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Persons diagnosed with COVID-19 in England in the Clinical Practice Research Datalink (CPRD): a cohort description

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ABSTRACT

Objective To create case definitions for confirmed COVID-19 diagnoses, COVID-19 vaccination status and three separate definitions of high risk of severe COVID-19, as well as to assess whether the implementation of these definitions in a cohort reflected the sociodemographic and clinical characteristics of COVID-19 epidemiology in England.

Design Retrospective cohort study.

Setting Electronic healthcare records from primary care (Clinical Practice Research Datalink, CPRD) linked to secondary care data (Hospital Episode Statistics) data covering 24% of the population in England.

Participants 2 271 072 persons aged 1 year and older diagnosed with COVID-19 in CPRD Aurum between 1 August 2020 and 31 January 2022.

Main outcome measures Age, sex and regional distribution of COVID-19 cases and COVID-19 vaccine doses received prior to diagnosis were assessed separately for the cohorts of cases identified in primary care and those hospitalised for COVID-19 (primary diagnosis code of ICD-10 U07.1 'COVID-19'). Smoking status, body mass index and Charlson Comorbidity Index were compared for the two cohorts, as well as for three separate definitions of high risk of severe disease used in the UK (National Health Service Highest Risk, PANORAMIC trial eligibility, UK Health Security Agency Clinical Risk prioritisation for vaccination).

Results Compared with national estimates, CPRD case estimates under-represented older adults in both the primary care (age 65–84: 6% in CPRD vs 9% nationally) and hospitalised (31% vs 40%) cohorts, and over-represented people living in regions with the highest median wealth areas of England (20% primary care and 20% hospital admitted cases in South East vs 15% nationally). The majority of non-hospitalised cases and all hospitalised cases had not completed primary series vaccination. In primary care, persons meeting high-risk definitions were older, more often smokers, overweight or obese, and had higher Charlson Comorbidity Index score.

Conclusions CPRD primary care data are a robust real-world data source and can be used for some COVID-19 research questions, however, limitations of the data availability should be carefully considered. Included in this publication are supplemental files for a total of over 28 000 codes to define each of three definitions of high risk of severe disease.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study used the Clinical Practice Research Datalink, a longitudinal and anonymised electronic health record database of primary healthcare interactions in England.
⇒ Definitions were built using reproducible methods with independent local clinician review.
⇒ Results were compared with government published COVID-19 case and vaccination counts to evaluate external validity of this data source.
⇒ Limitations of the data include data recency lag, with primary care data ending in April 2022 and hospitalisation data ending in March 2021.
⇒ Owing to the primary care setting of the data, this study does not represent people without a general practitioner, or those who presented directly to hospital without a prior COVID-19-related primary care encounter.

INTRODUCTION

As of 3 February 2023, there have been over 20 million confirmed COVID-19 cases and more than 183 000 related deaths in England.[1] COVID-19 severity ranges from asymptomatic cases to severe disease requiring hospital admission and sometimes death, with older adults and people with chronic health conditions at disproportionate risk.[2 3] Therefore, electronic health records (EHR) with long-standing capture of patients' medical history are uniquely positioned to answer population-based questions related to healthcare resource utilisation, economic impact and pharmaceutical intervention associated with COVID-19.

The Clinical Practice Research Datalink (CPRD) is a longitudinal and anonymised EHR database of primary healthcare

interactions in England.[4] Primary care is the cornerstone of healthcare in England, with over 98% of the population registered with a general practitioner (GP). From August 2020 to March 2022, all tests booked via the National Health Service (NHS) website for PCR tests for SARS-CoV-2, regardless of result, were reported to GP offices that use the EMIS EHR software.[5] Similarly, COVID-19 vaccines administered at any location in the country were also mandated to be reported to patient's GP.[6] Thus, during this period, CPRD can be considered a closed network of confirmed COVID-19 cases for persons in the network, with accurate information on COVID-19 vaccination status.

While the CPRD has been used in over 3000 peer-reviewed publications, it is not known whether interruptions in healthcare, particularly in-person primary care visits, during the first years of the COVID-19 pandemic affected the previously described characteristics of the CPRD population. The objective of this study was to create case definitions for COVID-19 diagnoses, COVID-19 vaccination and three separate definitions of high risk of severe COVID-19. Second, we aimed to evaluate these definitions in a sample of persons with COVID-19, using the CPRD, to assess whether this cohort's sociodemographic and clinical characteristics were generalisable to population-level COVID-19 epidemiology in England. The methodology developed in the study can be leveraged in future COVID-19 research in CPRD data.

METHODS

Study setting and population

CPRD Aurum contains data which are routinely collected from primary care practices that use the EMIS web digital clinical system that includes electronic patient records.[7] The May 2022 release of CPRD Aurum contained data from approximately 24% of persons in England.[8 9] Data captured include age, sex, body weight, medical diagnoses, referrals to specialists and/or secondary care, prescriptions issued in primary care, laboratory tests, vaccinations administered, smoking and alcohol consumption status, and all other types of care delivered as part of routine primary care practice.

CPRD Aurum was linked to Hospital Episode Statistics Admitted Patient Care (HES APC) records, using deterministic patient-level linkage with an eight-stage algorithm carried out by NHS Digital. Over 99% of practices contributing to CPRD Aurum participate in HES linkage. The HES APC dataset includes patient demographics, date and method of hospital admission and discharge, diagnoses, specialty care, and procedures. HES APC data from April 1997 to March 2021 were available in this study.

Inclusion and exclusion criteria

We included persons of any age diagnosed with COVID-19 (described below) from 1 August 2020 to 31 January 2022. First, we required records to be of acceptable research quality, as defined by CPRD. Second, we required people to be continuously registered with their GP practice for at least 365 days prior to COVID-19 diagnosis, to establish pre-COVID-19 health history. Third, we required persons to be HES APC linkage eligible to ensure the exclusion of patients where confirmed hospital admission status (via HES APC, during the time period available) could not be known. Fourth, we excluded persons who were admitted to the hospital with a primary diagnosis of U07.1 on or before their primary care recorded date of COVID-19 diagnosis. Due to mandatory reporting guidelines, the GP's date of notification from the hospital may be delayed from the date of true test collection, and therefore, may not accurately reflect date of diagnosis. Lastly, we excluded persons with a registration end date, practice last collection date or death date that was prior to their COVID-19 diagnosis.

COVID-19 case definition

With each monthly data release, CPRD publishes feasibility counts for SARS-CoV-2-related codes in CPRD primary care data with corresponding code lists.[8 10] The code types include vaccination, tests (including PCR, antibody and antigen tests), diagnosis, advice, possible cases and post-COVID-19 clinic referral codes. Three reviewers (KMA, QM and AS) independently screened the CPRD code list to determine which of the codes represented a confirmed and current infection. Discrepancies were adjudicated by a fourth reviewer (LJM), and the final definition for the COVID-19 case definition was reviewed by UK and non-UK clinicians (online supplemental table 1). We defined a current and confirmed COVID-19 episode as a diagnosis code, positive PCR or antigen test. We did not include COVID-19 vaccination, antibody tests, possible cases, exposure to COVID-19 or post-COVID-19 clinic referral codes in the COVID-19 case definition.

Hospitalisations for COVID-19 were defined as persons admitted with a primary diagnosis of COVID-19 (ICD-10 U07.1 'COVID-19') within 12 weeks of the initial diagnosis recorded in primary care. Non-hospitalised COVID-19 cases were defined as the subset of persons for whom secondary care data were available but had no record of hospital admission. Primary care COVID-19 cases were defined as persons who were not admitted to the hospital within 12 weeks of diagnosis, and those after 1 April 2021 for which hospital admission data were not available.

COVID-19 vaccination definition

The first COVID-19 vaccine dose in England was administered on 8 December 2020, with the initially limited supply prioritised for groups as outlined by the Joint Committee for Vaccinations and Immunisations (JCVI).[11] In England, COVID-19 vaccines produced by Pfizer-BioNTech and Moderna have been available since December 2020. In April 2021, JCVI announced that persons who received a first dose of an AstraZeneca vaccine would receive a second dose of the same brand but persons who had not yet received a vaccine dose would be 'preferentially offered an alternative'.[12] This study did not consider

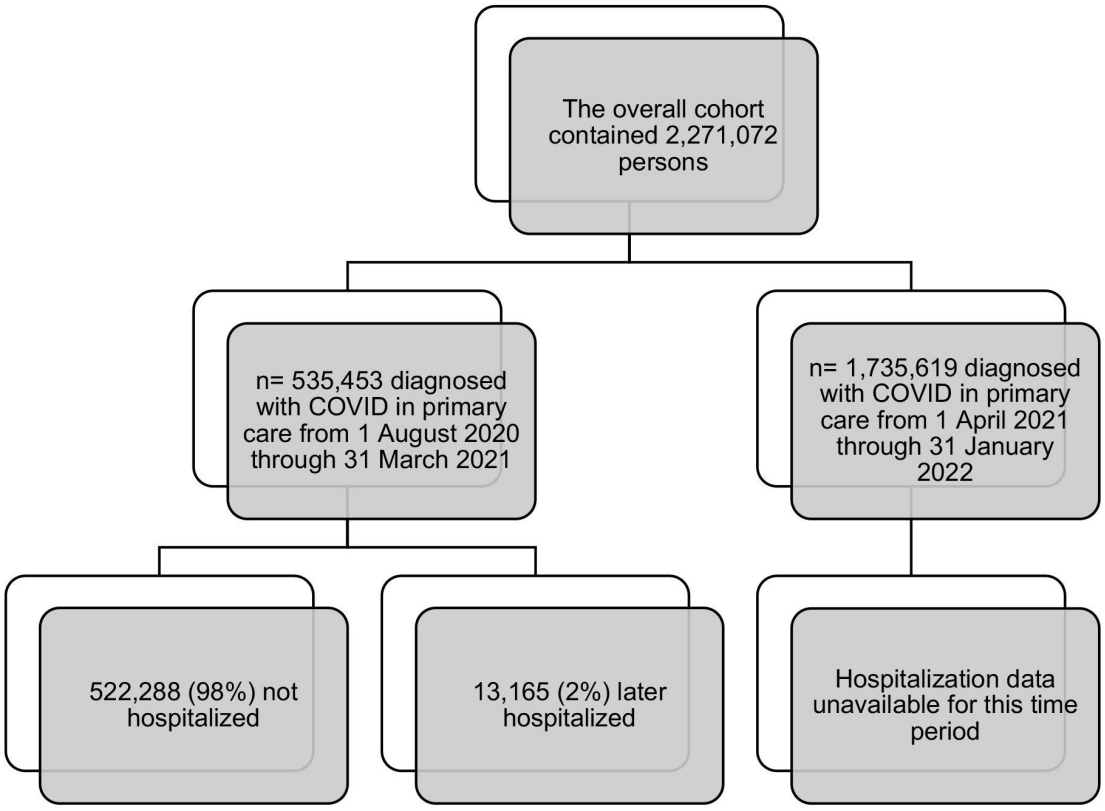

Figure 1 Cohort description. Attrition diagram of final cohort derivation. For further detail, see online supplemental table 6.

Novavax vaccinations, as it was approved for use after our index date, or the Janssen or Valneva vaccines, which have not been used in England as of February 2023.[13]

In phase 1 (December 2020–March 2021), people aged 50 and older, as well as front-line health and social care workers, clinically extremely vulnerable persons and persons aged 16 and older with underlying health conditions were eligible to receive two doses. In phase 2 (beginning April 2021), access broadened for persons aged 18–49 to receive two doses. Additionally, immunocompromised persons who received two doses in phase 1 were recommended to receive a third dose at least 8 weeks after their second dose in order to complete their primary series. Phase 3 included a single dose for 16–17 years in August 2021. In September 2021, 12–15 years could receive a single dose and a booster dose for adults was recommended at least 6 months after the completion of a primary series. In November 2021, 12–17 years could receive a second dose, and the recommendation for booster dose was shortened to at least 3 months after the completion of a primary series.[11]

We used a combination of product codes, which specify brand and dose of vaccine, as well as medical codes which indicated administration of a non-specific COVID-19 vaccine (online supplemental table 2). The code lists were derived from the published set by CPRD.[10] While patients may have multiple vaccination codes in their record on a given day, such as a code to indicate both the administration as well as a separate code for the specific product given, persons were not counted as receiving more than one vaccine dose per day.

Vaccination status at COVID-19 diagnosis date was reported, regardless of brand and separately for immunocompromised versus non-immunocompromised persons. Persons were considered unvaccinated if there was no record of COVID-19 vaccination, or for up to 13 days after first dose to account for time needed to build immunity following immunisation. Dose 1 was defined starting 14 days after the record of the first COVID-19 vaccine administration until 13 days after the receipt of second dose, or until end of follow-up. Dose 2 was defined starting 14 days after the record of the second COVID-19 vaccine administration and administered at least 21 days after the first dose. Persons were considered to have had two doses until 13 days before their next vaccine. For non-immunocompromised persons, the primary vaccination series was completed 14 days after second dose. For immunocompromised persons only, dose 3 was part of their primary series at least 21 days after their second dose. First booster doses (winter 2021) were defined 21 or more days after the receipt of the last dose in primary series. For all vaccination definitions, no upper limit on time between doses was applied.

COVID-19 risk status

We examined three separate definitions of COVID-19 risk status, each of which are set forth by different groups. While similarities exist, there are differences in the

Table 1 Characteristics of COVID-19 cases in CPRD Aurum, 1 August 2020–31 January 2022

	Primary care COVID-19 cases (n=2 257 907)	Hospitalised COVID-19 cases (n=13 165)
Age at COVID-19 diagnosis, years		
1–4	40 658 (2%)	15 (<1%)
5–11	260 186 (11%)	21 (<1%)
12–17	263 800 (11%)	24 (<1%)
18–49	1 161 843 (52%)	3127 (24%)
50–64	379 528 (17%)	4844 (37%)
65–74	92 573 (4%)	2386 (18%)
75–84	40 481 (2%)	1690 (13%)
85+	18 838 (1%)	1058 (8%)
Sex		
Male	1 046 275 (46%)	7537 (57%)
Female	1 211 592 (54%)	5628 (43%)
Unknown	40 (<1%)	0
General practitioner practice region		
North East	83 834 (4%)	467 (4%)
North West	471 195 (21%)	2886 (22%)
Yorkshire and The Humber	71 429 (3%)	340 (3%)
East Midlands	49 651 (2%)	214 (2%)
West Midlands	377 125 (17%)	2065 (16%)
East of England	95 139 (4%)	414 (3%)
London	424 908 (19%)	2984 (23%)
South East	448 536 (20%)	2682 (20%)
South West	235 785 (10%)	1113 (8%)
Unknown	305 (<1%)	0

CPRD, Clinical Practice Research Datalink.

populations. First, the NHS highest risk group, which was a list of conditions set forth by an advisory group commissioned by England's Deputy Chief Medical Officer to identify persons at the very highest risk of COVID-19 hospital admission and death.[14] Second, eligibility for the PANORAMIC (Platform Adaptive trial of NOvel antiviRals for eArly treatMent of COVID-19 In the Community) study, which began in December 2021 and is a platform randomised trial of antiviral therapeutic agents.[15] The persons who qualify for antiviral treatment in the trial are those at a higher risk of hospital admission and death. Third, UK Health Security Agency (UKHSA) clinical risk groups as outlined in 'The Green Book' chapter 14a, which is COVID-19 vaccination prioritisation from the JCVI.[16] For each of these three risk definitions, we operationalised the clinical conditions lists into SNOMED and ICD-10 (International Statistical Classification of Diseases and Related Health Problems, 10th revision) code lists. Where available, we used published code lists.[17–23] For concepts not found in the literature, we developed wildcard-based search terms in the CPRD code browser (online supplemental tables 3–5). At least one practising clinician from the UK, who was independent and external to Pfizer, reviewed each of the search term strategies, as well as ensuing code lists.

Comparison to publicly available data

We compared our results to estimates published on the UK Government's Coronavirus dashboard, and restricted results to those specific to England, as the CPRD Aurum population that is HES-linkage eligible contains data from England only.[24 25] The data in this manuscript reflect figures from the dashboard as accessed on 31 January 2023. Where possible, we restricted the dashboard to cases from 1 August 2020 to 31 January 2022 to reflect the study period, although age, sex and region-specific estimates were reported 'since the start of the pandemic'.[24 25] For whole country (non-COVID-19-related) comparisons, we used the Office of National Statistics' 2021 Census.[9]

Statistical analyses

All results are presented separately for the cohorts of persons with primary care versus hospitalised COVID-19 cases. Continuous variables are presented as means (SD) or medians (IQRs) and categorical variables as counts (percentages). Missing data for sex, region, smoking status and body mass index are shown in tables. The absence of codes for comorbidities was assumed to be the absence of the comorbidity rather than missing data. Standardised mean differences (SMDs) were used to compare groups, with SMD>10% indicating a significant difference. As per CPRD privacy rules, any cell with 10 persons or fewer (but not zero) was suppressed and other cells related to the small cell count were redacted to ensure no back-calculation could populate the count.

Data management and analyses for this study used SAS, V.9.4 (SAS Institute).

Patient and public involvement

There were no directly involved patients or public involvement in this study.

RESULTS

From 1 August 2020 to 31 January 2022, the UK Government's Coronavirus dashboard reported 14 744 991 COVID-19 cases in England.[24] The final CPRD cohort contained 2 271 072 persons diagnosed with COVID-19, regardless of care setting, in England in the same time period (online supplemental table 6). The case trends followed national estimates, with a series of peaks and troughs with a large peak in winter 2021 (online supplemental figures 1 and 2). Hospital admissions increased in fall 2020 and winter 2020 (online supplemental figure 3).

There were 2 257 907 persons with COVID-19 cases observed in primary care, which included persons who were not hospitalised during the period of time for which

hospital admission data was available (n=522 288) as well as all COVID-19 diagnoses recorded in the period where hospital admission data ended (n=1 735 619). Separately, there were 13 165 persons (2% of COVID-19 cases from August 2020 to March 2021) who were hospitalised within 12 weeks of initial COVID-19 diagnosis with a primary diagnosis of COVID-19 (figure 1).

Characteristics of COVID-19 cases

For both primary care and hospitalised cases, the majority of persons with COVID-19 in CPRD were adults aged 18–64 (table 1). The age distribution of CPRD primary care cases generally followed the national case count distribution, with young and middle-aged adults representing the largest groups, as well as the largest fraction of the English population (online supplemental table 7). Older adults were under-represented in both cohorts as compared with national population estimates. Within the primary care cohort, 6% of patients were aged 65–84 years, whereas 9% of national COVID-19 cases occurred in this age group. Notable differences were observed in the hospitalised cohort when compared with the national estimates; 31% vs 40% were aged 65–84 years and 8% vs 21% were aged >85 years, respectively.

The sex distribution of COVID-19 cases in the primary care cohort was comparable to national estimates, with 54% vs 55% female in each (table 1 and online supplemental table 7). There were more males (57%) than females in the hospitalised cohort; there are no national sex-specific hospital admission counts available.

The regional distributions of the CPRD primary care and hospitalised cohorts were similar to each other but not the overall country. Both of the study cohorts had larger proportions of persons with GP practices in higher-income regions of England as compared with national case counts.[26] For example, 20% of persons in the primary care cohort and 20% in the hospitalised cohort lived in South East region of England, the region with the highest median total household wealth as reported in March 2020. This is compared with 20% of CPRD contributing practices, 15% of all English cases and 16% of the population lived in London (online supplemental table 8). Similar trends are seen with lower median total household wealth regions being proportionally under-represented in the COVID-19 CPRD cohort as compared with national case estimates or population distribution.

COVID-19 vaccination status

At the time of COVID-19 diagnosis, 27% of non-immunocompromised persons and 36% of immunocompromised persons had completed a primary series of COVID-19 vaccination (table 2). Among the non-immunocompromised hospitalised COVID-19 cases, 98% were unvaccinated and none had completed a primary series. For immunocompromised hospitalised COVID-19 cases, 56% were unvaccinated, 44% had received one dose and none had completed a primary series. As of 1 December 2021, 86% of adults had ≥1 and 80% had ≥2 COVID-19 vaccine doses (2% and 0.2% lower than official reports, respectively).

Table 2 Vaccination status at COVID-19 diagnosis in CPRD Aurum, 1 August 2020–31 January 2022

	Primary care COVID-19 cases (n=2 257 907)	Hospitalised COVID-19 cases (n=13 165)
Non-immunocompromised	2 193 241 (100%)	12 984 (100%)
Unvaccinated	1 170 509 (53%)	12 744 (98%)
1 COVID-19 vaccine dose	173 853 (8%)	240 (2%)
2 COVID-19 vaccine doses	598 367 (27%)	0
First booster	250 512 (12%)	0
Immunocompromised	64 666 (100%)	181 (100%)
Unvaccinated	1306 (2%)	102 (56%)
1 COVID-19 vaccine dose	6033 (9%)	79 (44%)
2 COVID-19 vaccine doses	33 953 (53%)	0
3 COVID-19 vaccine doses	23 108 (36%)	0
First booster	266 (<1%)	0

CPRD, Clinical Practice Research Datalink.

Populations at risk of severe disease

After wildcard searches, clinicians reviewed nearly 50 000 codes to set the definitions for high-risk lists. The final lists contained 12 390 codes for NHS Highest Risk, 9132 codes for PANORAMIC trial criteria and 7343 codes for UKHSA Clinical Risk (code lists available on reasonable request). In the primary care cohort, 11% met NHS Highest Risk, 31% PANORAMIC and 10% UKHSA Clinical Risk criteria (table 3). With each definition, primary care cohort cases at high risk were more often current smokers (ranging 17%–21% vs 13% in full cohort) or former smokers (24%–28% vs 13%), overweight (16%–19% vs 9%) or obese (20%–28% vs 10%) and a larger proportion had at least 1 comorbidity in the Charlson Index (29%–54% vs 11%), where this was recorded. Primary care cases at high risk of severe disease were also older (mean age 49–55 years vs 34 years), more often female (55%–63% vs 54%) and had more recorded vaccine doses prior to COVID-19 diagnosis (online supplemental table 9).

Among hospitalised COVID-19 cases, 33% met NHS Highest Risk, 84% PANORAMIC and 41% UKHSA Clinical Risk criteria (table 4). The high-risk hospitalised groups were similar to the overall hospitalised cohort. Nearly half of persons were current smokers (13%–16% vs 13%) or former smokers (32%–39% vs 29%) and more than half were overweight (20%–23% vs 18%) or obese (37%–42% vs 35%). Among the hospital admitted cohort, people meeting each high-risk definition were older (mean age 65–66 years vs 60 years) (online supplemental table 10). Subgroups of patients with the NHS and UKHSA definitions had higher mean Charlson Comorbidity Indexes, and more females, than high-risk patients identified with the PANORAMIC criteria or the entire hospitalised population.

Table 3 Clinical characteristics of primary care COVID-19 cases in CPRD Aurum, by high-risk definitions

	All (n=2 257 907)	Meeting NHS highest risk conditions (n=249 972)	Meeting PANORAMIC criteria (n=691 593)	Meeting UKHSA clinical risk (n=225 051)
Primary care cases meeting definition	--	11%	31%	10%
Smoking status				
Current smoker	298 735 (13%)	44 365 (17%)	121 019 (18%)	46 436 (21%)
Former smoker	285 722 (13%)	67 637 (26%)	168 343 (24%)	63 124 (28%)
Never smoked	580 239 (26%)	87 217 (34%)	228 579 (33%)	77 157 (34%)
Unknown	1 093 211 (48%)	60 753 (23%)	173 652 (25%)	38 334 (17%)
Body mass index (kg/m^2)				
Mean (SD)	27.6 (7.1)	29.1 (6.9)	29.5 (6.7)	29.5 (7.5)
Underweight (< 18.5)	45 194 (2%)	3720 (1%)	5305 (1%)	5926 (3%)
Not overweight (18.5–24.9)	226 272 (10%)	35 766 (14%)	81 363 (12%)	36 716 (16%)
Overweight (25.0–29.9)	204 360 (9%)	45 261 (17%)	113 863 (16%)	43 758 (19%)
Obese (≥30.0)	219 253 (10%)	53 814 (21%)	138 035 (20%)	62 494 (28%)
Unknown	1 562 828 (69%)	121 411 (47%)	353 027 (51%)	76 157 (34%)
Charlson comorbidity index				
Mean (SD)	0.2 (0.6)	0.7 (1.3)	0.5 (1.0)	1.0 (1.3)
0	2 003 257 (89%)	165 823 (64%)	487 550 (71%)	102 790 (46%)
1 or 2	221 370 (10%)	74 805 (29%)	174 287 (25%)	99 830 (44%)
3 or 4	24 554 (1%)	12 659 (5%)	21 574 (3%)	15 961 (7%)
5+	8726 (<1%)	6685 (3%)	8182 (1%)	6470 (3%)

CPRD, Clinical Practice Research Datalink; NHS, National Health Service; PANORAMIC, Platform Adaptive trial of NOvel antiviRals for eArly treatMent of COVID-19 In the Community; UKHSA, UK Health Security Agency.

DISCUSSION

Key results

In this work, we defined and benchmark results from three key variables related to COVID-19 research using CPRD: index COVID-19 diagnoses, COVID-19 vaccinations and persons at high risk of severe disease.

We identified 2 271 072 COVID-19 cases in CPRD Aurum between 1 August 2020 and 31 January 2022. Younger age and lower socioeconomic deprivation have been consistently associated with reductions in COVID-19 incidence and severity.[27 28] These factors may explain why this CPRD cohort, which proportionally under-represented persons age 65 and older and over-represented persons living in the regions with higher median total household wealth, captured 15% of COVID-19 cases in a database that covers 24% of persons in England. The requirement for an NHS number in order for results to be shared may explain some of this attrition as well. Future work using CPRD for COVID-19 research will need to consider these limitations of under ascertainment of cases. Moving beyond this study's time period, the transition to at home testing, as well as the end of free PCR testing for the general public on 1 April 2022, will need to be additionally considered.

This manuscript reports results from a case definition of confirmed and current infection. We did not include codes for immunoglobulin titres, as measurable antibodies indicate a resolved infection rather than date of onset. We did not include codes indicating a sequela of prior infection, as these most often occur on a later date than index diagnosis. We did not include codes indicating a test without a result, as people with a negative test result should not be included in a COVID-19 case definition. Our results, therefore, identified fewer cases, although with greater specificity, than other studies in published literature that allow for such heterogeneity.[29]

COVID-19 vaccination events were well captured in the CPRD. This stands in stark contrast to most administrative claims and EHR databases in the USA, where less than 50% of COVID-19 vaccines are recorded in comparison to estimates provided by the Centers for Disease Control and Prevention.[30 31] England's national healthcare system, as well as the NHS data infrastructure to facilitate capture of COVID-19-related events and long-standing structure of GPs as the central node in a person's healthcare coordination, enabled the high coverage of COVID-19 vaccination records. Researchers can be more confident with CPRD data that the absence of a vaccination record indicates unvaccinated status than they otherwise would be with most other real-world datasets, which is a critical consideration for studies related to COVID-19 disease burden, vaccination or treatments.

The proportion of persons who had completed primary series vaccination prior to infection was low among primary care cases. Notably, among hospitalised cases, no

Table 4 Clinical characteristics of hospitalised COVID-19 cases in CPRD Aurum-HES linked data, by high-risk definitions

	All (n=13 165)	Meeting NHS highest risk conditions (n=4333)	Meeting PANORAMIC criteria (n=11 011)	Meeting UKHSA clinical risk (n=5353)
Hospitalised cases meeting definition	--	33%	84%	41%
Smoking status				
Current smoker	1690 (13%)	655 (15%)	1476 (13%)	840 (16%)
Former smoker	3810 (29%)	1574 (36%)	3544 (32%)	2070 (39%)
Never smoked	4205 (32%)	1362 (31%)	3513 (32%)	1746 (33%)
Unknown	3460 (26%)	742 (17%)	2478 (23%)	697 (13%)
Body mass index (kg/m^2)				
Mean (SD)	31.9 (7.5)	31.4 (7.5)	31.7 (7.4)	31.4 (7.7)
Underweight (<18.5)	96 (1%)	51 (1%)	90 (1%)	70 (1%)
Not overweight (18.5–24.9)	1162 (9%)	509 (12%)	1060 (10%)	729 (14%)
Overweight (25.0–29.9)	2390 (18%)	949 (22%)	2161 (20%)	1239 (23%)
Obese (≥30.0)	4586 (35%)	1662 (38%)	4053 (37%)	2231 (42%)
Unknown	4931 (37%)	1162 (27%)	3647 (33%)	1084 (20%)
Charlson Comorbidity Index				
Mean (SD)	1.0 (1.6)	1.9 (2.1)	1.2 (1.7)	2.0 (2.0)
0	7128 (54%)	1283 (30%)	5158 (47%)	894 (17%)
1 or 2	4241 (32%)	1833 (43%)	4094 (37%)	2.927 (55%)
3 or 4	1161 (9%)	711 (16%)	1129 (10%)	963 (18%)
5+	635 (5%)	506 (12%)	630 (6%)	569 (11%)

CPRD, Clinical Practice Research Datalink; HES, Hospital Episode Statistics; NHS, National Health Service; PANORAMIC, Platform Adaptive trial of NOvel antiviRals for eArly treatMent of COVID-19 In the Community; UKHSA, UK Health Security Agency.

patients had completed a primary COVID-19 vaccination series. These findings may be explained by several factors. First, the COVID-19 vaccine was first made available in England on 8 December 2020, and initially, second doses were given up to 12 weeks later to maximise limited supply for as many people as possible. Therefore, the calendar period under study allowed for most persons to have had a COVID-19 diagnosis in periods at which 'full vaccination' was not achievable. Second, it is possible that one vaccine offered protection against severe illness.[32–34]

We operationalised a total of over 28 000 codes, from an initial set of nearly 50 000, for three definitions of persons at risk of severe disease. We have made the search terms available, for reproducibility, as well as the resulting code lists, for other research groups to implement in their work. After the completion of this work, NHS Digital published a code list for 'Targeted Conditions', which includes each element in the NHS Highest Risk category. Among these, the NHS code list can be repurposed for 4 of the 14 conditions in PANORAMIC criteria and 3 of the 11 conditions in UKHSA Clinical Risk. To our knowledge, we offer the first publication of code lists for capture of all elements in the PANORAMIC criteria as well as UKHSA Clinical Risk criteria for these high-risk definitions, which can now be readily used in datasets that contain CPRD medical and product, ICD-10 and OPCS Classification of Interventions and Procedures codes.

While there are similarities between the three definitions, differences do exist. In the example of renal disease, NHS Highest Risk is defined as chronic kidney disease stage 4 or 5, PANORAMIC trial criteria stipulate stage 2 or 3 and UKHSA Clinical Risk are for stages 3–5. PANORAMIC trial eligibility capture persons with mild renal disease, as some antiviral treatments are not approved for use in persons with severe renal disease. However, UKHSA Clinical Risk prioritised vaccination access for persons at highest risk of disease, which would include persons with more advanced renal disease. Notably, persons who have renal disease as defined by PANORAMIC trial criteria by definition do not have renal disease by NHS definition, and people in each of these may (or may not) meet UKHSA prioritisation. The choice of which high-risk definition to implement in future studies will need to be guided by the study population and research question.

In the primary care cases, persons at high risk were older, more often smokers, had larger body sizes and higher Charlson Comorbidity Indices from the overall group of primary care cases. Among hospitalised cases, the high-risk groups were similar to the entire hospitalised

group. These findings are consistent with existing understanding of high-risk definitions, and perhaps provide reassurance that the code lists measure the purported phenomenon.

The study periods in this report represent the most recent data available from CPRD as of 3 February 2023. During the Autumn of 2022, the Aurum database experienced data quality issues related to the EMIS data flows from legacy systems, and no primary care data have been made available to researchers since the May 2022 release (data through March 2022, with some early view of April 2022). Separately, HES secondary care data have not been updated since March 2021, as NHS Digital has undergone a change in the way they process and link data. COVID-19 remains a serious disease for some people, and it is certain that some of the 1.7 million persons diagnosed with COVID-19 after 1 April 2021 would have been later admitted for COVID-19, but we do not have the hospital admission data to distinguish them from those whose cases were managed entirely in the community setting. Throughout, we have used the term 'primary care records' as the combined groups of those known to be non-hospitalised (cases where HES data were available, but the person was not hospitalised), as well as those whom we have GP encounters for but unknown eventual hospital admission status. It is difficult to approximate the number of hospital admissions that would be expected with full data availability. Carrying forward the 2% hospital admission incidence seen in the early pandemic period may not be appropriate, given 2021 introduced periods of increased (delta variant) and decreased (omicron variant) risk of hospital admission, as well the uptake of COVID-19 vaccinations and antiviral treatments. Finally, the population structure of this cohort outlined in this work further challenge the direct application of national estimates to CPRD cohorts.

This study does not capture persons not under GP care such as prisoners, some residential homes and persons without a place of residence. Additionally, CPRD Aurum, when linked with HES data, reduces the population to persons registered at eligible GP practices in England, and therefore, may not represent persons in other countries in the UK or countries outside the UK. This study does not include persons who presented directly to hospital without any prior GP interaction. In particular, persons with more severe disease such as older adults may require immediate hospital admission before seeking primary care, which could explain some of the gaps in representation we have reported. Given that CPRD is a primary care database, and the limited time period of hospital data availability, we decided to design our study as an initial cohort of persons with primary care records of COVID-19. Studies looking for complete capture of all hospitalised COVID-19 patients might consider other data sources.

CONCLUSION

In conclusion, we present a cohort of over 2 million COVID-19 cases in linked CPRD-HES data, using published definitions for COVID-19 cases, vaccinations and each of three UK-specific definitions of persons at increased risk of severe disease. CPRD primary care data are a robust real-world data source and can be used for COVID-19-related research questions; however, limitations of the data availability should be carefully considered.

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Contributors KMA, LJM, MR, DM, JLN, CT, DM and JY of Pfizer, as well as KKR and TT of Adelphi Real World which has received consulting fees from Pfizer, were involved in the study design (collection, analysis and interpretation of the data), writing of the report and in the decision to submit the article for publication. All authors had full access to all statistical reports and tables in the study and take responsibility for the integrity of the data and accuracy of the data analysis. All results presented in all tables were quality control verified by a non-Pfizer non-Adelphi employee. KMA as guarantor accepts full responsibility for the work and/or conduct of the study, had access to the data, and controlled the decision to publish.

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Competing interests KMA, LJM, MR, DM, JLN, CT, DM and JY are employees of Pfizer or Pfizer and may hold Pfizer stock or stock options. KKR and TT are employees of Adelphi Real World which has received consulting fees from Pfizer.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Electronic health records are considered sensitive data in the UK by the Data Protection Act and cannot be shared. The primary care data can be requested via application to the Clinical Practice Research Datalink, with secondary care data and mortality data through linkage on application. Information is available from https://www.cprd.com/research-applications.

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Supplemental file 1, Table 1: COVID Cohort Definition

Medcode	Term
6874141000006113	SARS-CoV
6604671000006111	SARS-CoV infection
13053051000006117	2019-nCoV (novel coronavirus) antigen detection result positive
12990741000006116	2019-nCoV (novel coronavirus) detected
13483601000006110	2019-nCoV (novel coronavirus) detection result positive at the limit of detection
13483161000006118	2019-nCoV (novel coronavirus) ribonucleic acid detected
14168601000006119	Acute COVID-19
13486461000006118	Acute COVID-19 infection
14168611000006116	Acute disease caused by Severe acute respiratory syndrome coronavirus 2
13486471000006113	Acute disease caused by severe acute respiratory syndrome coronavirus 2 infection
13486571000006112	Asymptomatic COVID-19
13486561000006117	Asymptomatic SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection
12802201000006117	Confirmed 2019-nCoV (novel coronavirus) infection
13012431000006117	COVID-19
13483031000006114	COVID-19
13012441000006110	COVID-19 caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2)
13002281000006117	COVID-19 confirmed by laboratory test
13002311000006115	COVID-19 confirmed clinically
13002291000006119	COVID-19 confirmed using clinical diagnostic criteria
13483951000006118	COVID-19 detected
12990531000006116	Detection of 2019-nCoV (novel coronavirus) using polymerase chain reaction technique
13485771000006110	Detection of COVID-19
13485471000006115	Detection of ribonucleic acid of 2019 novel coronavirus in nasopharyngeal swab
13485711000006118	Detection of ribonucleic acid of COVID- 19 using polymerase chain reaction
13485421000006116	Detection of ribonucleic acid of Severe acute respiratory syndrome coronavirus 2
13485461000006110	Detection of RNA (ribonucleic acid) of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) in nasopharyngeal swab
13485521000006117	Detection of RNA (ribonucleic acid) of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) in oropharyngeal swab
13485581000006118	Detection of RNA (ribonucleic acid) of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) in sputum
13485701000006116	Detection of RNA (ribonucleic acid) of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) using polymerase chain reaction
13485751000006117	Detection of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2)
13485381000006114	Detection of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) antigen
13012231000006116	Detection of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) using polymerase chain reaction technique

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13483041000006116	Disease caused by 2019 novel coronavirus
13483051000006119	Disease caused by 2019-nCoV
12991131000006119	Disease caused by 2019-nCoV (novel coronavirus)
13483061000006117	Disease caused by Severe acute respiratory syndrome coronavirus 2
12991141000006112	Disease caused by Wuhan 2019-nCoV (novel coronavirus)
13053041000006119	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) antigen detection result positive
13012301000006116	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) detected
13052351000006112	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) RNA (ribonucleic acid) detection result positive
13483141000006117	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) RNA (ribonucleic acid) detection result positive
13483591000006119	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) RNA (ribonucleic acid) detection result positive at the limit of detection
13483151000006115	Severe acute respiratory syndrome coronavirus 2 ribonucleic acid detected
12990751000006119	Wuhan 2019-nCoV (novel coronavirus) detected
13002301000006118	Probable COVID-19 confirmed using clinical diagnostic criteria
13483611000006113	SARS (severe acute respiratory syndrome) coronavirus 2 RNA
13484481000006118	SARS-CoV-2 - severe acute respiratory syndrome coronavirus 2
13039281000006117	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) detection result positive
13052381000006116	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) RNA (ribonucleic acid) qualitative existence in specimen
13483941000006115	Severe acute respiratory syndrome coronavirus 2 detected

Note: “SARS-CoV” or “SARS-CoV infection” may refer to the SARS illness of 2003. We allowed these terms, given the novelty of SARS-CoV-2 and potential for erroneous use of SARS-CoV terms, but required them to be used during the time period of COVID (August 2020 onwards).

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Supplemental file 1, Table 2: COVID Vaccination Definition

Product code	Term
13739441000033113	COVID-19 Vaccine AstraZeneca (ChAdOx1 S [recombinant]) 5x10,000,000,000 viral particles/0.5ml dose suspension for injection multidose vials (AstraZeneca UK Ltd)
13750541000033115	COVID-19 Vaccine Janssen (Ad26.COV2-S [recombinant]) 0.5ml dose suspension for injection multidose vials (Janssen-Cilag Ltd)
13860541000033111	COVID-19 Vaccine Medicago (CoVLP) 3.75micrograms/0.5ml dose emulsion for injection multidose vials (Medicago Inc)
13790341000033117	COVID-19 Vaccine Novavax (adjuvanted) 5micrograms/0.5ml dose suspension for injection multidose vials (Baxter Oncology GmbH)
13778941000033110	COVID-19 Vaccine Valneva (inactivated adjuvanted whole virus) 40antigen units/0.5ml dose suspension for injection multidose vials (Valneva UK Ltd)
13739541000033114	Comirnaty COVID-19 mRNA Vaccine 30micrograms/0.3ml dose concentrate for dispersion for injection multidose vials (Pfizer Ltd)
13764941000033111	Spikevax COVID-19 mRNA (nucleoside modified) Vaccine 0.1mg/0.5ml dose dispersion for injection multidose vials (Moderna, Inc)

Medical code	Term
12990501000006112	2019-nCoV (novel coronavirus) vaccination
13012221000006119	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) vaccination
13482981000006117	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) vaccination
13482991000006119	2019 novel coronavirus vaccination
13483001000006118	Severe acute respiratory syndrome coronavirus 2 vaccination
13483011000006115	COVID-19 vaccination
13483021000006111	2019-nCoV (novel coronavirus) vaccination
13483211000006110	Immunisation course to achieve immunity against SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2
13483221000006119	Immunisation course to achieve immunity against 2019-nCoV (novel coronavirus)
13483231000006116	Administration of first dose of SARS- CoV-2 (severe acute respiratory syndrome coronavirus 2) vaccine
13483241000006114	Administration of first dose of 2019- nCoV (novel coronavirus) vaccine
13483251000006111	Administration of second dose of SARS- CoV-2 (severe acute respiratory syndrome coronavirus 2) vaccine
13483261000006113	Administration of second dose of 2019- nCoV (novel coronavirus) vaccine
13483531000006118	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) immunisation course started
13483541000006111	2019-nCoV (novel coronavirus) immunisation course started
14169101000006118	COVID-19 mRNA vaccine
14170191000006111	SARS-CoV-2 antigen vaccine or SARS- CoV-2 mRNA vaccine
14170301000006118	Administration of first dose of SARS- CoV-2 mRNA vaccine
14170341000006116	First COVID-19 mRNA vaccination
14170411000006113	Administration of second dose of SARS- CoV-2 mRNA vaccine
14170431000006119	Second COVID-19 mRNA vaccination

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14233631000006113	Immunisation course to maintain protection against SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2
14233641000006115	Booster course to maintain protection against SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2)
14233671000006111	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) immunisation course completed
14233841000006119	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) protection maintenance course started
14233871000006110	SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) protection maintenance course completed
14233881000006113	Severe acute respiratory syndrome coronavirus 2 protection maintenance course done
14283421000006117	Administration of fourth dose of SARS- CoV-2 (severe acute respiratory syndrome coronavirus 2) vaccine
14283481000006118	Administration of fifth dose of SARS- CoV-2 (severe acute respiratory syndrome coronavirus 2) vaccine
14283541000006113	Administration of third dose of SARS- CoV-2 (severe acute respiratory syndrome coronavirus 2) vaccine

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Supplemental file 1, Table 3: Search Terms for NHS Highest Risk Definition

Note: this list reflects the report "Defining the highest-risk clinical subgroups upon community infection with SARS-CoV-2 when considering the use of neutralising monoclonal antibodies (nMABs) and antiviral drugs: independent advisory group report" version published on May 30, 2022.

Classification as defined by England's Deputy Chief Medical Officer	Concept as operationalized by Andersen et al	Search term
Down's syndrome and other genetic disorders	Down's syndrome or other chromosomal disorder known to affect immune competence	*down* *trisom* *mongol*
Solid cancer	We identified a code list "Clinical codelist – Cancer", which did not separate solid from liquid (blood) cancers. We systematically excluded blood cancers from the list by excluding the following terms, and had the resulting list reviewed by a clinician:	leuk Lymphoma lymphatic Lymphoid lymphosarc myeloma myeloid myeloscler myelofib myelosis myeloprol myelody walden anem anaem raeb nodular scler mycosis sezary zary hodgk heavy plasma marrow haemato hemota erythraem erythrem heilmeyer lymphadenopathy polycyt erythrocyt erythrodys thrombocyt

		franklin immunoprolif reticulosarc chloroma macroglob reticulosis kahler burkitt di guglielmo langer histiocytosis germinoblast letterer FAB Mastocytosis
Haematological diseases and recipients of haematological stem cell transplants	Amyloidosis	*amyloid*
	Graft Versus Host disease	*GVHD* *Graft V* *Graft-V* *reject* *trans* *fail* *trans*
	Myelodysplastic syndrome	*MDS* *myelod* *preleuk* *smouldering leuk*
	Chronic myelomonocytic leukaemia	*CMML* *chronic myelom*
	Sickle cell disease	*sickl* *SCD*
	Myeloma	*myelom* *kahler*
	Myelofibrosis	*myelof* *PMF* *idiopath* *fibrosis* *myelod metaplasia*
	Rare inherited anemia	*anaem* *anem*
	Chronic lymphocytic leukaemia and Follicular lymphoma	*lymphoma* *NHL* * hodgk* *nodular scler* *mycosis fung* *sezary* *walden*
	Thalassaemia	*thalass* *cooley* *mediterr* *constant spring* *haemoglobin h*

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		hemoglobin h *hb h* *haemoglobin bart* *hemoglobin bart* *hb bart*
Renal disease	Systemic anti-cancer treatments: Davidson, J, Warren-Gash, C and Mcdonald, H (2021). Clinical codelist - CPRD Aurum - Immuosuppressive conditions. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00002234. Davidson, J, Warren-Gash, C, Mcdonald, H, Evans, D and Clay, S (2021). Clinical codelist - chronic kidney disease. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00002406. CKD, stage 4 or 5	*CKD* *renal* *disease* *renal* *failure* *renal* *insufficiency* *renal* *disorder* *kidney* *disease* *kidney* *disorder* *kidney* *failure* *eGFR* *estimated* *glomerular* *filtration* *rate* *disease* *renal* *failure* *renal* *insufficiency* *renal* *disorder* *renal* *disease* *kidney* *disorder* *kidney* *failure* *kidney*
Liver disease	Cirrhosis	*cirrhos*
Solid organ transplant recipients	Solid organ transplant	*transplant* '*organ* *recipient*' '*heart* *recipient*' '*lung* *recipient*' '*pancreas* *recipient*' '*kidney* *recipient*' '*intestine* *recipient*' '*gland* *recipient*' '*stomach* *recipient*' '*spleen* *recipient*' '*liver* *recipient*' '*bladder* *recipient*'
Immune-mediated	People who have received a B-cell depleting therapy in the last 12 months	Obinutuzumab Ocrelizumab

inflammatory disorders		Ofatumumab Rituximab
	People who have been treated with cyclophosphamide (IV or oral) in the 6 months prior	Cyclophosphamide
	People who are on biologics or small molecule JAK-inhibitors (except anti-CD20 depleting monoclonal antibodies) or who have received these therapies within the last 6 months	Abatacept Adalimumab Baracitinib Belimumab Certolizumab pegol Etanercept Golimumab Infliximab Ixekizumab Sarilumab Secukinumab Tocilizumab Tofacitinib Upadacitinib Ustekinumab Vedolizumab
	People who are on corticosteroids (equivalent to greater than 10mg per day of prednisolone) for at least the 28 days prior	Betamethasone Cortisone Dexamethasone Hydrocortisone Methylprednisolone Prednisolone Prednisone Triamcinolone
	People who are on current treatment with: methotrexate (for interstitial lung disease) and/or ciclosporin	Mycophenolate Tacrolimus, oral Azathioprine with mercaptopurine Methotrexate Ciclosporin
	Giant cell arteritis	*giant cell arterit*
	Sarcoidosis	*sarcoid* *Besnier*
	Psoriatic arthritis or psoriasis	*arthr* *psoria*
	Autoimmune hepatitis	*autoimmune hep* *hepatitis auto* *AIH* *lupoid hep* *autoimmune chron* *autoimmune act* *autoimmune agg*
	Crohn’s disease	*crohn* *regional ent* *granulomatous ent* *ileocoli* *Jejunoileitis*

	granulomatous col
Type I diabetes	*type 1 dia*
	type I dia
	diabetes mellitus juv
	*diabetes mellitus *insulin dep*
	juvenile onset dia
	juvenile-onset dia
	*juvenile-onset
	diabetes mellitus type 1
	diabetes mellitus type I
	diabetes type 1
	diabetes type I
Ankylosing spondylitis	*ankylosing*
	Bekhterev
	Rheumatoid arthritis of spine
	spine rheum
	rheumatoid arthritis of
	rheumatoid *spine*
Rheumatoid arthritis	*rheumatoid*
	felty
	caplan
	rheum.
	atrophic art
	chronic rheumatic art
	prolif *art*
Systemic lupus erythematosus	*lupus*
Scleroderma	*scleroderma*
	systemic sclero
	crest s
	morphea
	morphoea
Ulcerative colitis	*ulcerative* *colitis*
	ulcerative *proctitis*
	rectosigmoiditis
	inflam *polyps*
	left *colitis*
	ulcerative *panc*
	extensive *colitis*
	proctosigmoiditis
	backwash *ileitis*
	distal *colitis*
	inflam *bowel*
Immunodeficiencies	*cvid*

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Immune deficiencies		*common* *immunodeficienc* *antibody* *deficienc* Hyper* *igm* *higm* *good* *syndrom* *thymom* *deficienc* *severe* *combin* *immunodeficienc* *SCID* *aps-1* *pas-2* * polygland* *autoimmune* *autoimmune* *polygland* *polyendocrinopath* *ectodermal dystroph* *apeced* *ifn* *signal* *interferon* *signal* *gammaglobulinaemi*
HIV/AIDS	HIV	*HIV* *immunodeficiency vir*
Rare neurological and severe complex life-limiting neurodisability conditions	Multiple sclerosis	*Multiple sclerosis* *sclerosis multiple* *encephalomyelit* *disseminat* * ms*
	Motor neurone disease	*motor* *neurone* disease* *kennedy* *amyotrophic* *lateral **sclerosis* *ALS* *primary* *lateral* *sclerosis* *progressive* *bulbar* *palsy* *progressive* *spinal* muscular* *atrophy*
	Huntington's disease	*huntington* *huntington* *disease* *Huntington* *chorea*

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Myasthenia gravis	*myasthenia* *gravis*

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Supplemental file 1, Table 4: Search Terms for PANORAMIC Eligibility Criteria Definition

Inclusion criteria as in PANORAMIC protocol	Concept as operationalized by Andersen et al	Search term
Chronic respiratory disease (including chronic obstructive pulmonary disease (COPD), cystic fibrosis and asthma requiring at least daily use of preventative and/or reliever medication)	Davidson, J, Warren-Gash, C and Mcdonald, H (2021). Clinical codelist - CPRD Aurum - chronic respiratory disease. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00002214. We also included product codes for asthma medications, using all drugs classified by the British National Formulary under the following categories: Short-acting beta agonists (SABA) Short-acting muscarinic antagonists (SAMA) Inhaled corticosteroids (ICS) Long-acting beta agonists (LABA) Long-acting muscarinic antagonist (LAMA) Methylxanthine PDE-4 inhibitor	
Chronic heart or vascular disease	Atherosclerosis/Arteriosclerosis Stenosis	*athero*;*arterioscl*;*ASVD*;*obliter*;*endart* *steno* *aort*;*steno* *vasc*;*steno* *heart*;*steno* *card*;*strict* *aort*;*strict* *vasc*;*heart* *stict*;*card* *strict*;
	Cerebrovascular disease (not including stroke/TIA - included in PANORAMIC)	*cerebro* *disea*;*subarac* *haem*;*vasc* *demen*;*arterio* *demen*;*infar* *demen*
	Pulmonary embolism	*pul* *embo*;
	Systolic/diastolic dysfunction	*syst* *dys*;*dia* *dys*;*dys* *syst*
	Chronic arrythmias	*AFL*;*atria* *flut*;*arrhyth*;*dysrhy*
	Myocardial infarction	*myo* *infarc*;*heart* *att*;* AMI
	Hypertension	*hyperten*;*high* *blood**pres*;* bp*;bp*;*bp*HBP*;*HTN*
	Venous thromboembolism/DVT	*VTE*;*thrombo*;*DVT*;*blood* clot*;*pulmon* *embolis*;* pe *;pe*;*pe;
	Heart failure	*CCF*;*CHF*;*hear* *fail*;*card* *fail*;*
	Atrial fibrillation	* fibrilla*;* fibrilla*;* af *;af*;*Afib*
	Ischaemic andperipheral heart disease	*hear* *diseas*; *artero* *diseas*; *vasc* *diseas*; *CAD*; *ihd*; *myocard* *isch*; *chd*
	Congenital heart/cardiac disease	*congen* *hear*;*congen* *card*;*CHD*
	Various	*Aneurysm* *May-Thurner* *Thoracic* *outlet* *Fibromuscular* *Klippel*

		lymphedema *hypoten* *Telangiect* *Vasculit* *body* *tumour* *Claudication* *Varicose* *Venous* *insufficiency* *artery* *dissection*
Renal disease: mild kidney disease (CKD) stage 2 and 3, with an eGFR measurement in the past 6 months	Renal disease, stage 2 or greater	*CKD* *renal* *disease* *renal* *failure* *renal* *insufficiency* *renal* *disorder* *kidney* *disease* *kidney* *disorder* *kidney* *failure* *eGFR* *estimated* *glomerular* *filtration* *rate* *disease* *renal* *failure* *renal* *insufficiency* *renal* *disorder* *renal* *disease* *kidney* *disorder* *kidney* *failure* *kidney*
Chronic liver disease	Chronic liver disease	'*biliary c*' '*destructive* *chol*' '*cirrhos*' '*sclero* *cholangit*' '*recurr* *cholangit*' '*chron* *cholangit*' '*chron* *hepat*' '*hepat* *chron*' '*acute* *yellow* *atroph*' '*hepat* *notif*' '*granul* *hepat*' '*alpha* *hepat*' '*hepat* *toxo*' '*toxop* *hepat*' '*acute hepatitis c*' '*alcoh* *hepat*' '*subacute* *hepat*' '*nonspec* *hepat*' '*nonalco* *liver* *dis*' '*hepat* *malaria*' '*malaria* *hepat*' '*autoimm* *hepat*' '*hepatitis c without*'

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		'*toxic* *hepat*' '*hepatitis C*' '*sequelae* *viral* *hep* '*chron* *liver* *dis*' '*oesoph* *varices*' '*varices* *oesoph*' '*hepat* *coma*' '**coma* *hepat*' '*enceph* *hepat*' 'hepat* *enceph*' '*sequelae* *liver*' '*liver* *sequelae*' '*portal* *hyperten*' '*hepatoren* *syndro*' '*syndro* *hepatoren*' '*eosophag* *varices*'
Chronic neurological disease (including dementia, stroke, epilepsy)	Davidson, J and Warren-Gash, C (2022). Clinical codelist - CPRD Aurum - chronic neurological disease. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00002817. PANORAMIC criteria details epilepsy and stroke as chronic neurological conditions which were not reflected in the existing code list, and were added using the following search terms	
	Epilepsy	*epilep*
	Stroke	*stroke* *stroke* *cerebr* *infarc* *cerebr* *acc* *CVA* *Tran* *ischemic*
Severe and profound learning disability	Severe and profound learning disability (including terms that 'definitely' indicate a learning disability)	*learning* *dis* *learning* *diff* *retard*
	Angelman syndrome	*angelman*
	Coffin-Lowry syndrome	*Coffin-lowry*
	Cornelia de lange syndrome	*cornelia* *lange*
	Cri du chat syndrome	*cri du chat* *5p Deletion* *cat* *cry*
	Dubowitz's syndrome	*dubowitz*
	Edward's syndrome	*edwards* *synd* *Trisomy* *18*
	Hurler's syndrome	*hurler* *mucopolysacc*
	Laurence-Moon Syndrome	*laurence-moon*
	Mowat-Wilson syndrome	*Mowat-Wilson*
	Patau syndrome	*Patau* *Trisomy* *13*

	Rett syndrome	*rett *
	Smith-Magenis syndrome	*Smith-Magenis* *Chromosome* *deletion*
	Wolff - Hirschorn syndrome	*wolf* *Hirs*
Down's syndrome	Down's syndrome	*down* *trisom* *mongol*
Diabetes mellitus (Type I or Type II)	Type I	*type 1 dia* *type I dia* *diabetes mellitus juv* *diabetes mellitus *insulin dep* *juvenile onset dia* *juvenile-onset dia* *juvenile-onset *diabetes mellitus type 1* *diabetes mellitus type I* *diabetes type 1* *diabetes type I*
	Type II	*type 2 dia* *type II dia* *adult onset dia* *adult-onset dia* *non-insulin dep* *noninsulin dep* *non-insulin-dep* *NIDDM* *T2D* *diabetes type 2* *diabetes mellitus type 2* *diabetes type II* *diabetes mellitus type II* type 2* type II* *diabetes mellitus adult*
Immunosuppression: primary (e.g., inherited immune disorders resulting from genetic mutations, usually present at birth and diagnosed in childhood) or secondary due to disease or treatment (e.g., sickle cell, HIV, cancer, chemotherapy)	Forbes, H (2020). Therapy Code List - Immunosuppression Aurum Therapy Codes. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00001589. We filtered among therapy codes for moderate immunosuppression for those drugs classified as chemotherapy.	

Solid organ, bone marrow and stem cell transplant recipients	Forbes, H (2020). Clinical Code List - Moderate Immunosuppression OPCS Codes. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00001587	
	Any transplant	*transplant*
	Solid organ transplant	*organ* *recipient* *heart* *recipient* *lung* *recipient* *pancreas* *recipient* *kidney* *recipient* *intestine* *recipient* *gland* *recipient* *stomach* *recipient* *spleen* *recipient* *liver* *recipient *bladder* *recipient
	Bone marrow transplant	*marrow* *graft* *graft* *marrow*
	Stem cell transplant	*stem* *transplant* *transplant* *stem* *stem* graft* *graft* *stem*
Morbid obesity (BMI > 35)		*obes* *BMI*
Severe mental illness	Severe mental illness, unspecified	*severe* *ment* *acute* *ment* *severe* *psy* *acute* *psy* *nervous break*
	Schizophrenia	*schiz* *psycot* *psychosis* * mania* mania* *manic*
	Bipolar disorder	*bipo*
	Self-harm	*self harm* *cutt* *self* *in* *self-i* *self-h*
	Obsessive-compulsive disorder	*OCD* *obsess*
	Eating disorder	*anor* *bulimia* *eating dis*
	Medicines for severe mental illness	Agomelatine Amoxapine Clomipramine hydrochloride Dosulepin hydrochloride Doxepin hydrochloride Imipramine hydrochloride

		Isocarboxazid Lofepramine hydrochloride Loxapine succinate Moclobemide Nefazodone hydrochloride Phenelzine sulfate Reboxetine mesilate Tranylcypromine sulfate Trazodone hydrochloride Trimipramine maleate Venlafaxine hydrochloride Vortioxetine hydrobromide
Community and care home resident		*nursing home* *home* *nursing* *care* *home* *home* *care* *residen* *care* *care* *resident*
Judged by recruiting medically qualified professional, research nurse, nurse prescriber, prescribing pharmacist, dependent on the ISA for the specific IMP involved, to be clinically vulnerable	Unable to define, given nature of secondary database research.	

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Supplemental file 1, Table 5: Search Terms for UK Health Security Agency Clinical Risk Group Definition

Classification as written in Green Book	Concept as written in Green Book	Search terms
Chronic respiratory disease – individuals with a severe lung condition	Poorly controlled asthma	Asthma with an oral corticosteroid use in the past 24 months
	Chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema	Davidson, J, Warren-Gash, C and Mcdonald, H (2021). Clinical codelist - CPRD Aurum - chronic respiratory disease. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00002214.
	Bronchiectasis	*bronchiec*
	Cystic fibrosis	Davidson, J, Warren-Gash, C and Mcdonald, H (2021). Clinical codelist - CPRD Aurum - chronic respiratory disease. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00002214.
	Interstitial lung fibrosis	*pulmon* *fibros* *lung* *fibros* *fibros* *lung* *ipf*
	Pneumoconiosis	*pneumocon* *asbestosis* *silicos*
	Bronchopulmonary dysplasia (BPD)	*broncho* *dysplas* *BDP*
Chronic heart disease and vascular disease	Congenital heart disease	*congen* *hear* *congen* *card* *CHD*
	Hypertension with cardiac complications	*hyperten* *high* *blood* *pres* * bp * *bp* *HBP* *HTN*
	Chronic heart failure	*CCF* *CHF* *hear* *fail* *card* *fail*
	Individuals requiring regular medication and/or follow-up for ischaemic heart disease (includes individuals with atrial	*hear* *diseas* *artero* *diseas* *vasc* *diseas* *CAD* *ihd*

	fibrillation, peripheral vascular disease or a history of venous thromboembolism)	*myocard* *isch* *chd* *fibrilla* *afib* *VTE* *thrombo* *DVT* *blood* *clot* *pulmon* *embolis* * pe *
Chronic kidney disease	At stage 3, 4 or 5 Chronic kidney failure	*CKD* *renal* *disease* *renal* *failure* *renal* *insufficiency* *renal* *disorder* *kidney* *disease* *kidney* *disorder* *kidney* *failure* *eGFR* *estimated* *glomerular* *filtration* *rate* *disease* *renal* *failure* *renal* *insufficiency* *renal* *disorder* *renal* *disease* *kidney* *disorder* *kidney* *failure* *kidney*
	Nephrotic syndrome	*nephro*
	Kidney transplantation	Davidson, J, Warren-Gash, C, Mcdonald, H, Evans, D and Clay, S (2021). Clinical codelist - chronic kidney disease. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00002406. We selected transplant-specific codes.
Chronic liver disease	Chronic hepatitis	*chron* *hepat*' *hepat* *chron*' *acute* *yellow* *atroph*' *hepat* *notif*' *granul* *hepat*' *alpha* *hepat*' *hepat* *toxo*' *toxop* *hepat*' *acute hepatitis c*' *alcoh* *hepat*' *subacute* *hepat*'

		nonspec *hepat*' *nonalco* *liver* *dis*' *hepat* *malaria*' *malaria* *hepat*' *autoimm* *hepat*' *hepatitis c without*' *toxic* *hepat*' *hepatitis C*' *sequelae* *viral* *hep* *chron* *liver* *dis*' *oesoph* *varices*' *varices* *oesoph*' *hepat* *coma*' **coma* *hepat*' *enceph* *hepat*' hepat* *enceph*' *sequelae* *liver*' *liver* *sequelae*' *portal* *hyperten*' *hepatoren* *syndro*' *syndro* *hepatoren*' *eosophag* *varices*'
	Cirrhosis	*cirrhos*'
	Biliary atresia	*biliary c*' *destructive* *chol*' *sclero* *cholangit*' *recurr* *cholangit*' *chron* *cholangit*'
Chronic neurological disease	Stroke	*stroke* *cerebr* *infarc* *cerebr* *acc* *CVA*
	Transient ischaemic attack (TIA)	*tran* *ischemic*
	Conditions in which respiratory function may be compromised due to neurological or neuromuscular disease (e.g. polio syndrome sufferers)	*polio* *infant* *parlay* *heine* *dis*
	Cerebral palsy	*cereb* *palsy* *cereb palsy* *cp*
	Severe or profound and multiple learning disabilities (PMLD) including all those on the learning disability register	*learning* *dis* *learning* *diff* *retard* *angelman* *Coffin-lowry* *cornelia* *lange*

		cri du chat
		5p Deletion
		cat *cry*
		dubowitz
		edwards *synd*
		Trisomy *18*
		hurler
		mucopolysacc
		laurence-moon
		Mowat-Wilson
		Patau
		Trisomy *13*
		*rett *
		Smith-Magenis
		Chromosome *deletion*
		wolf *Hirs*
	Down's syndrome	*down*
		trisomy
		mongol
	Multiple sclerosis	*multiple sclerosis*
		sclerosis multiple
		encephalomyelit *disseminat*
		ms
	Epilepsy	*epilep*
	Dementia	*demen*
		senil
	Parkinson's disease	*parkinson*
		hypo *rigid*
		parlay *agit*
		shak *pals*
		* pd *
	Motor neurone disease and related or similar conditions, hereditary and degenerative disease of the nervous system or muscles, severe neurological disability	*motor* *neurone* *disease*
		kennedy
		amyotrophic *lateral* *sclerosis*
		ALS
		primary *lateral* *sclerosis*
		progressive *bulbar* *palsy*
		progressive *spinal* *muscular* *atrophy*
		myo
Diabetes mellitus and other endocrine disorders	Type I	*type 1 dia*
		type I dia
		diabetes mellitus juv
		*diabetes mellitus
		insulin dep
		juvenile onset dia
		juvenile-onset dia
		*juvenile-onset
		diabetes mellitus type 1
		diabetes mellitus type I
		diabetes type 1

	Type II	*diabetes type I* *type 2 dia* *type II dia* *adult onset dia* *adult-onset dia* *non-insulin dep* *noninsulin dep* *non-insulin-dep* *NIDDM* *T2D* *diabetes type 2* *diabetes mellitus type 2* *diabetes type II* *diabetes mellitus type II* type 2* type II* *diabetes mellitus adult*
	Addison's disease	*Addison* *adren* *insuff* *hypocort* *hypoadren*
Immunosuppression due to disease or treatment	Patients undergoing chemotherapy leading to immunosuppression	Forbes, H (2020). Therapy Code List - Immunosuppression Aurum Therapy Codes. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00001589. We filtered among therapy codes for moderate immunosuppression for those drugs classified as chemotherapy.
	Patients undergoing radical radiotherapy	Davidson, J, Warren-Gash, C and Mcdonald, H (2021). Clinical codelist - CPRD Aurum - Immuosuppressive conditions. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00002234. We filtered for radiotherapy-specific codes.
	Solid organ transplant recipients	*transplant* *organ* *recipient*' *heart* *recipient*' *lung* *recipient*' *pancreas* *recipient*' *kidney* *recipient*' *intestine* *recipient*' *gland* *recipient*' *stomach* *recipient* *spleen* *recipient*' *liver* *recipient*'

		bladder *recipient*'
	Bone marrow or stem cell transplant recipients	LSHTM - Forbes, H (2020). Clinical Code List - Moderate Immunosuppression OPCS Codes. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom. https://doi.org/10.17037/DATA.00001587.
	HIV infection at all stages	*HIV* *immunodeficiency vir*
	Multiple myeloma or genetic disorders affecting the immune system (e.g. IRAK-4, NEMO, complement disorder, SCID)	*myelom* *kahler* *NEMO* *nuclear* *fact* *IKBKG* *mut* *NFKB* *complement* *SCID* *combin* *immune* *alympho* *glanz* *synd* *immunodef* *synd*
	Individuals who are receiving immunosuppressive or immunomodulating biological therapy including, but not limited to, anti-TNF, alemtuzumab, ofatumumab, rituximab, patients receiving protein kinase inhibitors or PARP inhibitors, and individuals treated with steroid sparing agents such as cyclophosphamide and mycophenolate mofetil	Adalimumab Etanercept Infliximab Golimumab Certolizumab pegol Abatacept Olaparib Rucaparib Niraparib Afatinib Axitinib Bosutinib Cetuximab Cobimetinib Crizotinib Cabozantinib Dacomitinib Dasatinib Entrectinib Erlotinib Fostamatinib Gefitinib Ibrutinib Imatinib Lapatinib Nilotinib Paxopanib Pegaptanib Ruxolitinib Sorafenib

		Sunitinib Vandetanib Vemurafenib
	Individuals treated with or likely to be treated with systemic steroids for more than a month at a dose equivalent to prednisolone at 20mg or more per day for adults	Betamethasone Cortisone Dexamethasone Hydrocortisone Methylprednisolone Prednisolone
	Anyone with a history of haematological malignancy, including leukaemia, lymphoma, and myeloma	*CMML* *chronic myelom* *lymph* *leuk* *CLL* *follic* *lymph* * fl *
	Those who require long term immunosuppressive treatment for conditions including but not limited to: systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, scleroderma, psoriasis	Using drugs listed above
Asplenia or dysfunction of the spleen. This includes conditions that may lead to splenic dysfunction	Asplenia	*asplen* *heterotax* *situs* *ambig*
	Homozygous sickle cell disease	*sickl* *SCD*
	Thalassemia major	*thal*
	Coeliac syndrome	*coelia* *celia* *sprue* *glut* *entero*
Morbid obesity (adults with a BMI >40kg/m$^{2)}$	Obesity with specification of BMI >40kgm^2	*obes* *BMI* Measured values using height and weight which calculate to >40 kgm/^{2}
Severe mental illness	Schizophrenia	*schiz* *psycot* *psychosis* * mania* mania* *manic*
	Bipolar disorder	*bipo* *severe* *ment*

	Any mental illness that causes severe functional impairment	*acute* *ment* *severe* *psy* *acute* *psy* *nervous break* *self harm* *cutt* *self* *in* *self-i* *self-h* *OCD* *obsess* *anor* *bulimia* *eating dis*
Pregnancy (all stages (first, second and third trimester))	Pregnancy	*pregnan* *trimest* *gestat*
	End of pregnancy	*birth* *deliver* *abortio*

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Supplemental file 1, Table 6: Cohort Attrition

	Unique person ID's
Persons of any age diagnosed with COVID from August 1, 2020 through January 31, 2022 using the May 2022 CPRD Aurum data release.	2,631,267
Files of "acceptable research quality", as defined by CPRD.	2,631,267
Continuously registered with CPRD GP practice for at least 365 days prior to COVID diagnosis, and did not have a registration end date, practice last collection date or death date prior to COVID diagnosis.	2,322,875
Hospital Episode Statistics (HES) Admitted Patient Care (APC) linkage eligible.	2,289,708
Once ONS data were received, 42 persons were noted that should have been excluded from the final cohort because ONS death data preceded index date.	2,289,666
Excluded persons who were admitted to the hospital on or before their primary care recorded date of COVID diagnosis. Due to mandatory GP reporting guidelines, this may be lagged from the date of true test collection and therefore not accurately reflect date of diagnosis.	2,271,072

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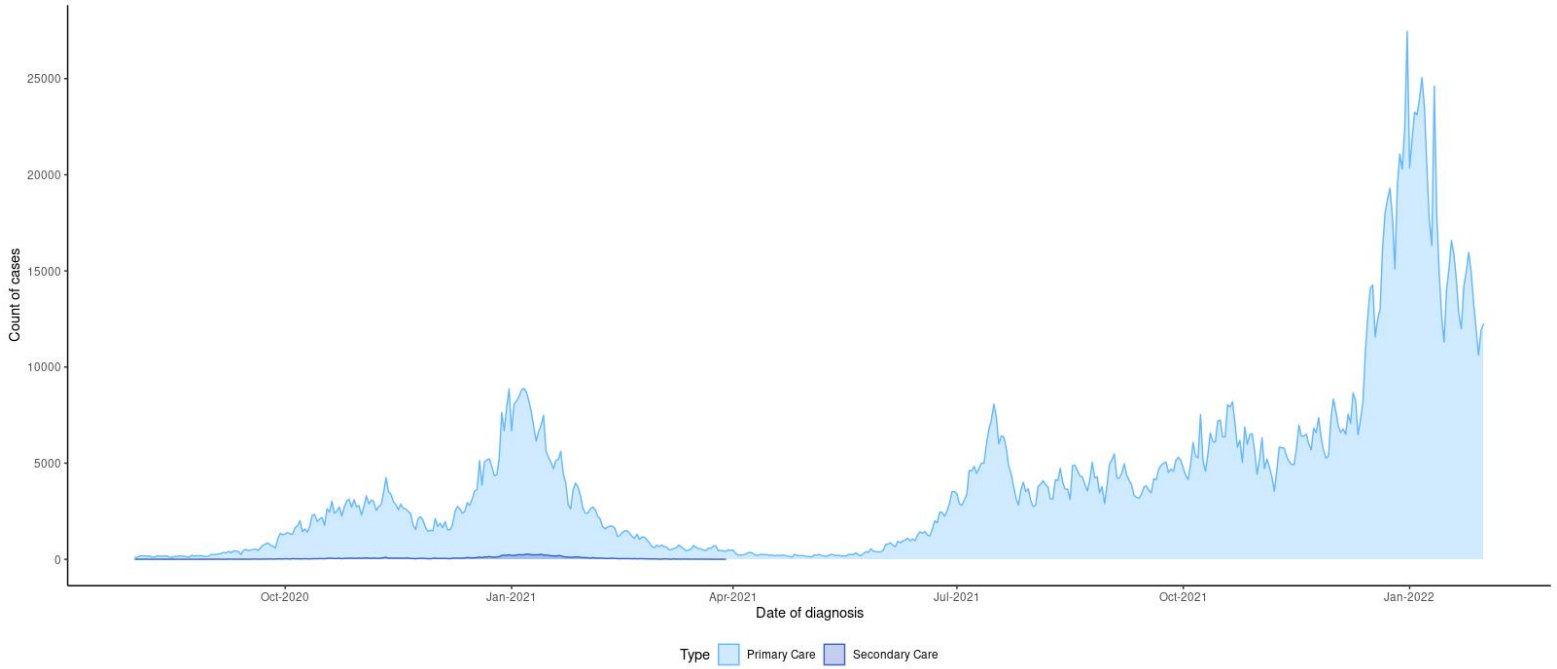
Supplemental file 1, Figure 1: Date of Diagnosis for 2,271,072 COVID Cases in CPRD Aurum, By Care Setting, August 1, 2020 through January 31, 2022



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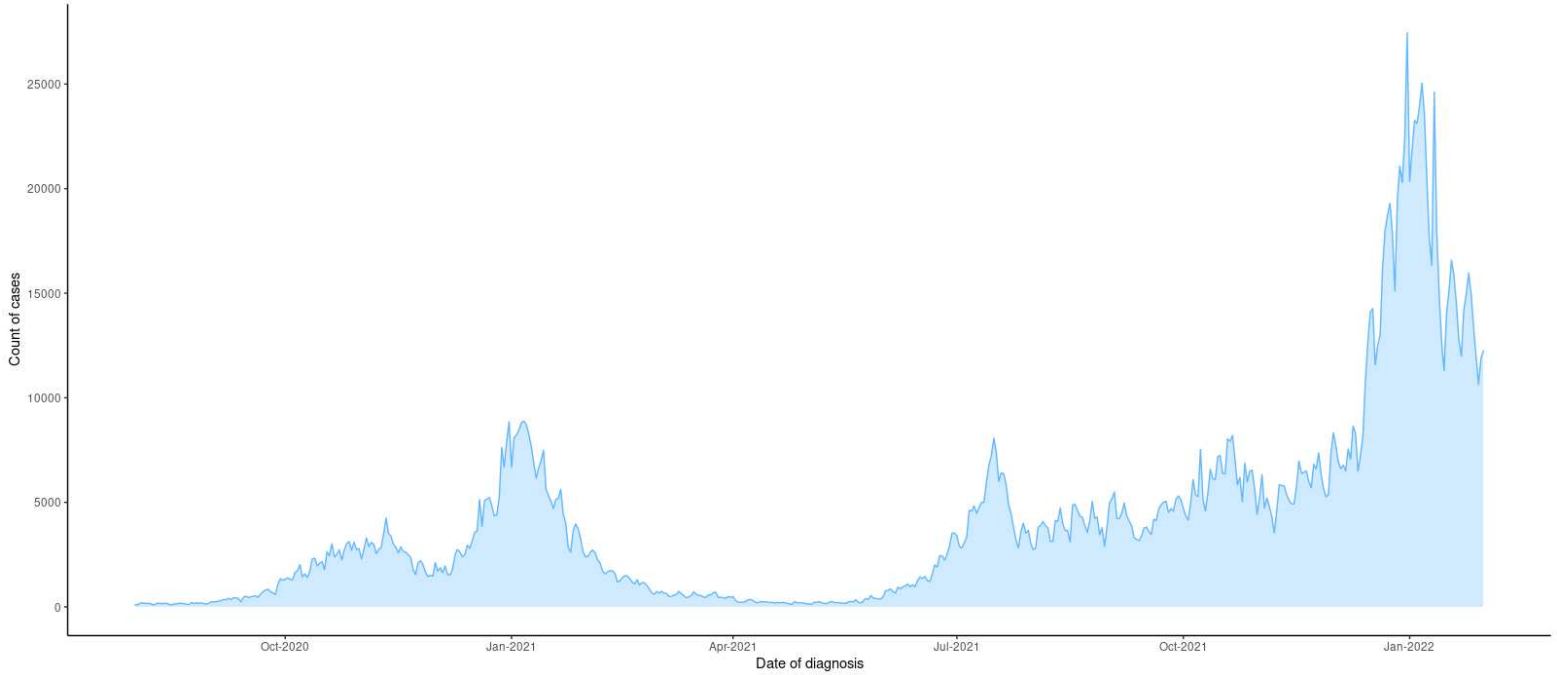
Supplemental file 1, Figure 2: Date of Diagnosis for 2,257,907 Primary Care COVID Cases in CPRD Aurum, August 1, 2020 through January 31, 2022



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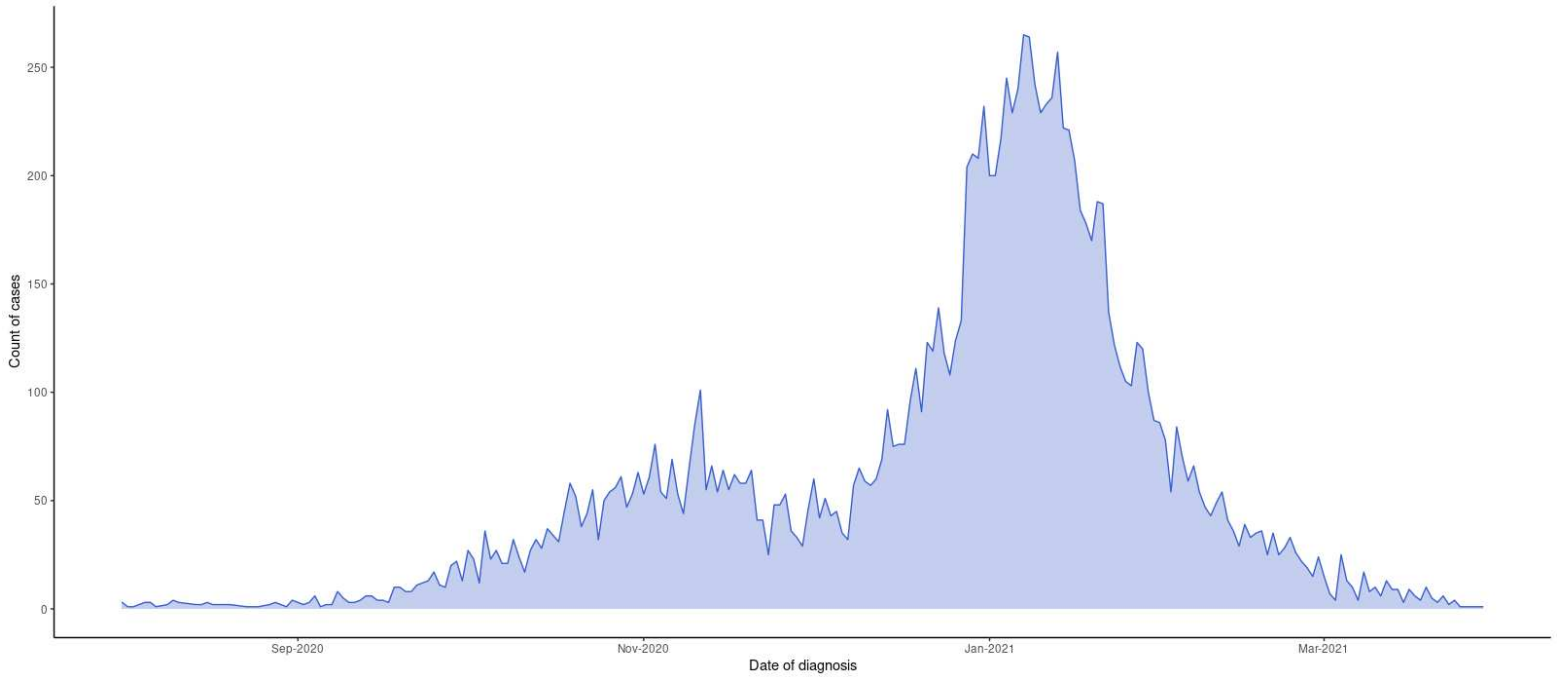
Supplemental file 1, Figure 3: Date of Primary Care Recorded Diagnosis in CPRD Aurum-HES Linked Data for 13,165 Hospitalised COVID Cases, August 1, 2020 through March 31, 2021



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Supplemental file 1, Table 7: Reference National Case Counts and Census Distributions for England

	All COVID Cases (n = 20,386,786)	COVID Admissions (n = 954,124)	Population of England (n = 56,489,800)
Age groups in years			
0-4	454,587 (2%)	--	3,077,000 (5%)
5-9	1,146,248 (6%)	--	3,348,600 (6%)
10-14	1,626,090 (8%)	--	3,413,100 (6%)
15-19	1,396,404 (7%)	--	3,218,900 (6%)
20-24	1,567,499 (8%)	--	3,414,400 (6%)
25-29	1,735,467 (9%)	--	3,715,400 (7%)
30-34	1,795,926 (9%)	--	3,952,600 (7%)
35-39	1,714,241 (8%)	--	3,795,400 (7%)
40-44	1,637,287 (8%)	--	3,580,400 (6%)
45-49	1,477,924 (7%)	--	3,602,600 (6%)
50-54	1,431,931 (7%)	--	3,907,700 (7%)
55-59	1,241,556 (6%)	--	3,806,300 (7%)
60-64	929,614 (5%)	--	3,256,100 (6%)
65-69	626,179 (3%)	--	2,767,500 (5%)
70-74	523,000 (3%)	--	2,796,600 (5%)
75-79	391,839 (2%)	--	2,038,800 (4%)
80-84	277,529 (1%)	--	1,427,900 (2%)
85-89	277,112 (1%)	--	872,200 (2%)
90+	192,353 (1%)	--	498,200 (< 1%)
0-5	--	20,400 (2%)	--
6-17	--	13,942 (1%)	--
18-64	--	335,675 (35%)	--
65-84	--	379,584 (40%)	--
85+	--	199,497 (21%)	--
Unknown	--	5,026 (1%)	--
Sex			
Male	9,245,295 (45%)	--	27,656,300 (49%)
Female	11,141,491 (55%)	--	28,833,500 (51%)
Region			
North East	948,543 (5%)	--	2,647,100 (5%)
North West	2,582,413 (13%)	--	7,417,300 (13%)
Yorkshire and The Humber	1,825,820 (9%)	--	5,480,800 (10%)
East Midlands	1,623,157 (8%)	--	4,880,200 (9%)
West Midlands	1,942,370 (10%)	--	5,950,800 (11%)
East of England	2,101,467 (10%)	--	6,334,500 (11%)
London	2,914,578 (14%)	--	8,799,800 (16%)
South East	3,125,838 (15%)	--	9,278,100 (16%)
South West	1,834,854 (9%)	--	5,701,200 (10%)
Unknown	1,487,746 (7%)	--	--

Note: coronavirus.data.gov.uk no longer publishes case counts by age, sex or region at the day level. It was not possible to limit to the study period of August 1, 2020 – January 31, 2022, and therefore the results

above reflect the figures as accessed on January 31, 2023 of the total number of cases since the start of the pandemic.

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PERSONS DIAGNOSED WITH COVID IN ENGLAND IN THE CPRD: A COHORT DESCRIPTION

Supplemental file 1, Table 8: Regional Distribution of CPRD COVID cohorts, CPRD Practices, COVID Cases and Population of England

	CPRD Aurum			England	
	Primary Care COVID Cases (n = 2,257,907)	Hospitalized COVID Cases (n = 13,165)	All CPRD Aurum Patients	All COVID Cases (n = 20,386,786)	Population (n = 56,489,800)
Region					
North East	4%	4%	5%	5%	5%
North West	21%	22%	17%	13%	13%
Yorkshire and The Humber	3%	3%	4%	9%	10%
East Midlands	2%)	2%	3%	8%	9%
West Midlands	17%	16%	18%	10%	11%
East of England	4%	3%	5%	10%	11%
London	19%	23%	16%	14%	16%
South East	20%	20%	20%	15%	16%
South West	10%	8%	14%	9%	10%
Unknown	< 1%	0		7%	--

All CPRD Aurum patients refers figures published in “Data resource profile: Clinical Practice Research Datalink (CPRD) Aurum” by Wolf et al (International Journal of Epidemiology 2019). We were unable to find more recent distributions by ONS region of all CPRD Aurum patients.

For all COVID cases, coronavirus.data.gov.uk no longer publishes case counts by region at the day level. It was not possible to limit to the study period of August 1, 2020 – January 31, 2022, and therefore the results above reflect the figures as accessed on January 31, 2023 of the total number of cases since the start of the pandemic.

For the population of England, we used ONS 2021 Census figures.

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PERSONS DIAGNOSED WITH COVID IN ENGLAND IN THE CPRD: A COHORT DESCRIPTION

Supplemental file 1, Table 9: Characteristics of Primary Care COVID Cases in CPRD Aurum, by High Risk Definitions

	All (n = 2,257,907)	Meeting NHS Highest Risk Conditions (n = 249,972)	Meeting PANORAMIC Criteria (n = 691,593)	Meeting UKHSA Clinical Risk (n = 225,051)
Cases meeting definition	--	11%	31%	10%
Age, mean (SD)	34 (19)	53 (18)	55 (15)	49 (21)
Sex				
Male	1,046,275 (46%)	37%	45%	42%
Female	1,211,592 (54%)	63%	55%	58%
Unknown	40 (< 1%)	< 1%	< 1%	< 1%
General Practitioner Practice Region				
North East	83,834 (4%)	12,776 (5%)	29,115 (4%)	9,678 (4%)
North West	471,195 (21%)	60,632 (23%)	157,317 (23%)	53,930 (24%)
Yorkshire and The Humber	71,429 (3%)	8,563 (3%)	23,079 (3%)	7,532 (3%)
East Midlands	49,651 (2%)	5,472 (2%)	14,001 (2%)	4,678 (2%)
West Midlands	377,125 (17%)	43,550 (17%)	118,027 (17%)	38,817 (17%)
East of England	95,139 (4%)	10,394 (4%)	28,546 (4%)	7,824 (3%)
London	424,908 (19%)	45,690 (18%)	118,663 (17%)	40,268 (18%)
South East	448,536 (20%)	45,430 (17%)	130,283 (19%)	38,808 (17%)
South West	235,785 (10%)	27,437 (11%)	72,473 (10%)	23,480 (10%)
Unknown	305 (< 1%)	28 (< 1%)	89 (< 1%)	36 (< 1%)
Non-immunocompromised	2,193,241 (100%)	218,912 (100%)	648,474 (100%)	196,621 (100%)
Unvaccinated	1,170,509 (53%)	82,484 (38%)	236,106 (36%)	96,498 (49%)
1 COVID vaccine dose	173,853 (8%)	9,527 (4%)	28,711 (5%)	12,469 (6%)
2 COVID vaccine doses	598,367 (27%)	73,907 (34%)	234,570 (36%)	54,869 (28%)
First booster	250,512 (12%)	52,994 (24%)	149,087 (23%)	32,785 (17%)
Immunocompromised	64,666 (100%)	41,060 (100%)	43,119 (100%)	28,430 (100%)
Unvaccinated	1,306 (2%)	832 (2%)	791 (2%)	675 (2%)
1 COVID vaccine dose	6,033 (9%)	3,556 (9%)	3,105 (7%)	2,661 (9%)
2 COVID vaccine doses	33,953 (53%)	20,928 (51%)	21,636 (50%)	14,416 (51%)
3 COVID vaccine doses	23,108 (36%)	15,544 (38%)	17,388 (40%)	10,542 (37%)
First booster	266 (< 1%)	200 (< 1%)	199 (< 1%)	136 (< 1%)

SD: standard deviation. Where necessary, to fulfill CPRD suppression rules of cells with 10 or fewer persons, categories are presented as percentages to prevent back-calculation.

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PERSONS DIAGNOSED WITH COVID IN ENGLAND IN THE CPRD: A COHORT DESCRIPTION

Supplemental file 1, Table 10: Characteristics of Hospitalized COVID Cases in CPRD Aurum-HES Linked Data, by High Risk Definitions

	All (n = 13,165)	Meeting NHS Highest Risk Conditions (n = 4,333)	Meeting PANORAMIC Criteria (n = 11,011)	Meeting UKHSA Clinical Risk (n = 5,353)
Hospitalized cases meeting definition	--	33%	84%	41%
Age, mean (SD)	60 (16)	66 (14)	65 (14)	66 (16)
Sex				
Male	7,537 (57%)	2,242 (52%)	6,280 (57%)	2,804 (52%)
Female	5,628 (43%)	2,091 (48%)	4,731 (43%)	2,549 (48%)
Unknown	0	0	0	0
General Practitioner Practice Region				
North East	467 (4%)	172 (4%)	397 (4%)	200 (4%)
North West	2,886 (22%)	962 (22%)	2,510 (23%)	1,263 (24%)
Yorkshire and The Humber	340 (3%)	126 (3%)	282 (3%)	156 (3%)
East Midlands	214 (2%)	73 (2%)	182 (2%)	97 (2%)
West Midlands	2,065 (16%)	708 (16%)	1,739 (16%)	891 (17%)
East of England	414 (3%)	147 (3%)	358 (3%)	175 (3%)
London	2,984 (23%)	943 (22%)	2,387 (22%)	1,105 (21%)
South East	2,682 (20%)	832 (19%)	2,235 (20%)	1,022 (19%)
South West	1,113 (8%)	370 (9%)	921 (8%)	444 (8%)
Unknown	0	0	0	0
Non-immunocompromised	12,984	4,179	10,832	5,208
Unvaccinated	12,744 (98%)	4,107 (98%)	10,602 (98%)	5,070 (97%)
1 COVID vaccine dose	240 (2%)	72 (2%)	230 (2%)	138 (3%)
2 COVID vaccine doses	0	0	0	0
First booster	0	0	0	0
Immunocompromised	181	154	179	145
Unvaccinated	102 (56%)	89 (58%)	100 (56%)	79 (54%)
1 COVID vaccine dose	79 (44%)	65 (42%)	79 (44%)	66 (46%)
2 COVID vaccine doses	0	0	0	0
3 COVID vaccine doses	0	0	0	0
First booster	0	0	0	0

SD: standard deviation.