(1.10-2.05)		1.6
Diagnosed 1-4.9 years ago		1.19	(1.04-1.35)		1.36	(1.13-1.65)		1.2
Diagnosed ≥5 years ago		0.97	(0.88-1.06)		0.92	(0.79-1.06)		1.0
Haematological malignancy								
None		1			1			
Diagnosed <1 year ago		3.52	(2.41-5.14)		2.60	(1.30-5.22)		3.5
Diagnosed 1-4.9 years ago		3.12	(2.50-3.89)		3.67	(2.66-5.06)		3.1
Diagnosed ≥5 years ago		1.88	(1.55-2.29)		1.64	(1.18-2.28)		1.9
Liver disease		1.61	(1.33-1.95)		1.86	(1.40-2.47)		1.6
Chronic neurological disease other than stroke or dementia*		2.46	(2.19-2.76)		2.28	(1.88-2.76)		2.5
Organ transplant		4.27	(3.20-5.70)		2.62	(1.51-4.57)		4.3
Spleen diseases†		1.41	(0.93-2.12)		1.87	(1.06-3.30)		1.4
Rheumatoid/lupus/psoriasis		1.23	(1.12-1.35)		1.31	(1.14-1.51)		1.2
Other immunosuppressive condition‡		1.69	(1.21-2.34)		2.01	(1.25-3.25)		1.8

*Includes motor neurone disease, myasthenia gravis, multiple sclerosis, Parkinson's disease, cerebral palsy, quadriplegia, hemiplegia, malignant primary brain tumour and progressive cerebellar disease.
†Includes splenectomy, or spleen dysfunction (e.g. from sickle cell disease).
‡Includes HIV, conditions inducing permanent immunodeficiency (ever diagnosed), aplastic anaemia, and temporary immunodeficiency recorded within the past year.

UPDATE 3: 29 JUNE 2020

In a prospective cohort study of all 800 cancer patients from a network of UK cancer centres who presented to hospital during 18 March to 26 April 2020 with symptomatic test-positive Covid-19, 226 (25%) died, almost all (211) because of the infection [3.6]. After adjustment for age, gender and comorbidities, there was no significant association of mortality either with chemotherapy in the preceding four weeks, or with other treatment modalities. However, little can be drawn from this in relation to our model of vulnerability because entry to the study was restricted to symptomatic Covid-19 presenting to hospital, and the risk estimates did not account for type, duration or severity of cancer.

A multicentre matched cohort study in Spain compared the risk of severe outcomes (death, invasive ventilation, admission to intensive care or serious complications) in 456 rheumatic patients with Covid-19 confirmed by PCR testing and 456 controls, also with confirmed Covid-19, but with no rheumatic disease [3.7]. After adjustment for sex, age and various comorbidities, risk was elevated in those with autoimmune/immune-mediated diseases (AI/IMD) such as SLE, Sjögren's syndrome, systemic sclerosis, polymyalgia rheumatica and vasculitis (OR 1.98, 95%CI 1.15-3.41), but not in those with inflammatory arthritides such as rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis. The results cannot be used to refine our currently adopted risk estimate for rheumatoid/lupus/psoriasis because of uncertainties about the selection of patients for the Covid-19 testing that qualified them for entry to the study. However, the findings suggest that within that broad diagnostic category, the vulnerability associated with AI/IMD may be greater than that associated with inflammatory arthritis.

UPDATE 4: 16 JULY 2020

The updated report from the OS study [4.1] indicates a need to modify slightly some of the adopted risk estimates in Table Y1. Table Y2 shows the HRs in the new report and indicates the relative risks that have now been adopted (those that have changed being marked by double asterisks).

Table Y2. Adjusted hazard ratios for other comorbidities from the updated report of the OS cohort [4.1], and relative risk estimates taken forward to risk model

Comorbidity		Follow-up censored at 6.5.20			Follow-up censored at 6.4.20			RR adopted for risk model
		HR	(95%CI)		HR	(95%CI)		
Non-haematological cancer								
None		1			1			
Diagnosed <1 year ago		1.72	(1.50-1.97)		1.66	(1.27-2.16)		1.7**
Diagnosed 1-4.9 years ago		1.15	(1.05-1.27)		1.34	(1.13-1.60)		1.2
Diagnosed ≥5 years ago		0.96	(0.91-1.03)		0.92	(0.81-1.04)		1.0
Haematological malignancy								
None		1			1			
Diagnosed <1 year ago		2.82	(2.09-3.81)		2.22	(1.15-4.27)		2.8**
Diagnosed 1-4.9 years ago		2.47	(2.06-2.96)		3.50	(2.61-4.69)		2.5**
Diagnosed ≥5 years ago		1.62	(1.39-1.88)		1.45	(1.07-1.98)		1.6**
Liver disease		1.75	(1.51-2.03)		1.92	(1.48-2.49)		1.8**
Chronic neurological disease other than stroke or dementia*		2.58	(2.38-2.79)		2.26	(1.91-2.68)		2.6**
Organ transplant		3.55	(2.79-4.52)		2.57	(1.60-4.13)		3.6**
Asplenia†		1.34	(0.98-1.83)		1.87	(1.13-3.11)		1.4
Rheumatoid/lupus/psoriasis		1.19	(1.11-1.27)		1.29	(1.14-1.46)		1.2
Other immunosuppressive condition‡		1.70	(1.34-2.16)		1.98	(1.32-2.96)		1.8

*Includes motor neurone disease, myasthenia gravis, multiple sclerosis, Parkinson's disease, cerebral palsy, quadriplegia, hemiplegia, and progressive cerebellar disease.
†Includes splenectomy, or spleen dysfunction (e.g. from sickle cell disease).
‡Includes HIV, conditions inducing permanent immunodeficiency (ever diagnosed), aplastic anaemia, and temporary immunodeficiency recorded within the past year.
**Adopted relative risk estimates that have changed

UPDATE 6: 13 AUGUST 2020

The new supplementary analysis of the OS cohort indicates importantly higher HRs at younger ages for several categories of comorbidity (Tables Y3 and Y4) [6.2]. To account for this observation, we have applied interpolation, extrapolation and a degree of smoothing to obtain newly adopted age-specific estimates of RR as set out in Tables Y5 and Y6. These estimates are liable to appreciable statistical uncertainty as well errors in the somewhat arbitrary smoothing, and we therefore regard them as provisional. Nevertheless, we expect

them to be more reliable than the previously adopted summary estimates of relative risk in all adults.

Table Y3. Adjusted hazard ratios for cancer, organ transplant and asplenia by age in the OpenSAFELY study

	Age (years)					
	18-69		18-49	50-59	60-69	70-79
	HR	(95%CI)	HR	HR	HR	HR
Non-haematological cancer						
None	1		1	1	1	1
Diagnosed <1 year ago	3.83	(2.90-5.05)	20.42	2.06	3.96	2.00
Diagnosed 1-4.9 years ago	1.85	(1.45-2.35)	8.05	2.58	1.62	1.21
Diagnosed ≥5 years ago	1.32	(1.06-1.66)	4.75	1.88	1.09	0.92
Haematological malignancy						
None	1		1	1	1	1
Diagnosed <1 year ago	6.64	(3.66-12.04)	24.55	8.57	7.61	3.20
Diagnosed 1-4.9 years ago	5.81	(4.02-8.40)	15.80	16.76	4.48	3.70
Diagnosed ≥5 years ago	2.02	(1.31-3.12)	6.94	2.91	1.94	1.75
Organ transplant	2.33	(1.69-3.22)	9.11	6.70	5.66	2.33
Asplenia	1.67	(0.92-3.03)	3.01	1.54	2.23	0.91

Table Y4. Adjusted hazard ratios for liver disease, other neurological disease and other immunosuppressive condition by age in the OpenSAFELY study

	Age (years)						
	18-69		18-39	40-49	50-59	60-69	70-79
	HR	(95%CI)	HR	HR	HR	HR	HR
Liver disease	2.15	(1.68-2.74)	16.29	2.66	3.70	2.36	1.51
Other neurological disease	4.75	(3.92-5.75)	7.66	15.54	5.84	4.17	3.43
Other immunosuppressive condition	2.97	(2.04-4.32)	33.36	4.00	4.04	2.61	1.63

Table Y5. Adopted relative risk estimates for cancers by year of true age

True age (years)	Non-haematological cancer by years since diagnosis						Haematological malignancy by years since diagnosis					
	<1		1-4.9		≥5		<1		1-4.9		≥5	
	RR	Added years	RR	Added years	RR	Added years	RR	Added years	RR	Added years	RR	Added years
20	33	34	13	25	6.4	18	30	33	27	32	8.7	21
21	30	33	13	25	6.4	18	30	33	24	31	8.7	21
22	30	33	13	25	6.4	18	27	32	24	31	8.7	21
23	27	32	12	24	6.4	18	27	32	24	31	8.7	21
24	27	32	12	24	5.8	17	27	32	22	30	8.7	21
25	24	31	12	24	5.8	17	27	32	22	30	7.8	20
26	24	31	11	23	5.8	17	24	31	22	30	7.8	20
27	22	30	11	23	5.2	16	24	31	20	29	7.8	20
28	22	30	10	22	5.2	16	24	31	20	29	7.8	20
29	20	29	10	22	5.2	16	24	31	20	29	7.8	20
30	20	29	10	22	4.7	15	22	30	18	28	7.8	20
31	18	28	8.7	21	4.7	15	22	30	18	28	7.1	19
32	18	28	8.7	21	4.7	15	22	30	18	28	7.1	19
33	16	27	8.7	21	4.2	14	22	30	16	27	7.1	19
34	16	27	7.8	20	4.2	14	20	29	16	27	7.1	19
35	15	26	7.8	20	3.8	13	20	29	16	27	6.4	18
36	15	26	7.1	19	3.8	13	20	29	15	26	6.4	18
37	13	25	7.1	19	3.4	12	20	29	15	26	6.4	18
38	13	25	6.4	18	3.4	12	18	28	13	25	6.4	18
39	12	24	6.4	18	3.1	11	18	28	13	25	5.8	17
40	12	24	6.4	18	3.1	11	18	28	13	25	5.8	17
41	11	23	5.8	17	3.1	11	18	28	12	24	5.8	17
42	11	23	5.8	17	2.8	10	16	27	12	24	5.8	17
43	10	22	5.2	16	2.8	10	16	27	11	23	5.2	16
44	10	22	5.2	16	2.8	10	16	27	11	23	5.2	16
45	8.7	21	5.2	16	2.5	9	15	26	10	22	5.2	16
46	8.7	21	4.7	15	2.5	9	15	26	10	22	4.7	15
47	7.8	20	4.7	15	2.5	9	15	26	10	22	4.7	15
48	7.8	20	4.2	14	2.3	8	13	25	10	22	4.2	14
49	7.1	19	3.8	13	2.3	8	13	25	10	22	4.2	14
50	7.1	19	3.8	13	2.3	8	12	24	8.7	21	3.8	13
51	6.4	18	3.4	12	2.1	7	12	24	8.7	21	3.4	12
52	6.4	18	3.1	11	2.1	7	11	23	8.7	21	3.4	12
53	5.8	17	3.1	11	2.1	7	11	23	8.7	21	3.1	11
54	5.2	16	2.8	10	1.9	6	10	22	7.8	20	3.1	11
55	5.2	16	2.8	10	1.9	6	10	22	7.8	20	2.8	10

56	4.7	15	2.5	9	1.9	6	8.7	21	7.8	20	2.8	10
57	4.7	15	2.5	9	1.7	5	8.7	21	7.1	19	2.8	10
58	4.2	14	2.3	8	1.7	5	7.8	20	7.1	19	2.5	9
59	4.2	14	2.3	8	1.5	4	7.8	20	6.4	18	2.5	9
60	3.8	13	2.3	8	1.5	4	7.1	19	6.4	18	2.5	9
61	3.8	13	2.1	7	1.4	3	7.1	19	5.8	17	2.3	8
62	3.4	12	2.1	7	1.4	3	6.4	18	5.8	17	2.3	8
63	3.4	12	2.1	7	1.2	2	5.8	17	5.2	16	2.3	8
64	3.1	11	1.9	6	1.2	2	5.8	17	5.2	16	2.1	7
65	3.1	11	1.9	6	1.1	1	5.2	16	4.7	15	2.1	7
66	2.8	10	1.9	6	1.1	1	5.2	16	4.7	15	2.1	7
67	2.8	10	1.7	5	1.1	1	4.7	15	4.2	14	2.1	7
68	2.5	9	1.7	5	1.1	1	4.7	15	4.2	14	1.9	6
69	2.5	9	1.5	4	1.0	0	4.2	14	3.8	13	1.9	6
70	2.5	9	1.5	4	1.0	0	4.2	14	3.8	13	1.9	6
71	2.3	8	1.4	3	1.0	0	3.8	13	3.4	12	1.9	6
72	2.3	8	1.4	3	1.0	0	3.8	13	3.4	12	1.7	5
73	2.3	8	1.4	3	1.0	0	3.4	12	3.1	11	1.7	5
74	2.1	7	1.2	2	1.0	0	3.4	12	3.1	11	1.7	5
75	2.1	7	1.2	2	1.0	0	3.1	11	3.1	11	1.7	5

Table Y6. Adopted relative risk estimates for rarer comorbidities by year of true age

True age (years)	Organ transplant		Asplenia		Liver disease		Other neurological disease		Other immunosuppressive condition	
	RR	Added years	RR	Added years	RR	Added years	RR	Added years	RR	Added years
20	13	25	4.2	14	27	32	11	23	22	30
21	13	25	4.2	14	24	31	11	23	22	30
22	12	24	3.8	13	24	31	10	22	20	29
23	12	24	3.8	13	22	30	10	22	20	29
24	12	24	3.8	13	22	30	10	22	18	28
25	12	24	3.8	13	20	29	10	22	18	28
26	12	24	3.8	13	20	29	10	22	16	27
27	12	24	3.8	13	18	28	10	22	16	27
28	12	24	3.8	13	18	28	10	22	15	26
29	12	24	3.8	13	16	27	10	22	15	26
30	11	23	3.8	13	16	27	10	22	13	25
31	11	23	3.8	13	15	26	10	22	13	25
32	11	23	3.8	13	15	26	8.7	21	12	24
33	11	23	3.4	12	13	25	8.7	21	12	24
34	11	23	3.4	12	13	25	8.7	21	11	23
35	11	23	3.4	12	12	24	8.7	21	11	23
36	10	22	3.4	12	12	24	8.7	21	10	22
37	10	22	3.4	12	11	23	8.7	21	10	22
38	10	22	3.4	12	11	23	8.7	21	8.7	21
39	10	22	3.4	12	10	22	7.8	20	8.7	21
40	10	22	3.1	11	10	22	7.8	20	7.8	20
41	10	22	3.1	11	8.7	21	7.8	20	7.8	20
42	8.7	21	3.1	11	8.7	21	7.8	20	7.1	19
43	8.7	21	3.1	11	7.8	20	7.8	20	7.1	19
44	8.7	21	3.1	11	7.8	20	7.8	20	6.4	18
45	8.7	21	3.1	11	7.1	19	7.8	20	5.8	17
46	8.7	21	2.8	10	7.1	19	7.1	19	5.8	17
47	7.8	20	2.8	10	6.4	18	7.1	19	5.2	16
48	7.8	20	2.8	10	5.8	17	7.1	19	5.2	16
49	7.8	20	2.8	10	5.8	17	7.1	19	4.7	15
50	7.1	19	2.5	9	5.2	16	6.4	18	4.7	15
51	7.1	19	2.5	9	4.7	15	6.4	18	4.7	15
52	7.1	19	2.5	9	4.7	15	6.4	18	4.2	14
53	6.4	18	2.3	8	4.2	14	6.4	18	4.2	14
54	6.4	18	2.3	8	4.2	14	5.8	17	3.8	13
55	6.4	18	2.3	8	3.8	13	5.8	17	3.8	13

56	5.8	17	2.3	8	3.8	13	5.8	17	3.8	13
57	5.8	17	2.1	7	3.4	12	5.2	16	3.4	12
58	5.2	16	2.1	7	3.4	12	5.2	16	3.4	12
59	5.2	16	2.1	7	3.1	11	5.2	16	3.1	11
60	4.7	15	1.9	6	3.1	11	5.2	16	3.1	11
61	4.7	15	1.9	6	2.8	10	4.7	15	3.1	11
62	4.2	14	1.9	6	2.8	10	4.7	15	2.8	10
63	4.2	14	1.7	5	2.5	9	4.7	15	2.8	10
64	3.8	13	1.7	5	2.5	9	4.2	14	2.5	9
65	3.8	13	1.7	5	2.3	8	4.2	14	2.5	9
66	3.4	12	1.7	5	2.3	8	4.2	14	2.5	9
67	3.4	12	1.5	4	2.1	7	4.2	14	2.3	8
68	3.1	11	1.5	4	2.1	7	3.8	13	2.3	8
69	3.1	11	1.4	3	1.9	6	3.8	13	2.1	7
70	2.8	10	1.4	3	1.9	6	3.8	13	2.1	7
71	2.8	10	1.2	2	1.9	6	3.8	13	2.1	7
72	2.5	9	1.2	2	1.7	5	3.4	12	1.9	6
73	2.5	9	1.1	1	1.7	5	3.4	12	1.9	6
74	2.3	8	1.1	1	1.5	4	3.4	12	1.7	5
75	2.3	8	1.0	0	1.5	4	3.4	12	1.7	5

In contrast to the comorbidities listed in Table Y5, there was no clear gradient in HRs by age band for the disease category “rheumatoid/lupus/psoriasis” [6.2], and taking into account the statistical uncertainty around the estimate for the youngest age band (95%CI 0.79-5.85), we think it is reasonable to retain the currently adopted RR estimate of 1.2 for all working ages.

UPDATE 7: 27 AUGUST 2020

A new report based on the OS cohort compared mortality from Covid-19 as registered on death certificates during 1 February to 22 June 2020 in 27,480 adults with a primary care record of HIV infection and 17,255,425 controls [7.3]. After adjustment for covariates (age, sex, ethnicity, social deprivation, obesity, smoking and various comorbidities including other immunosuppression), Cox regression indicated an increased risk (HR 2.30, 95%CI 1.55-3.41). There was no significant interaction with age, but with only 25 Covid-19 deaths among patients with HIV, an effect may have been missed. The observed association was said to be larger early in the epidemic, suggesting a possible effect of selective shielding.

Further evidence of increased vulnerability to Covid-19 in people with HIV infection comes from follow-up of hospitalised patients with laboratory-confirmed infection in the ISARIC study [7.4]. After adjustment for age, sex, ethnicity, possible hospital-acquisition of Covid-19, presentation date, 10 comorbidities, and severity at presentation, there was higher fatality at 28 days among 115 patients with HIV (HR 1.63, 1.07-2.48).

While the findings from these two new reports confirm greater vulnerability to Covid-19 among patients with HIV infection, we do not think that they are sufficiently strong and divergent to warrant adoption of separate risk estimates for HIV, distinct from those for immunosuppressive conditions more broadly.

UPDATE 8: 11 OCTOBER 2020

A new study from the UK analysed data on 1044 adult patients with active cancer (metastatic, undergoing anticancer treatment, or treated in past 12 months with surgery, systemic anti-cancer therapy or radiotherapy) and a positive RT-PCR test for SARSCov-2 registered during March 18 to May 8 2020 [8.13]. Patients with cancer of the skin or unspecified site were excluded. After adjustment for age and sex, all-cause inpatient case-fatality was higher for leukaemia, myeloma and lymphoma (ORs 1.65 to 2.25 relative to non-colorectal cancers of digestive organs), but there were no clear differences for other tumour types. This supports our higher adopted risk estimates for haematological as compared with non-haematological cancers, and does not indicate any need to change those risk estimates.

UPDATE 9: 28 OCTOBER 2020

Cancer

The QCovid paper [9.1] presents risk estimates for respiratory tract cancer, blood cancer, three categories of chemotherapy (grouped according to risk of febrile neutropenia or lymphopenia) in the past 12 months, radiotherapy in the past 6 months, and bone marrow or stem cell transplant in the past 6 months (Table Y7).

Table Y7. Adjusted hazard ratios in QCovid for cancer and cancer treatments

Risk factor	Women		Men	
	HR	(95%CI)	HR	(95%CI)
Respiratory tract cancer	1.70	(1.16-2.49)	1.27	(0.89-1.81)
Blood cancer	1.50	(1.06-2.12)	1.29	(0.97-1.71)
Chemotherapy grade A	2.30	(1.35-3.94)	1.74	(1.10-2.75)
Chemotherapy grade B	3.52	(2.29-5.42)	3.50	(2.54-4.82)
Chemotherapy grade C	17.31	(6.52-45.98)	3.37	(1.17-9.64)
Radiotherapy in past 6 months	2.11	(1.30-3.41)	2.09	(1.48-2.96)
Bose marrow or stem cell transplant in past 6 months	2.78	(0.22-34.55)	6.10	(1.11-33.54)

From the information given in Table 2 of the QCovid report, it appears that individuals could be assigned to only one grade of chemotherapy (presumably the highest that was applicable).

Comparison of these results with the currently adopted risk estimates for cancer in our model is complicated by differences in approach. There is agreement that haematological malignancies tend to be associated with greater vulnerability than solid cancers, and the associations with cancer treatments in QCovid accord with our current assessment that vulnerability is greater for cancers that have recently been diagnosed (although the treatments could be used for recurrent as well as newly diagnosed disease). However, our risk estimates do not directly take into account treatment. On the other hand, the QCovid estimates make no allowance for age interactions (for which there is good evidence from OpenSAFELY [6.2]).

Because of the differences in classification of risk factors, we do not think that the findings from QCovid can be used to modify our risk estimates for cancers. However, we note that within cancer patients, risk may be particularly high in patients who have recently been treated by radiotherapy or Group C chemotherapy as defined in the QCovid report Supplementary Box A (All ALL/AML regimens; BEP; highly immunosuppressive chemotherapy such as FluDAP, high dose methotrexate and cytarabine; trifuradine/tipracil). This should be taken into account when applying clinical judgement in the interpretation of estimated Covid-age.

Liver disease
The QCovid paper gives adjusted HRs for cirrhosis of the liver of 1.85 (95%CI 1.15-2.99) in women and 1.29 (95%CI 0.83-2.02) in men. These results accord with the summary (across all ages) RR of 1.8 for liver disease that we adopted at Update 4, before evidence emerged of age interactions. We do not think that the new evidence on liver disease warrants any change to our currently adopted risk estimates.

Chronic neurological disease other than stroke or dementia
Table Y8 shows risk estimates from the QCovid report [9.1] for categories of chronic neurological disease other than stroke (stroke is considered under cardiovascular disease – see Section G) and dementia (the more severe forms of which would normally be incompatible with employment).

Table Y8. Adjusted hazard ratios for chronic neurological disease from QCovid paper

Category of neurological disease	Women		Men	
	HR	(95%CI)	HR	(95%CI)
Parkinson's disease	1.13	(0.79-1.62)	1.93	(1.59-2.35)
Epilepsy	1.58	(1.23-2.03)	1.60	(1.30-1.97)
Motor neurone disease, multiple sclerosis, myasthenia gravis or Huntingdon's	2.75	(1.83-4.12)	1.99	(1.24-3.18)
Cerebral palsy	3.45	(1.10-10.78)	2.77	(1.23-6.23)

Overall, these risk estimates are a little lower than the summary (across all adult ages) RR of 2.6 that we adopted in Update 4 for neurological disease excluding stroke and dementia. However, the HR for Parkinson's disease may have been reduced by inclusion of residence in a care or nursing home as a variable in the regression model. Our currently adopted risk estimates take account of age interactions, and are higher (3.8 to 11). We do not think the new results indicate that any change is required.

Organ transplant
The QCovid paper gives risk estimates for organ transplant as set out in Table Y9 [9.1].

Table Y9. Risk estimates for organ transplant in QCovid paper

Category of transplant	Women		Men	
	HR	(95%CI)	HR	(95%CI)
CKD stage 5 with transplant	7.84	(3.38-18.17)	3.20	(1.62-6.33)
Solid organ transplant (excluding kidney and bone marrow)	1.46	(0.36-5.92)	1.72	(0.71-4.21)

These results seem compatible with the summary (across all adults) risk estimate of 3.6 for organ transplant that we adopted at Update 4. However, since then we have added allowance for important age interaction (RRs up to 13). We do not think the new findings warrant any change to our currently adopted risk estimates for organ transplant.

Diseases of spleen and immunodeficiency

The QCovid report gives adjusted hazard ratios for sickle cell disease or severe immunodeficiency of 5.94 (95%CI 1.89-18.67) in women and 4.41 (95%CI 1.41-13.81) in men [9.1]. It is unclear exactly how severe immunodeficiency was defined, or the extent to which splenectomy and other splenic pathology was covered. Therefore, we do not think the findings warrant any change to our currently adopted risk estimates for spleen diseases (ranging from 1.4 at age 70 to 4.2 at age 20) or other immunosuppressive conditions (2.1 to 22).

Autoimmune diseases

The QCovid report gives adjusted HRs for rheumatoid arthritis/SLE of 1.32 (95%CI 1.06-1.65) in women, and 1.02 (0.75-1.38) in men [9.1]. These risk estimates may have been reduced a little by inclusion of treatment with oral steroids as a separate term in the regression model (HRs 1.83 in women and 1.44 in men). However, they seem compatible with our currently adopted RR of 1.2 for rheumatoid/lupus/psoriasis, and we do not think that any change to that value is required.

UPDATE 10: 11 DECEMBER 2020

Cancer

A cohort study of 351 Dutch cancer patients with Covid-19, of whom 114 died, found that after adjustment for sex, age and other malignancy, risk of a fatal outcome was higher for those with lung cancer (OR 3.40, 95%CI 1.51-7.64) [10.7]. This suggests that vulnerability to Covid-19 may be higher for lung cancer than for other non-haematological malignancies.

Liver disease

A study of 745 patients with chronic liver disease and SARS-CoV-2 infection in 29 countries found substantially higher short-term mortality in those with cirrhosis (123/386) than the remainder (27/359) [10.8]. After adjustment for sex, age, ethnicity, smoking, obesity, and

eight categories of comorbidity, the elevated risk persisted, and increased progressively with severity of cirrhosis. The findings are not sufficiently robust to underpin specification of separate numerical risk estimates for sub-categories of chronic liver disease within our risk model, but they should be taken into account when applying clinical judgement to estimates of vulnerability from the model.

Organ transplant

Among 113 kidney transplant patients in London with SARS-CoV-2 infection confirmed by PCR testing during March to June 2020 or antibody testing during 1 June to 3 July 2020, 17 had died following infection [10.9]. Despite the small numbers, after allowance for age, and whether the transplant was from a living donor, risk of death was significantly higher in those with diabetes (OR 3.7). This finding gives limited support to the multiplicativity of RRs associated with organ transplantation and diabetes.

SECTION THREE: ESTIMATION OF INDIVIDUAL VULNERABILITY

Covid-age

Using the relative risk estimates that have been derived in the preceding sections of this report, it is possible to estimate the vulnerability of an individual should he or she at some stage contract Covid-19.

A major determinant of risk is age. Using the risk estimate for age from Section A, an increase in age of n years carries a relative risk of 1.0945^n. This implies that a relative risk, R, is equivalent to that from an increase in age of (log R)/(log 1.0945) years. Applying this formula, Table Z1 expresses the relative risks that are currently adopted for risk factors other than age as the additional years of age that would give an equivalent relative risk.

The analyses that were used to generate these risk estimates assumed that relative risks from different risk factors multiply, which in the absence of persuasive evidence to the contrary, seems a reasonable assumption. With that assumption, an individual's vulnerability can be assessed from Table Z1 by summing the added age equivalent for each risk factor that applies. For example, an Asian woman aged 50 with poorly controlled Type 2 diabetes would have an estimated vulnerability equivalent to that of a healthy white man aged 50 - 8 + 4 + 8 = 54 years.

We designate the age at which a healthy white man would have equivalent vulnerability, a person's "Covid-19-age".

Table Z1. Vulnerability from risk factors expressed as equivalence to added years of age

Risk factor	Relative risk	Equivalent added years of age	Robustness of risk estimate
Female sex	0.5	-8	Robust
Ethnicity			
Asian or Asian British	1.5	4	Moderately robust
Black	1.7	6	Moderately robust
Mixed	1.6	5	Provisional
Other non-white	1.3	3	Provisional
Body mass index (Kg/m^2)			
30-34.9	1.4	4	Provisional
35-39.9	1.6	5	Provisional
≥40	2.4	10	Provisional
Asthma			
Mild (no requirement for oral corticosteroids in past year)	1.1	1	Moderately robust
Severe (requiring oral corticosteroids in past year)	1.4	4	Moderately robust
Diabetes			
Type 1			
HbA1≤58 mmol/mol in past year	2.0	8	Moderately robust
HbA1>58 mmol/mol in past year	2.7	11	Moderately robust
HbA1c unknown	3.3	13	Moderately robust
Type 2 and other			
HbA1≤58 mmol/mol in past year	1.5	4	Moderately robust
HbA1>58 mmol/mol in past year	2.0	8	Moderately robust
HbA1c unknown	2.3	9	Moderately robust
Heart failure	2.2	9	Provisional
Other chronic heart disease	1.3	3	Provisional
Cerebrovascular disease	2.2	9	Provisional
Chronic respiratory disease (excluding asthma)	1.9	7	Moderately robust

Chronic kidney disease*	1.7	6	Moderately robust
Non-haematological cancer			
Diagnosed <1 year ago	1.6	5	Provisional
Diagnosed 1-4.9 years ago	1.2	2	Provisional
Diagnosed ≥5 years ago	1	0	Provisional
Haematological malignancy			
Diagnosed <1 year ago	3.5	14	Provisional
Diagnosed 1-4.9 years ago	3.1	13	Provisional
Diagnosed ≥5 years ago	1.9	7	Provisional
Liver disease	1.6	5	Provisional
Chronic neurological disease other than stroke or dementia**	2.5	10	Provisional
Organ transplant	4.3	16	Provisional
Spleen diseases†	1.4	4	Provisional
Rheumatoid/lupus/psoriasis	1.2	2	Provisional
Other immunosuppressive condition‡	1.8	7	Provisional

*Glomerular filtration rate <60mL/min/1.73m2, as estimated from the most recent serum creatinine measurement.
**Includes motor neurone disease, myasthenia gravis, multiple sclerosis, Parkinson's disease, cerebral palsy, quadriplegia, hemiplegia and progressive cerebellar disease.
†Includes splenectomy, or spleen dysfunction (e.g. from sickle cell disease).
‡Includes HIV, conditions inducing permanent immunodeficiency (ever diagnosed), aplastic anaemia, and temporary immunodeficiency recorded within the past year.

Case-fatality rates by Covid-age

To understand how Covid-age relates to case-fatality rate, an estimate is needed of the case-fatality rate for healthy white men at a specified age. Estimated relative risks by age can then be applied to estimate case-fatality at other ages.

As yet, no direct data are available from the UK on case-fatality by sex and age for all cases of Covid-19 including asymptomatic infection, or even for cases of symptomatic disease. Our starting point, therefore, was a report by Ferguson and colleagues [9], which presented estimates of infection fatality ratio (case-fatality rate) by sex and age, drawing on findings from a study by Verity and colleagues [10].

In the Ferguson report, the case fatality rate at 40-49 years of age in men and women combined was estimated to be 1.5 per 1000. Assuming a relative risk of 0.5 in women as compared with men (see Section B), this would imply a case fatality rate in men of 1.5*2/1.5 = 2 per thousand.

A limited check on the plausibility of this figure is possible using data on fatality rates among patients in the ISARIC study, who were admitted to British hospitals with Covid-19 [3]. From measurements of the lengths of bars in a bar chart, among men aged 40-49 years, approximately 22 had died by the time that data collection was censored, 241 had been discharged from hospital alive, and 58 were still in hospital. This implies a case-fatality rate of 1000*22/(22+241) = 83 per thousand among those whose final outcome was known. It is likely, however, that the true case fatality rate is somewhat higher than this because the cohort members who were still in hospital when data collection was censored, selectively included sicker patients who had failed to recover quickly. If the estimated fatality rate of 2 per 1000 in the general population were correct, a fatality rate of, say, 100 per 1000 in hospitalised cases, would imply that approximately one in fifty cases in the community lead to hospital admission. That figure seems plausible, for a relatively young age group, although there are major uncertainties about the frequency of asymptomatic infection.

Tentatively, therefore, we assumed an overall case-fatality rate of 2 per 1000 in men aged 45 (just above the mid-point of the age range under consideration), and that on average, the Covid-age of men with a true age of 45 might be 47 years. Thus, we assigned a case fatality rate of 2 per 1000 to a Covid-age of 47. Rates at other ages were then calculated by applying the previously determined relative risk of 1.0945 for each additional year of age (see Section A). Results are summarised in Table Z2.

In view of the many assumptions in these estimates of age-specific case fatality, we emphasise that they are subject to substantial uncertainty, and should be regarded only as provisional. A particular source of uncertainty is the unknown frequency of asymptomatic infection in the general population.

Table Z2. Relative risks of mortality from Covid-19 and estimated case fatality rates in healthy white males by age

Age (years)	Estimated risk relative to that at age 47 years (healthy white males)	Estimated case-fatality rate per 1000 in cases of Covid-19 infection (healthy white males)
20	0.1	0.2
25	0.1	0.3
30	0.2	0.4
35	0.3	0.7
40	0.5	1.1
45	0.8	1.7
47	1.0	2.0
50	1.3	2.6
52	1.6	3.1
54	1.9	3.8
56	2.3	4.5
58	2.7	5.4
60	3.2	6.5
62	3.9	7.7
64	4.6	9.3
66	5.6	11
68	6.7	13
70	8.0	16
72	9.6	19
74	11.5	23
76	13.7	27
78	16.4	33
80	19.7	39

UPDATE 3: 29 JUNE 2020

A national analysis of mortality from Covid-19 in Belgium during 8 March to 9 May 2020, in conjunction with estimated infection rates, suggested an infection fatality rate of 2.9 per 1000 among men aged 45-64 years [3.8]. It is unclear how reliably infection rates were estimated, and the fatality rate is for all men in the age band, including those with comorbidities. However, the finding is broadly consistent with our guarded estimate that case fatality among healthy men increases from 1.7 per 1000 at age 45 to 9.3 per 1000 at age 64.

UPDATE 4: 16 JULY 2020

In accordance with the rationale set out in the updates to Section 2, we have revised our adopted risk estimates as set out in Table Z3.

Table Z3. Vulnerability from risk factors expressed as equivalence to added years of age

Risk factor	Relative risk	Equivalent added years of age**	Robustness of risk estimate
Female sex	0.6	-5	Moderately robust
Ethnicity			
Asian or Asian British	1.5	4	Moderately robust
Black	1.7	5	Moderately robust
Mixed	1.4	3	Provisional
Other non-white	1.3	3	Provisional
Body mass index (Kg/m^2)			
30-34.9	1.3	3	Provisional
35-39.9	1.6	5	Provisional
≥40	2.4	9	Provisional
Hypertension (according to actual age)			
Age 20-26 years	3.3-3.6	12	Provisional
Age 27-33 years	3.0-3.3	11	Provisional
Age 34-39 years	2.7-2.9	10	Provisional
Age 40-44 years	2.4-2.6	9	Provisional
Age 45-49 years	2.2-2.4	8	Provisional
Age 50-54 years	2.0-2.1	7	Provisional
Age 55-57 years	1.8-1.9	6	Provisional
Age 58-61 years	1.6-1.8	5	Provisional
Age 62-64 years	1.5-1.6	4	Provisional
Age 65-67 years	1.3-1.4	3	Provisional
Age 68-70 years	1.2-1.3	2	Provisional
Age 71-72 years	1.1	1	Provisional
Age ≥73 years	1	0	Provisional
Heart failure	2.2	8	Provisional
Other chronic heart disease	1.3	3	Provisional
Cerebrovascular disease	2.2	8	Provisional

Asthma			
Mild (no requirement for oral corticosteroids in past year)	1.1	1	Moderately robust
Severe (requiring oral corticosteroids in past year)	1.4	3	Moderately robust
Chronic respiratory disease (excluding asthma)	1.9	6	Moderately robust
Diabetes			
Type 1			
HbA1≤58 mmol/mol in past year	2.0	7	Moderately robust
HbA1>58 mmol/mol in past year	2.7	10	Moderately robust
HbA1c unknown	3.3	12	Moderately robust
Type 2 and other			
HbA1≤58 mmol/mol in past year	1.5	4	Moderately robust
HbA1>58 mmol/mol in past year	2.0	7	Moderately robust
HbA1c unknown	2.3	8	Moderately robust
Chronic kidney disease			
Estimated GFR 30-60 mL/min	1.5	4	Moderately robust
Estimated GFR < 30 mL/min	3.0	11	Moderately robust
History of dialysis or end-stage renal failure	3.7	13	Moderately robust
Non-haematological cancer			
Diagnosed <1 year ago	1.7	5	Provisional
Diagnosed 1-4.9 years ago	1.2	2	Provisional
Diagnosed ≥5 years ago	1	0	Provisional
Haematological malignancy			
Diagnosed <1 year ago	2.8	10	Provisional
Diagnosed 1-4.9 years ago	2.5	9	Provisional
Diagnosed ≥5 years ago	1.6	5	Provisional
Liver disease	1.8	6	Provisional
Chronic neurological disease other than stroke or dementia*	2.6	9	Provisional
Organ transplant	3.6	12	Provisional
Spleen diseases†	1.4	3	Provisional
Rheumatoid/lupus/psoriasis	1.2	2	Provisional

Other immunosuppressive condition‡	1.8	6	Provisional

*Includes motor neurone disease, myasthenia gravis, multiple sclerosis, Parkinson's disease, cerebral palsy, quadriplegia, hemiplegia and progressive cerebellar disease.
†Includes splenectomy, or spleen dysfunction (e.g. from sickle cell disease).
‡Includes HIV, conditions inducing permanent immunodeficiency (ever diagnosed), aplastic anaemia, and temporary immunodeficiency recorded within the past year.
**Added years for hypertension are calculated from relative risks before rounding

The estimated case-fatality rates (both sexes and all ethnic groups) in the new report based on data from New York City [4.3] of 1.2 per 1000 at ages 25-44 years and 9.4 per 1000 at ages 45-64 years are broadly consistent with our previous estimate of 2 per 1000 for healthy white men aged 47 years. However, we have identified a need to adjust slightly our adopted relative risk by age. Taking account of this adjustment, Table Z4 sets out revised estimates of case-fatality in healthy white males by age.

Table Z4. Relative risks of mortality from Covid-19 and estimated case fatality rates in healthy white males by age

Age (years)	Estimated risk relative to that at age 47 years (healthy white males)	Estimated case-fatality rate per 1000 in cases of Covid-19 infection (healthy white males)
20	0.1	0.1
25	0.1	0.2
30	0.2	0.3
35	0.3	0.6
40	0.5	1.0
45	0.8	1.6
47	1.0	2.0
50	1.4	2.7
52	1.7	3.3
54	2.1	4.1
56	2.5	5.1
58	3.1	6.2
60	3.8	7.6
62	4.7	9.4
64	5.8	11.5
66	7.1	14.1
68	8.7	17.4
70	10.7	21.3
72	13.1	26.2
74	16.1	32.2
76	19.8	39.6
78	24.3	48.6
80	29.9	59.7

UPDATE 5: 27 JULY 2020

As described in Section 1, we are aware of growing suspicions that relative risks associated with some comorbidities may be higher in young adults and lower at older ages. Other than for hypertension, we do not as yet have usable quantitative estimates of any such variation in relative risks by age, but we highlight this as an uncertainty that should be taken into account when using the risk estimates in Table Z3. Other than for hypertension, those risk estimates should be viewed as averages across adults of all ages.

UPDATE 6: 13 AUGUST 2020

As described in Sections 1 and 2, in this update we are substantially revising and refining many of our adopted risk estimates to take account of new evidence from the OS study on variations by age. The revised relative risk estimates by year of true age are summarised in Table Z5. Table Z6 sets out the added years of age that are equivalent to those relative risks. Because of the complexity introduced by variations in relative risk by age, we will now provide a simple online calculator that shows impacts on Covid-age associated with different risk factors according to a person's true age.

Table Z5. Adopted estimates of relative risk by age as part of Update 6

Notes on Table

All estimates are approximate. Those in italics are classed as provisional. All others are classed as moderately robust.

*Chronic neurological disease other than stroke or dementia includes motor neurone disease, myasthenia gravis, multiple sclerosis, Parkinson's disease, cerebral palsy, quadriplegia, hemiplegia and progressive cerebellar disease.
†Spleen diseases include splenectomy, or spleen dysfunction (e.g. from sickle cell disease).
‡Other immunosuppressive condition includes HIV, conditions inducing permanent immunodeficiency (ever diagnosed), aplastic anaemia, and temporary immunodeficiency recorded within the past year.

True age (years)	20	21	22	23	24	25	26	27	28	29
Female sex	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity										
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)										
30-34.9	*2.1*	*2.1*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*	*1.9*	*1.9*	*1.9*
35-39.9	*7.1*	*7.1*	*7.1*	*6.4*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.8*
≥40	*13*	*13*	*12*	*12*	*12*	*11*	*11*	*11*	*10*	*10*
Hypertension	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*
Heart failure	*13*	*13*	*13*	*13*	*13*	*13*	*12*	*12*	*12*	*12*
Other chronic heart disease	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*7.1*
Cerebrovascular disease	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*
Asthma										
Mild	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Severe	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*4.2*
Other chronic respiratory disease	*5.8*	*5.8*	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*12*	*12*	*12*	*12*	*12*	*12*	*11*	*11*	*11*	*11*
HbA1>58 mmol/mol in past year	*16*	*16*	*16*	*16*	*16*	*16*	*15*	*15*	*15*	*15*
HbA1c unknown	*20*	*20*	*20*	*20*	*20*	*18*	*18*	*18*	*18*	*18*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*
HbA1>58 mmol/mol in past year	*11*	*11*	*11*	*11*	*11*	*10*	*10*	*10*	*10*	*10*
HbA1c unknown	*12*	*12*	*12*	*12*	*12*	*11*	*11*	*11*	*11*	*11*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*75*	*68*	*61*	*55*	*50*	*45*	*45*	*41*	*37*	*33*
Estimated GFR < 30 mL/min	*234*	*211*	*190*	*172*	*172*	*155*	*140*	*126*	*114*	*114*
Non-haematological cancer										
Diagnosed <1 year ago	*33*	*30*	*30*	*27*	*27*	*24*	*24*	*22*	*22*	*20*
Diagnosed 1-4.9 years ago	*13*	*13*	*13*	*12*	*12*	*12*	*11*	*11*	*10*	*10*
Diagnosed ≥5 years ago	*6.4*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*
Haematological malignancy										
Diagnosed <1 year ago	*30*	*30*	*27*	*27*	*27*	*27*	*24*	*24*	*24*	*24*
Diagnosed 1-4.9 years ago	*27*	*24*	*24*	*24*	*22*	*22*	*22*	*20*	*20*	*20*
Diagnosed ≥5 years ago	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*
Liver disease	*27*	*24*	*24*	*22*	*22*	*20*	*20*	*18*	*18*	*16*
Chronic neurological disease other than stroke or dementia*	*11*	*11*	*10*	*10*	*10*	*10*	*10*	*10*	*10*	*10*
Organ transplant	*13*	*13*	*12*	*12*	*12*	*12*	*12*	*12*	*12*	*12*
Spleen diseases†	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*22*	*22*	*20*	*20*	*18*	*18*	*16*	*16*	*15*	*15*

True age (years)	30	31	32	33	34	35	36	37	38	39
Female sex	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity										
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)										
30-34.9	*1.9*	*1.9*	*1.9*	*1.9*	*1.9*	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*
35-39.9	*5.8*	*5.2*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*
≥40	*10*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*6.4*
Hypertension	*3.1*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.8*	*2.8*	*2.8*
Heart failure	*12*	*11*	*11*	*11*	*10*	*10*	*10*	*10*	*8.7*	*8.7*
Other chronic heart disease	*7.1*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*
Cerebrovascular disease	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.7*
Asthma										
Mild	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Severe	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*
Other chronic respiratory disease	*5.2*	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*4.2*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*11*	*11*	*10*	*10*	*10*	*10*	*10*	*8.7*	*8.7*	*8.7*
HbA1>58 mmol/mol in past year	*15*	*15*	*13*	*13*	*13*	*13*	*13*	*13*	*12*	*12*
HbA1c unknown	*18*	*18*	*18*	*16*	*16*	*16*	*16*	*16*	*15*	*15*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*7.1*	*7.1*	*7.1*	*7.1*
HbA1>58 mmol/mol in past year	*10*	*10*	*10*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*
HbA1c unknown	*11*	*11*	*11*	*11*	*11*	*11*	*11*	*11*	*10*	*10*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*30*	*27*	*27*	*24*	*22*	*20*	*18*	*16*	*15*	*15*
Estimated GFR < 30 mL/min	*103*	*93*	*93*	*84*	*75*	*68*	*61*	*55*	*50*	*45*
Non-haematological cancer										
Diagnosed <1 year ago	*20*	*18*	*18*	*16*	*16*	*15*	*15*	*13*	*13*	*12*
Diagnosed 1-4.9 years ago	*10*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*	*6.4*
Diagnosed ≥5 years ago	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*
Haematological malignancy										
Diagnosed <1 year ago	*22*	*22*	*22*	*22*	*20*	*20*	*20*	*20*	*18*	*18*
Diagnosed 1-4.9 years ago	*18*	*18*	*18*	*16*	*16*	*16*	*15*	*15*	*13*	*13*
Diagnosed ≥5 years ago	*7.8*	*7.1*	*7.1*	*7.1*	*7.1*	*6.4*	*6.4*	*6.4*	*6.4*	*5.8*
Liver disease	*16*	*15*	*15*	*13*	*13*	*12*	*12*	*11*	*11*	*10*
Chronic neurological disease other than stroke or dementia*	*10*	*10*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*
Organ transplant	*11*	*11*	*11*	*11*	*11*	*11*	*10*	*10*	*10*	*10*
Spleen diseases†	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*13*	*13*	*12*	*12*	*11*	*11*	*10*	*10*	*8.7*	*8.7*

True age (years)	40	41	42	43	44	45	46	47	48	49
Female sex	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity										
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)										
30-34.9	*1.7*	*1.7*	*1.7*	*1.7*	*1.7*	*1.7*	*1.7*	*1.5*	*1.5*	*1.5*
35-39.9	*4.2*	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*
≥40	*6.4*	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*
Hypertension	*2.5*	*2.5*	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*	*2.3*	*2.3*
Heart failure	*8.7*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*6.4*	*6.4*	*6.4*
Other chronic heart disease	*5.2*	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*
Cerebrovascular disease	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*
Asthma										
Mild	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Severe	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*
Other chronic respiratory disease	*4.2*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*	*3.4*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*8.7*	*8.7*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*
HbA1>58 mmol/mol in past year	*12*	*12*	*12*	*11*	*11*	*11*	*11*	*10*	*10*	*10*
HbA1c unknown	*15*	*15*	*13*	*13*	*13*	*13*	*12*	*12*	*12*	*11*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*7.1*	*6.4*	*6.4*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.8*	*5.2*
HbA1>58 mmol/mol in past year	*8.7*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*6.4*
HbA1c unknown	*10*	*10*	*10*	*10*	*10*	*10*	*8.7*	*8.7*	*8.7*	*7.8*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*13*	*12*	*11*	*10*	*8.7*	*7.8*	*7.1*	*7.1*	*6.4*	*6.4*
Estimated GFR < 30 mL/min	*41*	*37*	*37*	*33*	*30*	*30*	*27*	*27*	*24*	*22*
Non-haematological cancer										
Diagnosed <1 year ago	*12*	*11*	*11*	*10*	*10*	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*
Diagnosed 1-4.9 years ago	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*3.8*
Diagnosed ≥5 years ago	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*
Haematological malignancy										
Diagnosed <1 year ago	*18*	*18*	*16*	*16*	*16*	*15*	*15*	*15*	*13*	*13*
Diagnosed 1-4.9 years ago	*13*	*12*	*12*	*11*	*11*	*10*	*10*	*10*	*10*	*10*
Diagnosed ≥5 years ago	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*
Liver disease	*10*	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*	*5.8*	*5.8*
Chronic neurological disease other than stroke or dementia*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*7.1*
Organ transplant	*10*	*10*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.8*
Spleen diseases†	*3.1*	*3.1*	*3.1*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.8*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*4.7*

True age (years)	50	51	52	53	54	55	56	57	58	59
Female sex	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity										
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)										
30-34.9	*1.5*	*1.5*	*1.5*	*1.4*	*1.4*	*1.4*	*1.5*	*1.4*	*1.4*	*1.4*
35-39.9	*3.4*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.8*	*2.5*	*2.5*
≥40	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*
Hypertension	*2.1*	*2.1*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*
Heart failure	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*
Other chronic heart disease	*3.8*	*3.4*	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*
Cerebrovascular disease	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*
Asthma										
Mild	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Severe	*2.5*	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*	*2.1*	*2.1*	*2.1*
Other chronic respiratory disease	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.5*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*6.4*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*
HbA1>58 mmol/mol in past year	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*6.4*	*6.4*	*5.8*
HbA1c unknown	*11*	*11*	*10*	*10*	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*
HbA1>58 mmol/mol in past year	*6.4*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*
HbA1c unknown	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.2*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*5.8*	*5.2*	*5.2*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*	*3.1*
Estimated GFR < 30 mL/min	*22*	*20*	*18*	*18*	*16*	*15*	*15*	*13*	*12*	*11*
Non-haematological cancer										
Diagnosed <1 year ago	*7.1*	*6.4*	*6.4*	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*
Diagnosed 1-4.9 years ago	*3.8*	*3.4*	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*
Diagnosed ≥5 years ago	*2.3*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*	*1.5*
Haematological malignancy										
Diagnosed <1 year ago	*12*	*12*	*11*	*11*	*10*	*10*	*8.7*	*8.7*	*7.8*	*7.8*
Diagnosed 1-4.9 years ago	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*
Diagnosed ≥5 years ago	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.5*	*2.5*
Liver disease	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*
Chronic neurological disease other than stroke or dementia*	*6.4*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*
Organ transplant	*7.1*	*7.1*	*7.1*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*
Spleen diseases†	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*	*2.3*	*2.1*	*2.1*	*2.1*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*

True age (years)	60	61	62	63	64	65	66	67	68	69
Female sex	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity										
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)										
30-34.9	*1.4*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
35-39.9	*2.5*	*2.3*	*2.3*	*2.3*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*	*1.7*
≥40	*2.8*	*2.8*	*2.8*	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*	*2.1*
Hypertension	*1.7*	*1.7*	*1.5*	*1.5*	*1.5*	*1.4*	*1.4*	*1.4*	*1.2*	*1.2*
Heart failure	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*
Other chronic heart disease	*2.5*	*2.3*	*2.3*	*2.1*	*2.1*	*1.9*	*1.9*	*1.7*	*1.7*	*1.7*
Cerebrovascular disease	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*
Asthma										
Mild	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Severe	1.9	1.9	1.7	1.7	1.5	1.5	1.5	1.5	1.4	1.4
Other chronic respiratory disease	*2.5*	*2.5*	2.3	2.3	2.3	2.1	2.1	2.1	2.1	2.1
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*
HbA1>58 mmol/mol in past year	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*
HbA1c unknown	*6.4*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*3.4*	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*
HbA1>58 mmol/mol in past year	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*
HbA1c unknown	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*3.1*	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*	*2.1*	*1.9*	*1.9*
Estimated GFR < 30 mL/min	*11*	*10*	*10*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*	*6.4*
Non-haematological cancer										
Diagnosed <1 year ago	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*	*2.5*
Diagnosed 1-4.9 years ago	*2.3*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*	*1.5*
Diagnosed ≥5 years ago	*1.5*	*1.4*	*1.4*	*1.2*	*1.2*	*1.1*	*1.1*	*1.1*	*1.1*	*1.0*
Haematological malignancy										
Diagnosed <1 year ago	*7.1*	*7.1*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*
Diagnosed 1-4.9 years ago	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*
Diagnosed ≥5 years ago	*2.5*	*2.3*	*2.3*	*2.3*	*2.1*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*
Liver disease	*3.1*	*2.8*	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*	*2.1*	*1.9*
Chronic neurological disease other than stroke or dementia*	*5.2*	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*
Organ transplant	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*
Spleen diseases†	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*	*1.7*	*1.7*	*1.5*	*1.5*	*1.4*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*

True age (years)	70	71	72	73	74	75
Female sex	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity						
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)						
30-34.9	*1.2*	*1.1*	*1.1*	*1.1*	*1.1*	*1.1*
35-39.9	*1.7*	*1.7*	*1.5*	*1.5*	*1.4*	*1.4*
≥40	*2.1*	*1.9*	*1.9*	*1.7*	*1.7*	*1.7*
Hypertension	*1.2*	*1.1*	*1.1*	*1.0*	*1.0*	*1.0*
Heart failure	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*
Other chronic heart disease	*1.5*	*1.5*	*1.5*	*1.4*	*1.4*	*1.4*
Cerebrovascular disease	*2.8*	*2.8*	*2.5*	*2.5*	*2.5*	*2.5*
Asthma						
Mild	1.1	1.1	1.1	1.1	1.1	1.1
Severe	1.4	1.4	1.2	1.2	1.2	1.2
Other chronic respiratory disease	1.9	1.9	1.9	1.9	1.9	1.9
Diabetes						
Type 1						
HbA1≤58 mmol/mol in past year	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*
HbA1>58 mmol/mol in past year	*3.8*	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*
HbA1c unknown	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.4*
Type 2 and other						
HbA1≤58 mmol/mol in past year	*2.1*	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*
HbA1>58 mmol/mol in past year	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*
HbA1c unknown	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*
Chronic kidney disease						
Estimated GFR 30-60 mL/min	*1.7*	1.7	1.5	1.5	1.4	1.4
Estimated GFR < 30 mL/min	*5.8*	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*
Non-haematological cancer						
Diagnosed <1 year ago	*2.5*	*2.3*	*2.3*	*2.3*	*2.1*	*2.1*
Diagnosed 1-4.9 years ago	*1.5*	*1.4*	*1.4*	*1.4*	*1.2*	*1.2*
Diagnosed ≥5 years ago	*1.0*	*1.0*	*1.0*	*1.0*	*1.0*	*1.0*
Haematological malignancy						
Diagnosed <1 year ago	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*
Diagnosed 1-4.9 years ago	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*
Diagnosed ≥5 years ago	*1.9*	*1.9*	*1.7*	*1.7*	*1.7*	*1.7*
Liver disease	*1.9*	*1.9*	*1.7*	*1.7*	*1.5*	*1.5*
Chronic neurological disease other than stroke or dementia*	*3.8*	*3.8*	*3.4*	*3.4*	*3.4*	*3.4*
Organ transplant	*2.8*	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*
Spleen diseases†	*1.4*	*1.2*	*1.2*	*1.1*	*1.1*	*1.0*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*2.1*	*2.1*	*1.9*	*1.9*	*1.7*	*1.7*

Table Z6. Adopted relative risks in Update 6 expressed as equivalence to added years of age.

To calculate a person's Covid-age, first find the column of the table corresponding to their true age. Then add to their true age the years in that column corresponding to each risk factor that applies.

For example, to calculate the Covid-age of an Asian woman aged 50 with poorly controlled Type 2 diabetes, first find the column of Table Z6 corresponding to a true age of 50. In that column the added years for being female are -5, for being Asian/Asian British +5, and for poorly controlled Type 2 diabetes + 18. Thus, her Covid-age would be 50 – 5 +5 +18 = 68 years

Notes on Table

All estimates are approximate. Those in italics are classed as provisional. All others are classed as moderately robust.

*Chronic neurological disease other than stroke or dementia includes motor neurone disease, myasthenia gravis, multiple sclerosis, Parkinson's disease, cerebral palsy, quadriplegia, hemiplegia and progressive cerebellar disease.
†Spleen diseases include splenectomy, or spleen dysfunction (e.g. from sickle cell disease).
‡Other immunosuppressive condition includes HIV, conditions inducing permanent immunodeficiency (ever diagnosed), aplastic anaemia, and temporary immunodeficiency recorded within the past year.

True age (years)	20	21	22	23	24	25	26	27	28	29
Female sex	-5	-5	-5	-5	-5	-5	-5	-5	-5	-5
Ethnicity										
Asian or Asian British	5	5	5	5	5	5	5	5	5	5
Black	7	7	7	7	7	7	7	7	7	7
Mixed	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Other non-white	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*
Body mass index (Kg/m^2)										
30-34.9	*7*	*7*	*7*	*7*	*7*	*6*	*6*	*6*	*6*	*6*
35-39.9	*19*	*19*	*19*	*18*	*18*	*18*	*18*	*17*	*17*	*17*
≥40	*25*	*25*	*24*	*24*	*24*	*23*	*23*	*23*	*22*	*22*
Hypertension	*12*	*12*	*12*	*12*	*12*	*12*	*12*	*11*	*11*	*11*
Heart failure	*25*	*25*	*25*	*25*	*25*	*25*	*24*	*24*	*24*	*24*
Other chronic heart disease	*20*	*20*	*20*	*20*	*20*	*20*	*19*	*19*	*19*	*19*
Cerebrovascular disease	*17*	*17*	*17*	*16*	*16*	*16*	*16*	*16*	*16*	*16*
Asthma										
Mild	1	1	1	1	1	1	1	1	1	1
Severe	*15*	*15*	*15*	*15*	*15*	*15*	*14*	*14*	*14*	*14*
Other chronic respiratory disease	*17*	*17*	*17*	*17*	*17*	*16*	*16*	*16*	*16*	*16*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*24*	*24*	*24*	*24*	*24*	*24*	*23*	*23*	*23*	*23*
HbA1>58 mmol/mol in past year	*27*	*27*	*27*	*27*	*27*	*27*	*26*	*26*	*26*	*26*
HbA1c unknown	*29*	*29*	*29*	*29*	*29*	*28*	*28*	*28*	*28*	*28*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*21*	*21*	*21*	*21*	*21*	*20*	*20*	*20*	*20*	*20*
HbA1>58 mmol/mol in past year	*23*	*23*	*23*	*23*	*23*	*22*	*22*	*22*	*22*	*22*
HbA1c unknown	*24*	*24*	*24*	*24*	*24*	*23*	*23*	*23*	*23*	*23*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*42*	*41*	*40*	*39*	*38*	*37*	*37*	*36*	*35*	*34*
Estimated GFR < 30 mL/min	*53*	*52*	*51*	*50*	*50*	*49*	*48*	*47*	*46*	*46*
Non-haematological cancer										
Diagnosed <1 year ago	*34*	*33*	*33*	*32*	*32*	*31*	*31*	*30*	*30*	*29*
Diagnosed 1-4.9 years ago	*25*	*25*	*25*	*24*	*24*	*24*	*23*	*23*	*22*	*22*
Diagnosed ≥5 years ago	*18*	*18*	*18*	*18*	*17*	*17*	*17*	*16*	*16*	*16*
Haematological malignancy										
Diagnosed <1 year ago	*33*	*33*	*32*	*32*	*32*	*32*	*31*	*31*	*31*	*31*
Diagnosed 1-4.9 years ago	*32*	*31*	*31*	*31*	*30*	*30*	*30*	*29*	*29*	*29*
Diagnosed ≥5 years ago	*21*	*21*	*21*	*21*	*21*	*20*	*20*	*20*	*20*	*20*
Liver disease	*32*	*31*	*31*	*30*	*30*	*29*	*29*	*28*	*28*	*27*
Chronic neurological disease other than stroke or dementia*	*23*	*23*	*22*	*22*	*22*	*22*	*22*	*22*	*22*	*22*
Organ transplant	*25*	*25*	*24*	*24*	*24*	*24*	*24*	*24*	*24*	*24*
Spleen diseases†	*14*	*14*	*13*	*13*	*13*	*13*	*13*	*13*	*13*	*13*
Rheumatoid/lupus/psoriasis	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
Other immunosuppressive condition‡	*30*	*30*	*29*	*29*	*28*	*28*	*27*	*27*	*26*	*26*

True age (years)	30	31	32	33	34	35	36	37	38	39
Female sex	-5	-5	-5	-5	-5	-5	-5	-5	-5	-5
Ethnicity										
Asian or Asian British	5	5	5	5	5	5	5	5	5	5
Black	7	7	7	7	7	7	7	7	7	7
Mixed	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Other non-white	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*
Body mass index (Kg/m^2)										
30-34.9	*6*	*6*	*6*	*6*	*6*	*6*	*6*	*6*	*5*	*5*
35-39.9	*17*	*16*	*16*	*16*	*16*	*15*	*15*	*15*	*15*	*15*
≥40	*22*	*21*	*21*	*21*	*20*	*20*	*19*	*19*	*19*	*18*
Hypertension	*11*	*11*	*11*	*11*	*10*	*10*	*10*	*10*	*10*	*10*
Heart failure	*24*	*23*	*23*	*23*	*22*	*22*	*22*	*22*	*21*	*21*
Other chronic heart disease	*19*	*18*	*18*	*18*	*17*	*17*	*17*	*17*	*16*	*16*
Cerebrovascular disease	*16*	*16*	*16*	*16*	*16*	*16*	*16*	*15*	*15*	*15*
Asthma										
Mild	1	1	1	1	1	1	1	1	1	1
Severe	*14*	*14*	*14*	*13*	*13*	*13*	*13*	*13*	*12*	*12*
Other chronic respiratory disease	*16*	*15*	*15*	*15*	*15*	*15*	*14*	*14*	*14*	*14*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*23*	*23*	*22*	*22*	*22*	*22*	*22*	*21*	*21*	*21*
HbA1>58 mmol/mol in past year	*26*	*26*	*25*	*25*	*25*	*25*	*25*	*25*	*24*	*24*
HbA1c unknown	*28*	*28*	*28*	*27*	*27*	*27*	*27*	*27*	*26*	*26*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*20*	*20*	*20*	*19*	*19*	*19*	*19*	*19*	*19*	*19*
HbA1>58 mmol/mol in past year	*22*	*22*	*22*	*21*	*21*	*21*	*21*	*21*	*21*	*21*
HbA1c unknown	*23*	*23*	*23*	*23*	*23*	*23*	*23*	*23*	*22*	*22*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*33*	*32*	*32*	*31*	*30*	*29*	*28*	*27*	*26*	*26*
Estimated GFR < 30 mL/min	*45*	*44*	*44*	*43*	*42*	*41*	*40*	*39*	*38*	*37*
Non-haematological cancer										
Diagnosed <1 year ago	*29*	*28*	*28*	*27*	*27*	*26*	*26*	*25*	*25*	*24*
Diagnosed 1-4.9 years ago	*22*	*21*	*21*	*21*	*20*	*20*	*19*	*19*	*18*	*18*
Diagnosed ≥5 years ago	*15*	*15*	*15*	*14*	*14*	*13*	*13*	*12*	*12*	*11*
Haematological malignancy										
Diagnosed <1 year ago	*30*	*30*	*30*	*30*	*29*	*29*	*29*	*29*	*28*	*28*
Diagnosed 1-4.9 years ago	*28*	*28*	*28*	*27*	*27*	*27*	*26*	*26*	*25*	*25*
Diagnosed ≥5 years ago	*20*	*19*	*19*	*19*	*19*	*18*	*18*	*18*	*18*	*17*
Liver disease	*27*	*26*	*26*	*25*	*25*	*24*	*24*	*23*	*23*	*22*
Chronic neurological disease other than stroke or dementia*	*22*	*22*	*21*	*21*	*21*	*21*	*21*	*21*	*21*	*20*
Organ transplant	*23*	*23*	*23*	*23*	*23*	*23*	*22*	*22*	*22*	*22*
Spleen diseases†	*13*	*13*	*13*	*12*	*12*	*12*	*12*	*12*	*12*	*12*
Rheumatoid/lupus/psoriasis	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
Other immunosuppressive condition‡	*25*	*25*	*24*	*24*	*23*	*23*	*22*	*22*	*21*	*21*

True age (years)	40	41	42	43	44	45	46	47	48	49
Female sex	-5	-5	-5	-5	-5	-5	-5	-5	-5	-5
Ethnicity										
Asian or Asian British	5	5	5	5	5	5	5	5	5	5
Black	7	7	7	7	7	7	7	7	7	7
Mixed	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Other non-white	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*
Body mass index (Kg/m^2)										
30-34.9	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*4*	*4*	*4*
35-39.9	*14*	*14*	*14*	*14*	*13*	*13*	*13*	*13*	*12*	*12*
≥40	*18*	*17*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*
Hypertension	*9*	*9*	*9*	*9*	*9*	*8*	*8*	*8*	*8*	*8*
Heart failure	*21*	*20*	*20*	*20*	*19*	*19*	*19*	*18*	*18*	*18*
Other chronic heart disease	*16*	*15*	*15*	*15*	*14*	*14*	*14*	*13*	*13*	*13*
Cerebrovascular disease	*15*	*15*	*15*	*15*	*15*	*15*	*15*	*14*	*14*	*14*
Asthma										
Mild	1	1	1	1	1	1	1	1	1	1
Severe	*12*	*12*	*12*	*11*	*11*	*11*	*11*	*10*	*10*	*10*
Other chronic respiratory disease	*14*	*13*	*13*	*13*	*13*	*13*	*13*	*12*	*12*	*12*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*21*	*21*	*20*	*20*	*20*	*20*	*20*	*19*	*19*	*18*
HbA1>58 mmol/mol in past year	*24*	*24*	*24*	*23*	*23*	*23*	*23*	*22*	*22*	*22*
HbA1c unknown	*26*	*26*	*25*	*25*	*25*	*25*	*24*	*24*	*24*	*23*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*19*	*18*	*18*	*18*	*18*	*18*	*17*	*17*	*17*	*16*
HbA1>58 mmol/mol in past year	*21*	*20*	*20*	*20*	*20*	*20*	*19*	*19*	*19*	*18*
HbA1c unknown	*22*	*22*	*22*	*22*	*22*	*22*	*21*	*21*	*21*	*20*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*25*	*24*	*23*	*22*	*21*	*20*	*19*	*19*	*18*	*18*
Estimated GFR < 30 mL/min	*36*	*35*	*35*	*34*	*33*	*33*	*32*	*32*	*31*	*30*
Non-haematological cancer										
Diagnosed <1 year ago	*24*	*23*	*23*	*22*	*22*	*21*	*21*	*20*	*20*	*19*
Diagnosed 1-4.9 years ago	*18*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*	*13*
Diagnosed ≥5 years ago	*11*	*11*	*10*	*10*	*10*	*9*	*9*	*9*	*8*	*8*
Haematological malignancy										
Diagnosed <1 year ago	*28*	*28*	*27*	*27*	*27*	*26*	*26*	*26*	*25*	*25*
Diagnosed 1-4.9 years ago	*25*	*24*	*24*	*23*	*23*	*22*	*22*	*22*	*22*	*22*
Diagnosed ≥5 years ago	*17*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*	*14*
Liver disease	*22*	*21*	*21*	*20*	*20*	*19*	*19*	*18*	*17*	*17*
Chronic neurological disease other than stroke or dementia*	*20*	*20*	*20*	*20*	*20*	*20*	*19*	*19*	*19*	*19*
Organ transplant	*22*	*22*	*21*	*21*	*21*	*21*	*21*	*20*	*20*	*20*
Spleen diseases†	*11*	*11*	*11*	*11*	*11*	*11*	*10*	*10*	*10*	*10*
Rheumatoid/lupus/psoriasis	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
Other immunosuppressive condition‡	*20*	*20*	*19*	*19*	*18*	*17*	*17*	*16*	*16*	*15*

True age (years)	50	51	52	53	54	55	56	57	58	59
Female sex	-5	-5	-5	-5	-5	-5	-5	-5	-5	-5
Ethnicity										
Asian or Asian British	5	5	5	5	5	5	5	5	5	5
Black	7	7	7	7	7	7	7	7	7	7
Mixed	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Other non-white	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*
Body mass index (Kg/m^2)										
30-34.9	*4*	*4*	*4*	*3*	*3*	*3*	*4*	*3*	*3*	*3*
35-39.9	*12*	*11*	*11*	*11*	*10*	*10*	*10*	*10*	*9*	*9*
≥40	*14*	*14*	*13*	*13*	*12*	*12*	*12*	*11*	*11*	*11*
Hypertension	*7*	*7*	*7*	*7*	*7*	*6*	*6*	*6*	*5*	*5*
Heart failure	*17*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*	*14*
Other chronic heart disease	*13*	*12*	*12*	*12*	*12*	*11*	*11*	*10*	*10*	*9*
Cerebrovascular disease	*14*	*14*	*14*	*13*	*13*	*13*	*13*	*13*	*12*	*12*
Asthma										
Mild	1	1	1	1	1	1	1	1	1	1
Severe	*9*	*9*	*9*	*9*	*8*	*8*	*8*	*7*	*7*	*7*
Other chronic respiratory disease	*12*	*12*	*11*	*11*	*11*	*11*	*10*	*10*	*10*	*9*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*18*	*18*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*
HbA1>58 mmol/mol in past year	*21*	*21*	*20*	*20*	*19*	*19*	*19*	*18*	*18*	*17*
HbA1c unknown	*23*	*23*	*22*	*22*	*21*	*21*	*20*	*20*	*19*	*19*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*16*	*16*	*15*	*15*	*14*	*14*	*14*	*13*	*13*	*12*
HbA1>58 mmol/mol in past year	*18*	*18*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*
HbA1c unknown	*20*	*20*	*19*	*19*	*18*	*18*	*18*	*17*	*17*	*16*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*17*	*16*	*16*	*15*	*14*	*14*	*13*	*13*	*12*	*11*
Estimated GFR < 30 mL/min	*30*	*29*	*28*	*28*	*27*	*26*	*26*	*25*	*24*	*23*
Non-haematological cancer										
Diagnosed <1 year ago	*19*	*18*	*18*	*17*	*16*	*16*	*15*	*15*	*14*	*14*
Diagnosed 1-4.9 years ago	*13*	*12*	*11*	*11*	*10*	*10*	*9*	*9*	*8*	*8*
Diagnosed ≥5 years ago	*8*	*7*	*7*	*7*	*6*	*6*	*6*	*5*	*5*	*4*
Haematological malignancy										
Diagnosed <1 year ago	*24*	*24*	*23*	*23*	*22*	*22*	*21*	*21*	*20*	*20*
Diagnosed 1-4.9 years ago	*21*	*21*	*21*	*21*	*20*	*20*	*20*	*19*	*19*	*18*
Diagnosed ≥5 years ago	*13*	*12*	*12*	*11*	*11*	*10*	*10*	*10*	*9*	*9*
Liver disease	*16*	*15*	*15*	*14*	*14*	*13*	*13*	*12*	*12*	*11*
Chronic neurological disease other than stroke or dementia*	*18*	*18*	*18*	*18*	*17*	*17*	*17*	*16*	*16*	*16*
Organ transplant	*19*	*19*	*19*	*18*	*18*	*18*	*17*	*17*	*16*	*16*
Spleen diseases†	*9*	*9*	*9*	*8*	*8*	*8*	*8*	*7*	*7*	*7*
Rheumatoid/lupus/psoriasis	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
Other immunosuppressive condition‡	*15*	*15*	*14*	*14*	*13*	*13*	*13*	*12*	*12*	*11*

True age (years)	60	61	62	63	64	65	66	67	68	69
Female sex	-5	-5	-5	-5	-5	-5	-5	-5	-5	-5
Ethnicity										
Asian or Asian British	5	5	5	5	5	5	5	5	5	5
Black	7	7	7	7	7	7	7	7	7	7
Mixed	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Other non-white	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*
Body mass index (Kg/m^2)										
30-34.9	*3*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
35-39.9	*9*	*8*	*8*	*8*	*7*	*7*	*7*	*6*	*6*	*5*
≥40	*10*	*10*	*10*	*9*	*9*	*9*	*8*	*8*	*7*	*7*
Hypertension	*5*	*5*	*4*	*4*	*4*	*3*	*3*	*3*	*2*	*2*
Heart failure	*13*	*13*	*12*	*12*	*11*	*11*	*11*	*10*	*10*	*10*
Other chronic heart disease	*9*	*8*	*8*	*7*	*7*	*6*	*6*	*5*	*5*	*5*
Cerebrovascular disease	*12*	*12*	*12*	*11*	*11*	*11*	*11*	*11*	*10*	*10*
Asthma										
Mild	1	1	1	1	1	1	1	1	1	1
Severe	6	6	5	5	4	4	4	4	3	3
Other chronic respiratory disease	*9*	*9*	8	8	8	7	7	7	7	7
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*14*	*13*	*13*	*12*	*12*	*11*	*11*	*11*	*10*	*10*
HbA1>58 mmol/mol in past year	*17*	*16*	*16*	*15*	*15*	*14*	*14*	*14*	*13*	*13*
HbA1c unknown	*18*	*18*	*17*	*17*	*16*	*16*	*15*	*15*	*14*	*14*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*12*	*11*	*11*	*10*	*10*	*9*	*9*	*8*	*8*	*7*
HbA1>58 mmol/mol in past year	*14*	*13*	*13*	*12*	*12*	*11*	*11*	*11*	*10*	*10*
HbA1c unknown	*16*	*15*	*15*	*14*	*14*	*13*	*13*	*13*	*12*	*12*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*11*	*10*	*9*	*9*	*8*	*8*	*7*	*7*	*6*	*6*
Estimated GFR < 30 mL/min	*23*	*22*	*22*	*21*	*20*	*20*	*19*	*19*	*18*	*18*
Non-haematological cancer										
Diagnosed <1 year ago	*13*	*13*	*12*	*12*	*11*	*11*	*10*	*10*	*9*	*9*
Diagnosed 1-4.9 years ago	*8*	*7*	*7*	*7*	*6*	*6*	*6*	*5*	*5*	*4*
Diagnosed ≥5 years ago	*4*	*3*	*3*	*2*	*2*	*1*	*1*	*1*	*1*	*0*
Haematological malignancy										
Diagnosed <1 year ago	*19*	*19*	*18*	*17*	*17*	*16*	*16*	*15*	*15*	*14*
Diagnosed 1-4.9 years ago	*18*	*17*	*17*	*16*	*16*	*15*	*15*	*14*	*14*	*13*
Diagnosed ≥5 years ago	*9*	*8*	*8*	*8*	*7*	*7*	*7*	*7*	*6*	*6*
Liver disease	*11*	*10*	*10*	*9*	*9*	*8*	*8*	*7*	*7*	*6*
Chronic neurological disease other than stroke or dementia*	*16*	*15*	*15*	*15*	*14*	*14*	*14*	*14*	*13*	*13*
Organ transplant	*15*	*15*	*14*	*14*	*13*	*13*	*12*	*12*	*11*	*11*
Spleen diseases†	*6*	*6*	*6*	*5*	*5*	*5*	*5*	*4*	*4*	*3*
Rheumatoid/lupus/psoriasis	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
Other immunosuppressive condition‡	*11*	*11*	*10*	*10*	*9*	*9*	*9*	*8*	*8*	*7*

True age (years)	70	71	72	73	74	75
Female sex	-5	-5	-5	-5	-5	-5
Ethnicity						
Asian or Asian British	5	5	5	5	5	5
Black	7	7	7	7	7	7
Mixed	5	5	5	5	5	5
Other non-white	4	4	4	4	4	4
Body mass index (Kg/m^2)						
30-34.9	2	1	1	1	1	1
35-39.9	5	5	4	4	3	3
≥40	7	6	6	5	5	5
Hypertension	2	1	1	0	0	0
Heart failure	9	9	9	8	8	8
Other chronic heart disease	4	4	4	3	3	3
Cerebrovascular disease	10	10	9	9	9	9
Asthma						
Mild	1	1	1	1	1	1
Severe	3	3	2	2	2	2
Other chronic respiratory disease	6	6	6	6	6	6
Diabetes						
Type 1						
HbA1≤58 mmol/mol in past year	10	9	9	8	8	8
HbA1>58 mmol/mol in past year	13	12	12	12	11	11
HbA1c unknown	14	13	13	12	12	12
Type 2 and other						
HbA1≤58 mmol/mol in past year	7	6	6	6	5	5
HbA1>58 mmol/mol in past year	9	9	9	8	8	8
HbA1c unknown	11	11	11	10	10	9
Chronic kidney disease						
Estimated GFR 30-60 mL/min	5	5	4	4	3	3
Estimated GFR < 30 mL/min	17	17	16	16	15	15
Non-haematological cancer						
Diagnosed <1 year ago	9	8	8	8	7	7
Diagnosed 1-4.9 years ago	4	3	3	3	2	2
Diagnosed ≥5 years ago	0	0	0	0	0	0
Haematological malignancy						
Diagnosed <1 year ago	14	13	13	12	12	11
Diagnosed 1-4.9 years ago	13	12	12	11	11	11
Diagnosed ≥5 years ago	6	6	5	5	5	5
Liver disease	6	6	5	5	4	4
Chronic neurological disease other than stroke or dementia*	13	13	12	12	12	12
Organ transplant	10	10	9	9	8	8
Spleen diseases†	3	2	2	1	1	0
Rheumatoid/lupus/psoriasis	2	2	2	2	2	2
Other immunosuppressive condition‡	7	7	6	6	5	5

UPDATE 7: 27 AUGUST 2020

Tables Z7 and Z8 show adopted risk estimates by age that have been updated to incorporate the changes for Type 2 diabetes with unknown HbA1c that are described in Section 2F.

Table Z7. Adopted estimates of relative risk by age as part of Update 7

Notes on Table

All estimates are approximate. Those in italics are classed as provisional. All others are classed as moderately robust.

*Chronic neurological disease other than stroke or dementia includes motor neurone disease, myasthenia gravis, multiple sclerosis, Parkinson's disease, cerebral palsy, quadriplegia, hemiplegia and progressive cerebellar disease.
†Spleen diseases include splenectomy, or spleen dysfunction (e.g. from sickle cell disease).
‡Other immunosuppressive condition includes HIV, conditions inducing permanent immunodeficiency (ever diagnosed), aplastic anaemia, and temporary immunodeficiency recorded within the past year.

True age (years)	20	21	22	23	24	25	26	27	28	29
Female sex	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity										
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)										
30-34.9	*2.1*	*2.1*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*	*1.9*	*1.9*	*1.9*
35-39.9	*7.1*	*7.1*	*7.1*	*6.4*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.8*
≥40	*13*	*13*	*12*	*12*	*12*	*11*	*11*	*11*	*10*	*10*
Hypertension	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*
Heart failure	*13*	*13*	*13*	*13*	*13*	*13*	*12*	*12*	*12*	*12*
Other chronic heart disease	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*7.1*
Cerebrovascular disease	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*
Asthma										
Mild	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Severe	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*4.2*
Other chronic respiratory disease	*5.8*	*5.8*	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*12*	*12*	*12*	*12*	*12*	*12*	*11*	*11*	*11*	*11*
HbA1>58 mmol/mol in past year	*16*	*16*	*16*	*16*	*16*	*16*	*15*	*15*	*15*	*15*
HbA1c unknown	*20*	*20*	*20*	*20*	*20*	*18*	*18*	*18*	*18*	*18*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*
HbA1>58 mmol/mol in past year	*11*	*11*	*11*	*11*	*11*	*10*	*10*	*10*	*10*	*10*
HbA1c unknown	*9.6*	*9.6*	*9.6*	*9.6*	*9.6*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*75*	*68*	*61*	*55*	*50*	*45*	*45*	*41*	*37*	*33*
Estimated GFR < 30 mL/min	*234*	*211*	*190*	*172*	*172*	*155*	*140*	*126*	*114*	*114*
Non-haematological cancer										
Diagnosed <1 year ago	*33*	*30*	*30*	*27*	*27*	*24*	*24*	*22*	*22*	*20*
Diagnosed 1-4.9 years ago	*13*	*13*	*13*	*12*	*12*	*12*	*11*	*11*	*10*	*10*
Diagnosed ≥5 years ago	*6.4*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*
Haematological malignancy										
Diagnosed <1 year ago	*30*	*30*	*27*	*27*	*27*	*27*	*24*	*24*	*24*	*24*
Diagnosed 1-4.9 years ago	*27*	*24*	*24*	*24*	*22*	*22*	*22*	*20*	*20*	*20*
Diagnosed ≥5 years ago	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*
Liver disease	*27*	*24*	*24*	*22*	*22*	*20*	*20*	*18*	*18*	*16*
Chronic neurological disease other than stroke or dementia*	*11*	*11*	*10*	*10*	*10*	*10*	*10*	*10*	*10*	*10*
Organ transplant	*13*	*13*	*12*	*12*	*12*	*12*	*12*	*12*	*12*	*12*
Spleen diseases†	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*22*	*22*	*20*	*20*	*18*	*18*	*16*	*16*	*15*	*15*

True age (years)	30	31	32	33	34	35	36	37	38	39
Female sex	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity										
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)										
30-34.9	*1.9*	*1.9*	*1.9*	*1.9*	*1.9*	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*
35-39.9	*5.8*	*5.2*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*
≥40	*10*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*6.4*
Hypertension	*3.1*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.8*	*2.8*	*2.8*
Heart failure	*12*	*11*	*11*	*11*	*10*	*10*	*10*	*10*	*8.7*	*8.7*
Other chronic heart disease	*7.1*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*
Cerebrovascular disease	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.7*
Asthma										
Mild	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Severe	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*
Other chronic respiratory disease	*5.2*	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*4.2*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*11*	*11*	*10*	*10*	*10*	*10*	*10*	*8.7*	*8.7*	*8.7*
HbA1>58 mmol/mol in past year	*15*	*15*	*13*	*13*	*13*	*13*	*13*	*13*	*12*	*12*
HbA1c unknown	*18*	*18*	*18*	*16*	*16*	*16*	*16*	*16*	*15*	*15*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*7.1*	*7.1*	*7.1*	*7.1*
HbA1>58 mmol/mol in past year	*10*	*10*	*10*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*
HbA1c unknown	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*30*	*27*	*27*	*24*	*22*	*20*	*18*	*16*	*15*	*15*
Estimated GFR < 30 mL/min	*103*	*93*	*93*	*84*	*75*	*68*	*61*	*55*	*50*	*45*
Non-haematological cancer										
Diagnosed <1 year ago	*20*	*18*	*18*	*16*	*16*	*15*	*15*	*13*	*13*	*12*
Diagnosed 1-4.9 years ago	*10*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*	*6.4*
Diagnosed ≥5 years ago	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*
Haematological malignancy										
Diagnosed <1 year ago	*22*	*22*	*22*	*22*	*20*	*20*	*20*	*20*	*18*	*18*
Diagnosed 1-4.9 years ago	*18*	*18*	*18*	*16*	*16*	*16*	*15*	*15*	*13*	*13*
Diagnosed ≥5 years ago	*7.8*	*7.1*	*7.1*	*7.1*	*7.1*	*6.4*	*6.4*	*6.4*	*6.4*	*5.8*
Liver disease	*16*	*15*	*15*	*13*	*13*	*12*	*12*	*11*	*11*	*10*
Chronic neurological disease other than stroke or dementia*	*10*	*10*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*
Organ transplant	*11*	*11*	*11*	*11*	*11*	*11*	*10*	*10*	*10*	*10*
Spleen diseases†	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*	*3.4*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*13*	*13*	*12*	*12*	*11*	*11*	*10*	*10*	*8.7*	*8.7*

True age (years)	40	41	42	43	44	45	46	47	48	49
Female sex	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity										
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)										
30-34.9	*1.7*	*1.7*	*1.7*	*1.7*	*1.7*	*1.7*	*1.7*	*1.5*	*1.5*	*1.5*
35-39.9	*4.2*	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*
≥40	*6.4*	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*
Hypertension	*2.5*	*2.5*	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*	*2.3*	*2.3*
Heart failure	*8.7*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*6.4*	*6.4*	*6.4*
Other chronic heart disease	*5.2*	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*
Cerebrovascular disease	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*
Asthma										
Mild	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Severe	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*
Other chronic respiratory disease	*4.2*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*	*3.4*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*8.7*	*8.7*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*
HbA1>58 mmol/mol in past year	*12*	*12*	*12*	*11*	*11*	*11*	*11*	*10*	*10*	*10*
HbA1c unknown	*15*	*15*	*13*	*13*	*13*	*13*	*12*	*12*	*12*	*11*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*7.1*	*6.4*	*6.4*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.8*	*5.2*
HbA1>58 mmol/mol in past year	*8.7*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*6.4*
HbA1c unknown	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*6.4*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*13*	*12*	*11*	*10*	*8.7*	*7.8*	*7.1*	*7.1*	*6.4*	*6.4*
Estimated GFR < 30 mL/min	*41*	*37*	*37*	*33*	*30*	*30*	*27*	*27*	*24*	*22*
Non-haematological cancer										
Diagnosed <1 year ago	*12*	*11*	*11*	*10*	*10*	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*
Diagnosed 1-4.9 years ago	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*3.8*
Diagnosed ≥5 years ago	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*
Haematological malignancy										
Diagnosed <1 year ago	*18*	*18*	*16*	*16*	*16*	*15*	*15*	*15*	*13*	*13*
Diagnosed 1-4.9 years ago	*13*	*12*	*12*	*11*	*11*	*10*	*10*	*10*	*10*	*10*
Diagnosed ≥5 years ago	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*
Liver disease	*10*	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*	*5.8*	*5.8*
Chronic neurological disease other than stroke or dementia*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*7.1*
Organ transplant	*10*	*10*	*8.7*	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.8*
Spleen diseases†	*3.1*	*3.1*	*3.1*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.8*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*4.7*

True age (years)	50	51	52	53	54	55	56	57	58	59
Female sex	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity										
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)										
30-34.9	*1.5*	*1.5*	*1.5*	*1.4*	*1.4*	*1.4*	*1.4*	*1.4*	*1.4*	*1.4*
35-39.9	*3.4*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.8*	*2.5*	*2.5*
≥40	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*
Hypertension	*2.1*	*2.1*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*
Heart failure	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*
Other chronic heart disease	*3.8*	*3.4*	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*
Cerebrovascular disease	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*
Asthma										
Mild	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Severe	*2.5*	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*	*2.1*	*2.1*	*2.1*
Other chronic respiratory disease	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.5*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*6.4*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*
HbA1>58 mmol/mol in past year	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*	*7.1*	*6.4*	*6.4*	*5.8*
HbA1c unknown	*11*	*11*	*10*	*10*	*8.7*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*
HbA1>58 mmol/mol in past year	*6.4*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*
HbA1c unknown	*6.4*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*5.8*	*5.2*	*5.2*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*	*3.1*
Estimated GFR < 30 mL/min	*22*	*20*	*18*	*18*	*16*	*15*	*15*	*13*	*12*	*11*
Non-haematological cancer										
Diagnosed <1 year ago	*7.1*	*6.4*	*6.4*	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*
Diagnosed 1-4.9 years ago	*3.8*	*3.4*	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*
Diagnosed ≥5 years ago	*2.3*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*	*1.5*
Haematological malignancy										
Diagnosed <1 year ago	*12*	*12*	*11*	*11*	*10*	*10*	*8.7*	*8.7*	*7.8*	*7.8*
Diagnosed 1-4.9 years ago	*8.7*	*8.7*	*8.7*	*8.7*	*7.8*	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*
Diagnosed ≥5 years ago	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*	*2.5*	*2.5*
Liver disease	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*
Chronic neurological disease other than stroke or dementia*	*6.4*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.8*	*5.2*	*5.2*	*5.2*
Organ transplant	*7.1*	*7.1*	*7.1*	*6.4*	*6.4*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*
Spleen diseases†	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*	*2.3*	*2.1*	*2.1*	*2.1*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*

True age (years)	60	61	62	63	64	65	66	67	68	69
Female sex	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity										
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)										
30-34.9	*1.4*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
35-39.9	*2.5*	*2.3*	*2.3*	*2.3*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*	*1.7*
≥40	*2.8*	*2.8*	*2.8*	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*	*2.1*
Hypertension	*1.7*	*1.7*	*1.5*	*1.5*	*1.5*	*1.4*	*1.4*	*1.4*	*1.2*	*1.2*
Heart failure	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*	*2.8*
Other chronic heart disease	*2.5*	*2.3*	*2.3*	*2.1*	*2.1*	*1.9*	*1.9*	*1.7*	*1.7*	*1.7*
Cerebrovascular disease	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*
Asthma										
Mild	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Severe	1.9	1.9	1.7	1.7	1.5	1.5	1.5	1.5	1.4	1.4
Other chronic respiratory disease	*2.5*	*2.5*	2.3	2.3	2.3	2.1	2.1	2.1	2.1	2.1
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*
HbA1>58 mmol/mol in past year	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*
HbA1c unknown	*6.4*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*3.4*	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*
HbA1>58 mmol/mol in past year	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*
HbA1c unknown	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*	*2.8*	*2.8*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*3.1*	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*	*2.1*	*1.9*	*1.9*
Estimated GFR < 30 mL/min	*11*	*10*	*10*	*8.7*	*7.8*	*7.8*	*7.1*	*7.1*	*6.4*	*6.4*
Non-haematological cancer										
Diagnosed <1 year ago	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*	*2.5*
Diagnosed 1-4.9 years ago	*2.3*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*	*1.5*
Diagnosed ≥5 years ago	*1.5*	*1.4*	*1.4*	*1.2*	*1.2*	*1.1*	*1.1*	*1.1*	*1.1*	*1.0*
Haematological malignancy										
Diagnosed <1 year ago	*7.1*	*7.1*	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*
Diagnosed 1-4.9 years ago	*6.4*	*5.8*	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*
Diagnosed ≥5 years ago	*2.5*	*2.3*	*2.3*	*2.3*	*2.1*	*2.1*	*2.1*	*2.1*	*1.9*	*1.9*
Liver disease	*3.1*	*2.8*	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*	*2.1*	*1.9*
Chronic neurological disease other than stroke or dementia*	*5.2*	*4.7*	*4.7*	*4.7*	*4.2*	*4.2*	*4.2*	*4.2*	*3.8*	*3.8*
Organ transplant	*4.7*	*4.7*	*4.2*	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*
Spleen diseases†	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*	*1.7*	*1.7*	*1.5*	*1.5*	*1.4*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*3.1*	*3.1*	*2.8*	*2.8*	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*

True age (years)	70	71	72	73	74	75
Female sex	0.6	0.6	0.6	0.6	0.6	0.6
Ethnicity						
Asian or Asian British	1.7	1.7	1.7	1.7	1.7	1.7
Black	2.0	2.0	2.0	2.0	2.0	2.0
Mixed	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*	*1.6*
Other non-white	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*	*1.5*
Body mass index (Kg/m^2)						
30-34.9	*1.2*	*1.1*	*1.1*	*1.1*	*1.1*	*1.1*
35-39.9	*1.7*	*1.7*	*1.5*	*1.5*	*1.4*	*1.4*
≥40	*2.1*	*1.9*	*1.9*	*1.7*	*1.7*	*1.7*
Hypertension	*1.2*	*1.1*	*1.1*	*1.0*	*1.0*	*1.0*
Heart failure	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*
Other chronic heart disease	*1.5*	*1.5*	*1.5*	*1.4*	*1.4*	*1.4*
Cerebrovascular disease	*2.8*	*2.8*	*2.5*	*2.5*	*2.5*	*2.5*
Asthma						
Mild	1.1	1.1	1.1	1.1	1.1	1.1
Severe	1.4	1.4	1.2	1.2	1.2	1.2
Other chronic respiratory disease	1.9	1.9	1.9	1.9	1.9	1.9
Diabetes						
Type 1						
HbA1≤58 mmol/mol in past year	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*
HbA1>58 mmol/mol in past year	*3.8*	*3.4*	*3.4*	*3.4*	*3.1*	*3.1*
HbA1c unknown	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.4*
Type 2 and other						
HbA1≤58 mmol/mol in past year	*2.1*	*1.9*	*1.9*	*1.9*	*1.7*	*1.7*
HbA1>58 mmol/mol in past year	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.3*
HbA1c unknown	*2.5*	*2.5*	*2.5*	*2.3*	*2.3*	*2.1*
Chronic kidney disease						
Estimated GFR 30-60 mL/min	*1.7*	1.7	1.5	1.5	1.4	1.4
Estimated GFR < 30 mL/min	*5.8*	*5.8*	*5.2*	*5.2*	*4.7*	*4.7*
Non-haematological cancer						
Diagnosed <1 year ago	*2.5*	*2.3*	*2.3*	*2.3*	*2.1*	*2.1*
Diagnosed 1-4.9 years ago	*1.5*	*1.4*	*1.4*	*1.4*	*1.2*	*1.2*
Diagnosed ≥5 years ago	*1.0*	*1.0*	*1.0*	*1.0*	*1.0*	*1.0*
Haematological malignancy						
Diagnosed <1 year ago	*4.2*	*3.8*	*3.8*	*3.4*	*3.4*	*3.1*
Diagnosed 1-4.9 years ago	*3.8*	*3.4*	*3.4*	*3.1*	*3.1*	*3.1*
Diagnosed ≥5 years ago	*1.9*	*1.9*	*1.7*	*1.7*	*1.7*	*1.7*
Liver disease	*1.9*	*1.9*	*1.7*	*1.7*	*1.5*	*1.5*
Chronic neurological disease other than stroke or dementia*	*3.8*	*3.8*	*3.4*	*3.4*	*3.4*	*3.4*
Organ transplant	*2.8*	*2.8*	*2.5*	*2.5*	*2.3*	*2.3*
Spleen diseases†	*1.4*	*1.2*	*1.2*	*1.1*	*1.1*	*1.0*
Rheumatoid/lupus/psoriasis	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*	*1.2*
Other immunosuppressive condition‡	*2.1*	*2.1*	*1.9*	*1.9*	*1.7*	*1.7*

Table Z8. Adopted relative risks in Update 7 expressed as equivalence to added years of age.

To calculate a person's Covid-age, first find the column of the table corresponding to their true age. Then add to their true age the years in that column corresponding to each risk factor that applies.

For example, to calculate the Covid-age of an Asian woman aged 50 with poorly controlled Type 2 diabetes, first find the column of Table Z6 corresponding to a true age of 50. In that column the added years for being female are -5, for being Asian/Asian British +5, and for poorly controlled Type 2 diabetes + 18. Thus, her Covid-age would be 50 – 5 +5 +18 = 68 years

Notes on Table

All estimates are approximate. Those in italics are classed as provisional. All others are classed as moderately robust.

*Chronic neurological disease other than stroke or dementia includes motor neurone disease, myasthenia gravis, multiple sclerosis, Parkinson's disease, cerebral palsy, quadriplegia, hemiplegia and progressive cerebellar disease.
†Spleen diseases include splenectomy, or spleen dysfunction (e.g. from sickle cell disease).
‡Other immunosuppressive condition includes HIV, conditions inducing permanent immunodeficiency (ever diagnosed), aplastic anaemia, and temporary immunodeficiency recorded within the past year.

True age (years)	20	21	22	23	24	25	26	27	28	29
Female sex	-5	-5	-5	-5	-5	-5	-5	-5	-5	-5
Ethnicity										
Asian or Asian British	5	5	5	5	5	5	5	5	5	5
Black	7	7	7	7	7	7	7	7	7	7
Mixed	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Other non-white	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*
Body mass index (Kg/m^2)										
30-34.9	*7*	*7*	*7*	*7*	*7*	*6*	*6*	*6*	*6*	*6*
35-39.9	*19*	*19*	*19*	*18*	*18*	*18*	*18*	*17*	*17*	*17*
≥40	*25*	*25*	*24*	*24*	*24*	*23*	*23*	*23*	*22*	*22*
Hypertension	*12*	*12*	*12*	*12*	*12*	*12*	*12*	*11*	*11*	*11*
Heart failure	*25*	*25*	*25*	*25*	*25*	*25*	*24*	*24*	*24*	*24*
Other chronic heart disease	*20*	*20*	*20*	*20*	*20*	*20*	*19*	*19*	*19*	*19*
Cerebrovascular disease	*17*	*17*	*17*	*16*	*16*	*16*	*16*	*16*	*16*	*16*
Asthma										
Mild	1	1	1	1	1	1	1	1	1	1
Severe	*15*	*15*	*15*	*15*	*15*	*15*	*14*	*14*	*14*	*14*
Other chronic respiratory disease	*17*	*17*	*17*	*17*	*17*	*16*	*16*	*16*	*16*	*16*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*24*	*24*	*24*	*24*	*24*	*24*	*23*	*23*	*23*	*23*
HbA1>58 mmol/mol in past year	*27*	*27*	*27*	*27*	*27*	*27*	*26*	*26*	*26*	*26*
HbA1c unknown	*29*	*29*	*29*	*29*	*29*	*28*	*28*	*28*	*28*	*28*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*21*	*21*	*21*	*21*	*21*	*20*	*20*	*20*	*20*	*20*
HbA1>58 mmol/mol in past year	*23*	*23*	*23*	*23*	*23*	*22*	*22*	*22*	*22*	*22*
HbA1c unknown	*22*	*22*	*22*	*22*	*22*	*21*	*21*	*21*	*21*	*21*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*42*	*41*	*40*	*39*	*38*	*37*	*37*	*36*	*35*	*34*
Estimated GFR < 30 mL/min	*53*	*52*	*51*	*50*	*50*	*49*	*48*	*47*	*46*	*46*
Non-haematological cancer										
Diagnosed <1 year ago	*34*	*33*	*33*	*32*	*32*	*31*	*31*	*30*	*30*	*29*
Diagnosed 1-4.9 years ago	*25*	*25*	*25*	*24*	*24*	*24*	*23*	*23*	*22*	*22*
Diagnosed ≥5 years ago	*18*	*18*	*18*	*18*	*17*	*17*	*17*	*16*	*16*	*16*
Haematological malignancy										
Diagnosed <1 year ago	*33*	*33*	*32*	*32*	*32*	*32*	*31*	*31*	*31*	*31*
Diagnosed 1-4.9 years ago	*32*	*31*	*31*	*31*	*30*	*30*	*30*	*29*	*29*	*29*
Diagnosed ≥5 years ago	*21*	*21*	*21*	*21*	*21*	*20*	*20*	*20*	*20*	*20*
Liver disease	*32*	*31*	*31*	*30*	*30*	*29*	*29*	*28*	*28*	*27*
Chronic neurological disease other than stroke or dementia*	*23*	*23*	*22*	*22*	*22*	*22*	*22*	*22*	*22*	*22*
Organ transplant	*25*	*25*	*24*	*24*	*24*	*24*	*24*	*24*	*24*	*24*
Spleen diseases†	*14*	*14*	*13*	*13*	*13*	*13*	*13*	*13*	*13*	*13*
Rheumatoid/lupus/psoriasis	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
Other immunosuppressive condition‡	*30*	*30*	*29*	*29*	*28*	*28*	*27*	*27*	*26*	*26*

True age (years)	30	31	32	33	34	35	36	37	38	39
Female sex	-5	-5	-5	-5	-5	-5	-5	-5	-5	-5
Ethnicity										
Asian or Asian British	5	5	5	5	5	5	5	5	5	5
Black	7	7	7	7	7	7	7	7	7	7
Mixed	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Other non-white	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*
Body mass index (Kg/m^2)										
30-34.9	*6*	*6*	*6*	*6*	*6*	*6*	*6*	*6*	*5*	*5*
35-39.9	*17*	*16*	*16*	*16*	*16*	*15*	*15*	*15*	*15*	*15*
≥40	*22*	*21*	*21*	*21*	*20*	*20*	*19*	*19*	*19*	*18*
Hypertension	*11*	*11*	*11*	*11*	*10*	*10*	*10*	*10*	*10*	*10*
Heart failure	*24*	*23*	*23*	*23*	*22*	*22*	*22*	*22*	*21*	*21*
Other chronic heart disease	*19*	*18*	*18*	*18*	*17*	*17*	*17*	*17*	*16*	*16*
Cerebrovascular disease	*16*	*16*	*16*	*16*	*16*	*16*	*16*	*15*	*15*	*15*
Asthma										
Mild	1	1	1	1	1	1	1	1	1	1
Severe	*14*	*14*	*14*	*13*	*13*	*13*	*13*	*13*	*12*	*12*
Other chronic respiratory disease	*16*	*15*	*15*	*15*	*15*	*15*	*14*	*14*	*14*	*14*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*23*	*23*	*22*	*22*	*22*	*22*	*22*	*21*	*21*	*21*
HbA1>58 mmol/mol in past year	*26*	*26*	*25*	*25*	*25*	*25*	*25*	*25*	*24*	*24*
HbA1c unknown	*28*	*28*	*28*	*27*	*27*	*27*	*27*	*27*	*26*	*26*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*20*	*20*	*20*	*19*	*19*	*19*	*19*	*19*	*19*	*19*
HbA1>58 mmol/mol in past year	*22*	*22*	*22*	*21*	*21*	*21*	*21*	*21*	*21*	*21*
HbA1c unknown	*21*	*21*	*21*	*21*	*21*	*21*	*21*	*21*	*20*	*20*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*33*	*32*	*32*	*31*	*30*	*29*	*28*	*27*	*26*	*26*
Estimated GFR < 30 mL/min	*45*	*44*	*44*	*43*	*42*	*41*	*40*	*39*	*38*	*37*
Non-haematological cancer										
Diagnosed <1 year ago	*29*	*28*	*28*	*27*	*27*	*26*	*26*	*25*	*25*	*24*
Diagnosed 1-4.9 years ago	*22*	*21*	*21*	*21*	*20*	*20*	*19*	*19*	*18*	*18*
Diagnosed ≥5 years ago	*15*	*15*	*15*	*14*	*14*	*13*	*13*	*12*	*12*	*11*
Haematological malignancy										
Diagnosed <1 year ago	*30*	*30*	*30*	*30*	*29*	*29*	*29*	*29*	*28*	*28*
Diagnosed 1-4.9 years ago	*28*	*28*	*28*	*27*	*27*	*27*	*26*	*26*	*25*	*25*
Diagnosed ≥5 years ago	*20*	*19*	*19*	*19*	*19*	*18*	*18*	*18*	*18*	*17*
Liver disease	*27*	*26*	*26*	*25*	*25*	*24*	*24*	*23*	*23*	*22*
Chronic neurological disease other than stroke or dementia*	*22*	*22*	*21*	*21*	*21*	*21*	*21*	*21*	*21*	*20*
Organ transplant	*23*	*23*	*23*	*23*	*23*	*23*	*22*	*22*	*22*	*22*
Spleen diseases†	*13*	*13*	*13*	*12*	*12*	*12*	*12*	*12*	*12*	*12*
Rheumatoid/lupus/psoriasis	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
Other immunosuppressive condition‡	*25*	*25*	*24*	*24*	*23*	*23*	*22*	*22*	*21*	*21*

True age (years)	40	41	42	43	44	45	46	47	48	49
Female sex	-5	-5	-5	-5	-5	-5	-5	-5	-5	-5
Ethnicity										
Asian or Asian British	5	5	5	5	5	5	5	5	5	5
Black	7	7	7	7	7	7	7	7	7	7
Mixed	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Other non-white	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*
Body mass index (Kg/m^2)										
30-34.9	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*4*	*4*	*4*
35-39.9	*14*	*14*	*14*	*14*	*13*	*13*	*13*	*13*	*12*	*12*
≥40	*18*	*17*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*
Hypertension	*9*	*9*	*9*	*9*	*9*	*8*	*8*	*8*	*8*	*8*
Heart failure	*21*	*20*	*20*	*20*	*19*	*19*	*19*	*18*	*18*	*18*
Other chronic heart disease	*16*	*15*	*15*	*15*	*14*	*14*	*14*	*13*	*13*	*13*
Cerebrovascular disease	*15*	*15*	*15*	*15*	*15*	*15*	*15*	*14*	*14*	*14*
Asthma										
Mild	1	1	1	1	1	1	1	1	1	1
Severe	*12*	*12*	*12*	*11*	*11*	*11*	*11*	*10*	*10*	*10*
Other chronic respiratory disease	*14*	*13*	*13*	*13*	*13*	*13*	*13*	*12*	*12*	*12*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*21*	*21*	*20*	*20*	*20*	*20*	*20*	*19*	*19*	*18*
HbA1>58 mmol/mol in past year	*24*	*24*	*24*	*23*	*23*	*23*	*23*	*22*	*22*	*22*
HbA1c unknown	*26*	*26*	*25*	*25*	*25*	*25*	*24*	*24*	*24*	*23*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*19*	*18*	*18*	*18*	*18*	*18*	*17*	*17*	*17*	*16*
HbA1>58 mmol/mol in past year	*21*	*20*	*20*	*20*	*20*	*20*	*19*	*19*	*19*	*18*
HbA1c unknown	*20*	*20*	*20*	*20*	*20*	*20*	*19*	*19*	*19*	*18*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*25*	*24*	*23*	*22*	*21*	*20*	*19*	*19*	*18*	*18*
Estimated GFR < 30 mL/min	*36*	*35*	*35*	*34*	*33*	*33*	*32*	*32*	*31*	*30*
Non-haematological cancer										
Diagnosed <1 year ago	*24*	*23*	*23*	*22*	*22*	*21*	*21*	*20*	*20*	*19*
Diagnosed 1-4.9 years ago	*18*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*	*13*
Diagnosed ≥5 years ago	*11*	*11*	*10*	*10*	*10*	*9*	*9*	*9*	*8*	*8*
Haematological malignancy										
Diagnosed <1 year ago	*28*	*28*	*27*	*27*	*27*	*26*	*26*	*26*	*25*	*25*
Diagnosed 1-4.9 years ago	*25*	*24*	*24*	*23*	*23*	*22*	*22*	*22*	*22*	*22*
Diagnosed ≥5 years ago	*17*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*	*14*
Liver disease	*22*	*21*	*21*	*20*	*20*	*19*	*19*	*18*	*17*	*17*
Chronic neurological disease other than stroke or dementia*	*20*	*20*	*20*	*20*	*20*	*20*	*19*	*19*	*19*	*19*
Organ transplant	*22*	*22*	*21*	*21*	*21*	*21*	*21*	*20*	*20*	*20*
Spleen diseases†	*11*	*11*	*11*	*11*	*11*	*11*	*10*	*10*	*10*	*10*
Rheumatoid/lupus/psoriasis	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
Other immunosuppressive condition‡	*20*	*20*	*19*	*19*	*18*	*17*	*17*	*16*	*16*	*15*

True age (years)	50	51	52	53	54	55	56	57	58	59
Female sex	-5	-5	-5	-5	-5	-5	-5	-5	-5	-5
Ethnicity										
Asian or Asian British	5	5	5	5	5	5	5	5	5	5
Black	7	7	7	7	7	7	7	7	7	7
Mixed	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Other non-white	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*
Body mass index (Kg/m^2)										
30-34.9	*4*	*4*	*4*	*3*	*3*	*3*	*3*	*3*	*3*	*3*
35-39.9	*12*	*11*	*11*	*11*	*10*	*10*	*10*	*10*	*9*	*9*
≥40	*14*	*14*	*13*	*13*	*12*	*12*	*12*	*11*	*11*	*11*
Hypertension	*7*	*7*	*7*	*7*	*7*	*6*	*6*	*6*	*5*	*5*
Heart failure	*17*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*	*14*
Other chronic heart disease	*13*	*12*	*12*	*12*	*12*	*11*	*11*	*10*	*10*	*9*
Cerebrovascular disease	*14*	*14*	*14*	*13*	*13*	*13*	*13*	*13*	*12*	*12*
Asthma										
Mild	1	1	1	1	1	1	1	1	1	1
Severe	*9*	*9*	*9*	*9*	*8*	*8*	*8*	*7*	*7*	*7*
Other chronic respiratory disease	*12*	*12*	*11*	*11*	*11*	*11*	*10*	*10*	*10*	*9*
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*18*	*18*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*
HbA1>58 mmol/mol in past year	*21*	*21*	*20*	*20*	*19*	*19*	*19*	*18*	*18*	*17*
HbA1c unknown	*23*	*23*	*22*	*22*	*21*	*21*	*20*	*20*	*19*	*19*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*16*	*16*	*15*	*15*	*14*	*14*	*14*	*13*	*13*	*12*
HbA1>58 mmol/mol in past year	*18*	*18*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*
HbA1c unknown	*18*	*18*	*17*	*17*	*16*	*16*	*16*	*15*	*15*	*14*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*17*	*16*	*16*	*15*	*14*	*14*	*13*	*13*	*12*	*11*
Estimated GFR < 30 mL/min	*30*	*29*	*28*	*28*	*27*	*26*	*26*	*25*	*24*	*23*
Non-haematological cancer										
Diagnosed <1 year ago	*19*	*18*	*18*	*17*	*16*	*16*	*15*	*15*	*14*	*14*
Diagnosed 1-4.9 years ago	*13*	*12*	*11*	*11*	*10*	*10*	*9*	*9*	*8*	*8*
Diagnosed ≥5 years ago	*8*	*7*	*7*	*7*	*6*	*6*	*6*	*5*	*5*	*4*
Haematological malignancy										
Diagnosed <1 year ago	*24*	*24*	*23*	*23*	*22*	*22*	*21*	*21*	*20*	*20*
Diagnosed 1-4.9 years ago	*21*	*21*	*21*	*21*	*20*	*20*	*20*	*19*	*19*	*18*
Diagnosed ≥5 years ago	*13*	*12*	*12*	*11*	*11*	*10*	*10*	*10*	*9*	*9*
Liver disease	*16*	*15*	*15*	*14*	*14*	*13*	*13*	*12*	*12*	*11*
Chronic neurological disease other than stroke or dementia*	*18*	*18*	*18*	*18*	*17*	*17*	*17*	*16*	*16*	*16*
Organ transplant	*19*	*19*	*19*	*18*	*18*	*18*	*17*	*17*	*16*	*16*
Spleen diseases†	*9*	*9*	*9*	*8*	*8*	*8*	*8*	*7*	*7*	*7*
Rheumatoid/lupus/psoriasis	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
Other immunosuppressive condition‡	*15*	*15*	*14*	*14*	*13*	*13*	*13*	*12*	*12*	*11*

True age (years)	60	61	62	63	64	65	66	67	68	69
Female sex	-5	-5	-5	-5	-5	-5	-5	-5	-5	-5
Ethnicity										
Asian or Asian British	5	5	5	5	5	5	5	5	5	5
Black	7	7	7	7	7	7	7	7	7	7
Mixed	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Other non-white	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*	*4*
Body mass index (Kg/m^2)										
30-34.9	*3*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
35-39.9	*9*	*8*	*8*	*8*	*7*	*7*	*7*	*6*	*6*	*5*
≥40	*10*	*10*	*10*	*9*	*9*	*9*	*8*	*8*	*7*	*7*
Hypertension	*5*	*5*	*4*	*4*	*4*	*3*	*3*	*3*	*2*	*2*
Heart failure	*13*	*13*	*12*	*12*	*11*	*11*	*11*	*10*	*10*	*10*
Other chronic heart disease	*9*	*8*	*8*	*7*	*7*	*6*	*6*	*5*	*5*	*5*
Cerebrovascular disease	*12*	*12*	*12*	*11*	*11*	*11*	*11*	*11*	*10*	*10*
Asthma										
Mild	1	1	1	1	1	1	1	1	1	1
Severe	6	6	5	5	4	4	4	4	3	3
Other chronic respiratory disease	*9*	*9*	8	8	8	7	7	7	7	7
Diabetes										
Type 1										
HbA1≤58 mmol/mol in past year	*14*	*13*	*13*	*12*	*12*	*11*	*11*	*11*	*10*	*10*
HbA1>58 mmol/mol in past year	*17*	*16*	*16*	*15*	*15*	*14*	*14*	*14*	*13*	*13*
HbA1c unknown	*18*	*18*	*17*	*17*	*16*	*16*	*15*	*15*	*14*	*14*
Type 2 and other										
HbA1≤58 mmol/mol in past year	*12*	*11*	*11*	*10*	*10*	*9*	*9*	*8*	*8*	*7*
HbA1>58 mmol/mol in past year	*14*	*13*	*13*	*12*	*12*	*11*	*11*	*11*	*10*	*10*
HbA1c unknown	*14*	*13*	*13*	*12*	*12*	*11*	*11*	*11*	*10*	*10*
Chronic kidney disease										
Estimated GFR 30-60 mL/min	*11*	*10*	*9*	*9*	*8*	*8*	*7*	*7*	*6*	*6*
Estimated GFR < 30 mL/min	*23*	*22*	*22*	*21*	*20*	*20*	*19*	*19*	*18*	*18*
Non-haematological cancer										
Diagnosed <1 year ago	*13*	*13*	*12*	*12*	*11*	*11*	*10*	*10*	*9*	*9*
Diagnosed 1-4.9 years ago	*8*	*7*	*7*	*7*	*6*	*6*	*6*	*5*	*5*	*4*
Diagnosed ≥5 years ago	*4*	*3*	*3*	*2*	*2*	*1*	*1*	*1*	*1*	*0*
Haematological malignancy										
Diagnosed <1 year ago	*19*	*19*	*18*	*17*	*17*	*16*	*16*	*15*	*15*	*14*
Diagnosed 1-4.9 years ago	*18*	*17*	*17*	*16*	*16*	*15*	*15*	*14*	*14*	*13*
Diagnosed ≥5 years ago	*9*	*8*	*8*	*8*	*7*	*7*	*7*	*7*	*6*	*6*
Liver disease	*11*	*10*	*10*	*9*	*9*	*8*	*8*	*7*	*7*	*6*
Chronic neurological disease other than stroke or dementia*	*16*	*15*	*15*	*15*	*14*	*14*	*14*	*14*	*13*	*13*
Organ transplant	*15*	*15*	*14*	*14*	*13*	*13*	*12*	*12*	*11*	*11*
Spleen diseases†	*6*	*6*	*6*	*5*	*5*	*5*	*5*	*4*	*4*	*3*
Rheumatoid/lupus/psoriasis	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*	*2*
Other immunosuppressive condition‡	*11*	*11*	*10*	*10*	*9*	*9*	*9*	*8*	*8*	*7*

True age (years)	70	71	72	73	74	75
Female sex	-5	-5	-5	-5	-5	-5
Ethnicity						
Asian or Asian British	5	5	5	5	5	5
Black	7	7	7	7	7	7
Mixed	5	5	5	5	5	5
Other non-white	4	4	4	4	4	4
Body mass index (Kg/m^2)						
30-34.9	2	1	1	1	1	1
35-39.9	5	5	4	4	3	3
≥40	7	6	6	5	5	5
Hypertension	2	1	1	0	0	0
Heart failure	9	9	9	8	8	8
Other chronic heart disease	4	4	4	3	3	3
Cerebrovascular disease	10	10	9	9	9	9
Asthma						
Mild	1	1	1	1	1	1
Severe	3	3	2	2	2	2
Other chronic respiratory disease	6	6	6	6	6	6
Diabetes						
Type 1						
HbA1≤58 mmol/mol in past year	10	9	9	8	8	8
HbA1>58 mmol/mol in past year	13	12	12	12	11	11
HbA1c unknown	14	13	13	12	12	12
Type 2 and other						
HbA1≤58 mmol/mol in past year	7	6	6	6	5	5
HbA1>58 mmol/mol in past year	9	9	9	8	8	8
HbA1c unknown	9	9	9	8	8	7
Chronic kidney disease						
Estimated GFR 30-60 mL/min	5	5	4	4	3	3
Estimated GFR < 30 mL/min	17	17	16	16	15	15
Non-haematological cancer						
Diagnosed <1 year ago	9	8	8	8	7	7
Diagnosed 1-4.9 years ago	4	3	3	3	2	2
Diagnosed ≥5 years ago	0	0	0	0	0	0
Haematological malignancy						
Diagnosed <1 year ago	14	13	13	12	12	11
Diagnosed 1-4.9 years ago	13	12	12	11	11	11
Diagnosed ≥5 years ago	6	6	5	5	5	5
Liver disease	6	6	5	5	4	4
Chronic neurological disease other than stroke or dementia*	13	13	12	12	12	12
Organ transplant	10	10	9	9	8	8
Spleen diseases†	3	2	2	1	1	0
Rheumatoid/lupus/psoriasis	2	2	2	2	2	2
Other immunosuppressive condition‡	7	7	6	6	5	5

Two new reports provide estimates of infection fatality rates (IFRs). In the REACT-2 study [7.6], summary IFRs for men and women combined were 0.3 per 1000, 5.2 per 1000 and 31.3 per 1000 at ages 15-44, 45-64 and 65-74 years respectively.

In a similar analysis from Spain, the IFR was estimated as 0.8 to 0.9 per 1000 in men aged 40-49 years, and 3.3-3.8 per 1000 in men aged 50-59 [7.7].

The Spanish data suggest that our previous estimates of case fatality by Covid-age may have been a little too high, but results from the English study are reasonably compatible with what we estimated previously. On balance, we do not think that a change to Table Z4 is justified at this stage.

UPDATE 8: 11 OCTOBER 2020

A new report [8.14] gives estimates for age-specific IFRs (in both sexes combined) in England, one using ONS data on deaths within 28 days of a positive test, and the other using data from the REACT 2 survey [7.6]. The calculated values from these two sources at age 45 years were $10^{(-3.267+0.0523*45)}$ = 1.2 per 1000 and $10^{(-2.964+0.0505*45)}$ = 2.0 per 1000.

A study in the USA combined prevalence estimates from a state-wide random sample of community-dwelling Indiana residents aged 12 years and older (corrected for non-response) with data on mortality from Covid-19 to estimate IFRs by age, sex, race and ethnicity [8.15]. The overall estimate of IFR at ages 40-59 was 1.2 per 1000 (95%CI 0.9-1.9).

In a systematic review and meta-analysis of 28 studies 17 countries, the log of IFR for both sexes combined was estimated as -3.27 + 0.0524*age, giving a value for IFR at age 45 of 10 (-3.27 + 0.0524*age) = 1.2 per 1000 [8.16].

Uncertainties remain in the estimation of IFRs for Covid-19. In some studies, failure fully to ascertain infections because of the incomplete sensitivity of antibody tests may have caused overestimation, while incomplete ascertainment of deaths from Covid-19 may have led to bias in the opposite direction. Bias could also have occurred because of selective participation in surveys to estimate the prevalence of infection. And there is a possibility that IFR has fallen over the course of the pandemic as treatment has improved.

Nevertheless, we think the evidence on IFR is now sufficiently strong that our online calculator should include an approximate estimate (expressed as a range of uncertainty) of the IFR corresponding to each calculated Covid-age. To support this, we revisited the estimates of IFR in Table Z4.

Our starting point was an estimate of IFR for men and women combined in England and Wales at age 45 years. Given the latest findings from the UK [8.14], we judged it reasonable to assume a value of 1.8 per 1000, a level which is broadly consistent with estimates from other countries.

Next, it was necessary to estimate the "average" Covid-age of people aged 45 years in the general population. For that purpose, we assumed as an approximation that relative risks from relevant risk factors combine multiplicatively, and that the occurrence of each risk factor is independent. In those circumstances, the presence of a risk factor with prevalence, P, and relative risk, R, will increase the "average" risk of the population by a factor of {1 + (R-1)*P}, and the overall impact of multiple risk factors will be obtained as the product of such terms for each factor. The added years of age equivalent to the final population relative risk can then be calculated, assuming as before, that risk increases by a factor of 1.1084 for each added year.

Risk factors would contribute materially to the calculation where their prevalence in the general population was sufficiently high, given the relative risk with which they are associated. Following review of the estimated relative risks at age 45 years in Table Z7 and taking into account the likely prevalence of each risk factor at that age, we carried out a rough calculation using the parameters set out in Table Z9. The table also shows the basis for the assumed estimate of prevalence, and the factor by which each risk factor was estimated to increase the "average" risk in the population. It can be seen that the largest expected impacts were for female sex, obesity, hypertension and diabetes.

Table Z9. Estimated impact of relevant risk factors on "average" risk of population aged 45 years

Risk factor	Assumed relative risk	Assumed prevalence in general population at age 45 years	Basis for assumed prevalence	Estimated impact on population risk (expressed as factor by which it is increased)
Female sex	0.6	0.5	ONS population estimates	0.80
Non-white ethnicity	1.7	0.1	UK government statistics	1.07
Obese	2	0.3	Health Survey for England 2018	1.30
Hypertension	2.3	0.2	Health Survey for England 2018	1.30
Severe asthma	3.1	0.02	OpenSAFELY study sample	1.04
Diabetes	8	0.04	Health Survey for England 2018	1.30
Chronic kidney disease	10	0.01	Health Survey for England 2016	1.09

The estimated overall impact of these risk factors (i.e. the product of the individual impacts listed in the right-hand column of Table Z9) was to increase the risk of the 45-yearold population by a factor of 2, which equates to an added 7 years of age. Thus, the estimated IFR of 1.8 per 1000 for people aged 45 years, which we took as the starting point for calculations (see above) would correspond to that for a Covid-age of 45 + 7 = 52 years. From this, IFRs at other ages were calculated by applying the previously adopted relative risk of 1.1084 for each one-year increase in age (Table Z10). Because of the uncertainties in these calculations and in the underpinning data, we consider that these estimates could

be inaccurate by a factor of 2 in either direction. To reflect this, Table Z10 also presents the range within which each IFR might be expected to lie.

Table Z10. Estimated infection fatality rates by Covid-age

Covid-age	Estimated risk relative to a Covid-age of 52 years	Estimated infection fatality rate (per 1000) and range of uncertainty		
		Point estimate	Lower bound	Upper bound
20	0.04	0.07	0.04	0.1
21	0.04	0.08	0.04	0.2
22	0.05	0.09	0.05	0.2
23	0.05	0.1	0.05	0.2
24	0.06	0.1	0.06	0.2
25	0.06	0.1	0.06	0.2
26	0.07	0.1	0.07	0.3
27	0.08	0.2	0.08	0.3
28	0.08	0.2	0.08	0.3
29	0.09	0.2	0.09	0.4
30	0.1	0.2	0.1	0.4
31	0.1	0.2	0.1	0.5
32	0.1	0.3	0.1	0.5
33	0.1	0.3	0.1	0.6
34	0.2	0.3	0.2	0.6
35	0.2	0.3	0.2	0.7
36	0.2	0.4	0.2	0.8
37	0.2	0.4	0.2	0.9
38	0.2	0.5	0.2	0.9
39	0.3	0.5	0.3	1.0
40	0.3	0.6	0.3	1.2
41	0.3	0.6	0.3	1.3
42	0.4	0.7	0.4	1.4
43	0.4	0.8	0.4	1.6
44	0.4	0.9	0.4	1.8
45	0.5	1.0	0.5	1.9
46	0.5	1.1	0.5	2.2
47	0.6	1.2	0.6	2.4
48	0.7	1.3	0.7	2.7
49	0.7	1.5	0.7	2.9
50	0.8	1.6	0.8	3.3
51	0.9	1.8	0.9	3.6
52	1.0	2.0	1.0	4.0
53	1.1	2.2	1.1	4.4
54	1.2	2.5	1.2	4.9
55	1.4	2.7	1.4	5.4
56	1.5	3.0	1.5	6.0
57	1.7	3.3	1.7	6.7
58	1.9	3.7	1.9	7.4

59	2.1	4.1	2.1	8.2
60	2.3	4.6	2.3	9.1
61	2.5	5.1	2.5	10
62	2.8	5.6	2.8	11
63	3.1	6.2	3.1	12
64	3.4	6.9	3.4	14
65	3.8	7.6	3.8	15
66	4.2	8.4	4.2	17
67	4.7	9.4	4.7	19
68	5.2	10	5.2	21
69	5.8	12	5.8	23
70	6.4	13	6.4	26
71	7.1	14	7.1	28
72	7.8	16	7.8	31
73	8.7	17	8.7	35
74	9.6	19	9.6	38
75	11	21	11	43
76	12	24	12	47
77	13	26	13	52
78	15	29	15	58
79	16	32	16	64
80	18	36	18	71
81	20	40	20	79
82	22	44	22	88
83	24	49	24	97
84	27	54	27	108
85	30	60	30	119

UPDATE 10: 11 DECEMBER 2020

Two studies, one of critical care patients in England [10.10], and the other of hospitalised patients in Sweden [10.11], suggest that over the first three months of the Covid-19 epidemic in those countries, case-fatality rates fell importantly. The reductions may in part have been influenced by changes in case-mix, but they raise the possibility that IFRs based on outcomes over the early phase of the pandemic may overestimate those that now pertain, reinforcing the uncertainties that we have expressed in our estimates of IFR by Covid-age.

Using data on mortality from 45 countries, and results from 22 sero-prevalence studies in a subset of 16 countries (including England and Scotland), a new analysis has estimated an IFR of 1.68 per 1000 for men aged 45-49 years [10.12]. This is a little lower than the value of 1.8 per 1000 that we assumed for people (both sexes combined) aged 45 years in Update 8. However, it is compatible with the range of uncertainty that we proposed around our estimates of IFR.

UPDATE 12: 14 DECEMBER 2021

Our original estimates of IFRs by Covid-age were based on data from unvaccinated populations during the early phases of the pandemic. Because of improvements in treatment, and possible differences in the severity of disease caused by more recent variants of SARSCov-2, we think those estimates are now less reliable as an indication of risk in people who are unvaccinated. In view of this uncertainty, and also the widespread uptake of vaccination among people of working age in the UK, we consider that they are no longer sufficiently useful for inclusion in our calculator, and accordingly have removed them. This does not, however, affect the use of Covid-Age as a measure of relative risk of death in unvaccinated individuals who contract infection.

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