

The prevalence of long COVID in people with diabetes mellitus—evidence from a UK cohort

Adrian H. Heald,^{a,b,*} Richard Williams,^{c,d} David A. Jenkins,^{c,d} Stuart Stewart,^{e,i} Nawar Diar Bakerly,^{c,f,h} Kevin Mccay,^g and William Ollier^g

^aThe School of Medicine and Manchester Academic Health Sciences Centre, The University of Manchester, Manchester, UK

^bDepartment of Diabetes and Endocrinology, Salford Royal Hospital, Salford, UK

^cDivision of Informatics, Imaging and Data Science, Faculty of Biology, Medicine and Health, University of Manchester, Manchester Academic Health Science Centre, Manchester, UK

^dNIHR Applied Research Collaboration Greater Manchester, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

^eCentre for Primary Care & Health Services Research, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

^fDepartment of Respiratory Medicine, Salford Royal Hospital, Salford, UK

^gFaculty of Science and Engineering, Manchester Metropolitan University, Manchester, UK

^hSchool of Biological Sciences, Manchester Metropolitan University, Manchester, UK

ⁱDonal O'Donoghue Renal Research Centre, Northern Care Alliance Research & Innovation, Salford Royal NHS Foundation Trust, Salford, UK

Summary

Background It was apparent from the early phase of the SARS-CoV-2 virus (COVID-19) pandemic that a multi-system syndrome can develop in the weeks following a COVID-19 infection, now referred to as Long COVID. Given that people living with diabetes are at increased risk of hospital admission/poor outcomes following COVID-19 infection we hypothesised that they may also be more susceptible to developing Long COVID. We describe here the prevalence of Long COVID in people living with diabetes when compared to matched controls in a Northwest UK population.

Methods This was a retrospective cohort study of people who had a recorded diagnosis of type 1 diabetes (T1D) or type 2 diabetes (T2D) who were alive on 1st January 2020 and who had a proven COVID-19 infection. We used electronic health record data from the Greater Manchester Care Record collected from 1st January 2020 to 16th September 2023, we determined the prevalence of Long COVID in people with T1D and T2D vs matched individuals without diabetes (non-DM).

Findings There were 3087 T1D individuals with 14,077 non-diabetes controls and 3087 T2D individuals with 14,077 non-diabetes controls and 29,700 T2D individuals vs 119,951 controls. For T1D, there was a lower proportion of Long COVID diagnosis and/or referral to a Long COVID service at 0.33% vs 0.48% for matched controls. The prevalence of Long COVID in T2D individuals was 0.53% vs 1:3 matched controls 0.54%. For T2D, there were differences by sex in the prevalence of Long COVID in comparison with 1:3 matched controls. For Long COVID between males with T2D and their matched controls, the prevalence was lower in matched controls at 0.46% vs 0.54% (0.008). When considering the prevalence of LC between females with T2D and their matched controls, the prevalence was higher in matched controls at 0.61% vs 0.53% (0.007). The prevalence of Long COVID in males with T2D vs females was not different. T2D patients at older vs younger age were at reduced risk of developing Long COVID (OR 0.994 [95% CI] [0.989, 0.999]). For females there was a minor increase of risk (OR 1.179, 95% CI [1.002, 1.387]). Presence of a higher body mass index (BMI) was also associated an increased risk of developing Long COVID (OR 1.013, 95% CI [1.001, 1.026]). The estimated general population prevalence of Long COVID based on general practice coding (not self-reported) of this diagnosis was 0.5% of people with a prior acute COVID-19 diagnosis.

Interpretation Recorded Long COVID was more prevalent in men with T2D than in matched non-T2D controls with the opposite seen for T2D women, with recorded Long COVID rates being similar for T2D men and women. Younger age, female sex and higher BMI were all associated with a greater likelihood of developing Long COVID when taken as individual variables. There remains an imperative for continuing awareness of Long COVID as a differential diagnosis for multi-system symptomatic presentation in the context of a previous acute COVID-19 infection.

*Corresponding author. The School of Medicine and Manchester Academic Health Sciences Centre, The University of Manchester, Manchester, UK.
E-mail address: adrian.heald@nca.nhs.uk (A.H. Heald).



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Research in context

Evidence before this study

There is now a large body of literature concerning the phenomenology and natural history of Long COVID and an increasing understanding of predisposing factors. However less work has been done that relates to the prevalence of Long COVID at a population level and how the prevalence of Long COVID may vary according by specific underlying conditions.

Added value of this study

We here have approached this question in a UK population including people who are living with diabetes. The prevalence of Long COVID in males with T2D and vs females was not different in contrast to much higher rates in females for the population as a whole. The estimated general population prevalence of Long COVID based on general practice coding

(not self-reported) of this diagnosis was lower than studies using self report, at 0.5% of people with a prior acute COVID-19 diagnosis.

Implications of all the available evidence

The evidence so far suggest that younger age, female sex, mixed ethnicity and higher BMI were all associated with a greater likelihood of developing Long COVID. There remains an imperative for continuing awareness of Long COVID as a differential diagnosis for multi-system symptomatic presentation following acute COVID-19, in people with T2D as in the wider population. The similar rates of Long COVID in men and women with T2D are intriguing and suggest that diabetes reviews in both sexes should include a question about Long COVID symptoms in the short to intermediate term.

Introduction

Globally, the vast majority of people infected with the Severe Acute Respiratory Syndrome Related Coronavirus (SARS-Cov-2) (COVID-19) virus from early 2020 survived—the case fatality rate was reported in a global review as 1.3%,¹ although numbers do vary. A large body of evidence now exists in relation to the predictive factors regarding more adverse sequelae of an acute COVID-19 infection in individuals with a history of diabetes mellitus.^{2–6} It was apparent from the early phase of the pandemic that a multi-system syndrome can develop in the weeks after a COVID-19 infection.^{6,7} The generally agreed diagnostic term for this is now Long COVID.

Long COVID is characterised by fatigue, muscles weakness, malaise, breathlessness and concentration impairment/brain fog, among other less frequent symptoms such as excess perspiration, chest pain, sore throat, anxiety and headaches.⁸ At least 65 million people across the world are estimated to have Long COVID. Similarities with other viral-onset illnesses such as myalgic encephalomyelitis/chronic fatigue syndrome and postural orthostatic tachycardia syndrome have laid the groundwork for research in the field⁹ with mindfulness of diagnostic uncertainty.¹⁰

A significant proportion of the population in the United Kingdom (UK) and in many other parts of the world, were infected by COVID-19, many more than once. Those that survive fall into three groups—those

left with devastating and disabling consequences, those with Long COVID and the those who are completely unaffected. It is the second of these groups that we are examining here.

There is now a large body of literature concerning the phenomenology and natural history of Long COVID and an increasing understanding of predisposing factors.^{11,12} However less work has been done that relates to the prevalence of Long COVID at a population level and how the prevalence of Long COVID may vary by specific underlying conditions. A number of studies have examined this question. These have included discussion of the biological factors that may lead to Long COVID in people with diabetes^{13,14} and analysis of the consequences of Long COVID in relation to metabolic control.¹³

We here have approached this question in a UK population including people who are living with diabetes.

Greater Manchester UK has a city-wide database for Primary Health Care on a population of approximately 2.87 million¹⁵ This is called the Greater Manchester Care Record.¹⁶ Access to anonymised data from this resource for research purposes permitted an analysis to investigate the long term consequences of COVID infection.¹⁷ Both T1D and T2D are conditions associated with significant comorbidity as people go through their lives with these conditions. Many people with T1D and T2D experienced either severe acute COVID-19

infections and/or had to shield for much of 2020 and the first half of 2021. For these reasons it is relevant to explore the effects of COVID-19 in the longer term for these individuals. Here we have examined the prevalence of Long COVID in people with T2D and the related predisposing factors in a large population sample.

Our primary aim was to determine whether an underlying diagnosis of diabetes (type 1 diabetes (T1D) or type 2 diabetes (T2D) predisposed people to develop Long COVID following an acute COVID-19 infection and to determine the predisposing factors for Long COVID in people with diabetes compared with non-diabetes individuals. A further aim was to estimate the prevalence of Long COVID within the conurbation of Greater Manchester.

Methods

Study design and participants

This was a retrospective observational cohort study using data collected from 1st January 2020 to 16th September 2023. The primary outcome was a diagnosis of Long COVID following an acute COVID-19 infection.

Retrospective analyses of primary care electronic health record (EHR) data from the GMCR¹⁶ were undertaken. The GMCR pools EHR data for 2.85 million citizens across 433 general practices (99.67%) across the conurbation. Data were de-identified at source and were extracted from the GMCR according to eligibility criteria. Thus the base population is nearly everyone who resides in Greater Manchester. All primary care coded data including laboratory test results is available for analysis. The available data included everyone alive on 1 January 2020. The diagnoses of T1D and T2D were based on general practice coded diagnoses. The diagnosis of diabetes preceded the diagnosis of Long COVID. We did not include people with a diagnosis of diabetes post-acute COVID-19 infection. The data was validated and cleaned prior to analysis by RW (co-author).

This study follows reporting instructions from STROBE (Strengthening the Reporting of Observational studies in Epidemiology) guidelines.¹⁸

Study participants included all people who had a recorded diagnosis of T1D or T2D who were alive on 1 January 2020 and who had a proven COVID-19 infection, based on a recorded positive test noted in the electronic health record (EHR) based on accredited laboratory polymerase chain reaction (PCR) testing. Each individual with diabetes (T1D or T2D) was matched with 3 controls (1:3 matching)—that is 3 people who did not have a diagnosis of diabetes matched for age and sex who had also tested positive (both groups) within a 28-day period for a COVID-19 infection (Fig. 1). There were no children or adolescents (age <18 years) included in the sample. Women pregnant at the time of

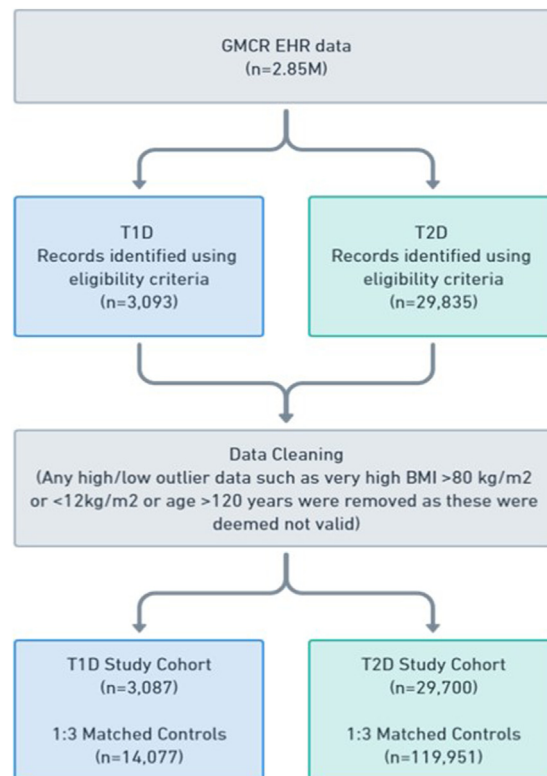


Fig. 1: Flow chart of analysis plan.

acute COVID-19 test positive were excluded. There was no upper limit to the age. The control group does not contain anyone coded as pre-diabetes = non-diabetic hyperglycaemia. The analysis was based on any COVID-19 positive result.

Patients were identified using a variety of diagnostic read codes for diabetes (SNOMED CT, CTV2, EMIS). The specific characteristics of Long COVID included weakness, general malaise, fatigue, concentration impairment and breathlessness plus reduced quality of life⁸ (please also see the [Appendix](#)).

Following data cleaning, the participants were split into 2 cohorts:

Those with T1D and their controls (approximately 1:3 matching as is standard for studies using GMCR data).

Those with T2D and their controls (approximately 1:3 matching as is standard for studies using GMCR data).

Outcome

Clinical code sets for Long COVID were created.^{19,20} The primary outcome was a diagnosis of Long COVID. Patients were considered to have Long COVID if they either had a Long COVID diagnosis code, or a Long COVID referral code. This is in-line with previous work on Long COVID in databases of routinely collected data

in the UK.¹⁹ A secondary outcome was to estimate the prevalence of Long COVID within the conurbation of Greater Manchester.

Statistics

A total of 3093 T1D individuals and 29,835 T2D individuals were identified according to the eligibility criteria. After data cleaning, 3087 T1D individuals and 29,700 T2D individuals were included in the final study. Any high/low outlier data were removed as these were deemed not valid.

Predictor variables included sex, age, ethnicity, body mass index (BMI), glycated haemoglobin (HbA1c) and socioeconomic status as measured using the Townsend Index.²¹ The 2001 census and NHS 5 groups were used to define ethnicity.²² BMI was included only if recorded within 6 months of the positive COVID-19 test. BMI measurements <12 kg/m² and >100 kg/m² were excluded as erroneous outliers.

Digital health records often contain missing data, particularly for diagnoses. We assumed that missing data for these variables meant that individuals were did not have a specific diagnosis. Therefore, a complete case analysis was conducted. Comparison between continuous and categorical variables was performed using multiple logistic regression. All analyses were undertaken in R (version 3.6.2) (R Foundation for Statistical Computing, Vienna, Austria). Data presented is mean ± standard deviation, unless stated otherwise. BMI was missing for many individuals in the matched cohorts in the time period examined, leading to 111,897 records being unused in the logistic regression due to missingness. Therefore, we performed matched logistic regression with demographic factors and BMI and without BMI. Glycosylated haemoglobin (HbA1c) and systolic blood pressure were included in the regression models. T1D and T2D individuals were analysed separately in relation to the logistic regression.

Ethics

The legal basis for use of patient data in this study was defined in the national Control of Patient Information (COPI) notice (Notice under Regulation 3(4) of the Health Service Control of Patient Information Regulations of 2002) which gives NHS organisations a legal requirement to share data for the purposes of the COVID-19 response. The study was also reviewed and

approved by the Greater Manchester Care Record (GMCR) Expert Research Group (ERG) reference number R 2020 020. The data used in the analyses presented was obtained with the permission of the Greater Manchester Care Record Board and was fully anonymised prior to being made available to the investigators.

Role of funding source

The time of RW was supported by the NIHR Applied Research Collaboration Greater Manchester (NIHR200174) and the NIHR Manchester Biomedical Research Centre (NIHR203308).

Results

For T1D there was a lower rate of diagnosis and/or referral to a Long COVID service (Table 1) at 0.33% vs 0.48% for matched controls (p = 0.009). Mean age of the T1D individuals was 47 years. For T1D sub categorisation in relation to sex, BMI and other factors was not possible because of low overall cases. All T1D individuals were treated with insulin.

Mean age of the T2D individuals was 65 years. The prevalence of Long COVID In T2D individuals was 0.53% (matched controls 0.54%). 12% of T2D individuals were treated with insulin in addition to oral hypoglycaemic agents. For T2D individuals there was no difference in the prevalence of Long COVID in comparison with 1:3 matched controls (Table 2). Prevalence was based on diagnosis or referral to a Long COVID assessment clinic. The prevalence of Long COVID in males with T2D was 0.54% whereas the prevalence of Long COVID in females with T2D was 0.53% (p NS), showing no difference. When considering the prevalence of recorded Long COVID between males with T2D and their matched controls, the prevalence was lower in matched controls at 0.46%.vs 0.54% vs men without T2D (p = 0.008). When considering the prevalence of Long COVID between females with T2D and their matched controls, the prevalence was higher in matched controls at 0.61% vs 0.53% in women with T2D (p = 0.007).

Logistic regression including age, sex, Townsend index, ethnicity, a patient’s most recent BMI and whether a patient has T1D or T2D indicated that younger age, female sex, being of mixed ethnicity, and higher BMI were associated with a higher likelihood of a

	T1D	Controls
Total number of patients	3087 (100%)	14,077 (100%)
Mean age (95% Confidence Interval (CI)) in years	47.2 (44.7-49.7)	47.8 (46.8-48.8)
With long COVID diagnosis	<10	46 (0.33%)
With diagnosis and/or referral	10 (0.32%)	68 (0.48%)

Table 1: Type 1 diabetes (T1D).

	T2D	Controls
Total number of patients	29,700 (100%)	119,951 (100%)
Mean age 95% Confidence Interval (CI) in years	65 (63.9–66.1)	64.6 (64.0–65.2)
With Long COVID diagnosis	115 (0.39%)	446 (0.37%)
With Diagnosis and/or Referral	156 (0.53%)	647 (0.54%)
Sex		
Male	15,469 (52.5%)	57,938 (48.3%)
Male with Long COVID	83 (0.54%)	267 (0.46%)
Female	13,769 (47.4%)	62,013 (51.7%)
Female with Long COVID	73 (0.53%)	380 (0.61%)
BMI		
BMI ≥ 30	13,342 (44.9%)	18,617 (15.5%)
BMI ≥ 30 with Long COVID	77 (0.58%)	137 (0.74%)
BMI < 30	10,641 (35.8%)	36,229 (30.2%)
BMI < 30 with Long COVID	55 (0.52%)	211 (0.58%)
Unknown BMI	5717 (19.3%)	65,105 (54.3%)
Unknown BMI with Long COVID	24 (0.42%)	299 (0.46%)
Ethnicity		
White	20,892 (70.3%)	96,751 (80.7%)
White + Long COVID	117 (0.56%)	550 (0.57%)
Black	911 (3.07%)	1940 (1.62%)
Black + Long COVID	<10	<10
Asian	5171 (17.4%)	6898 (5.75%)
Asian + Long COVID	20 (0.39%)	41 (0.59%)
Mixed	278 (0.94%)	952 (0.79%)
Mixed + Long COVID	<10	<10
Other	1901 (6.4%)	10,284 (8.57%)
Other + Long COVID	<10	29 (0.28%)
Unknown	547 (1.84%)	3126 (2.61%)
Unknown + Long COVID	<10	13 (0.42%)

Long COVID % refers to the proportion within each category. For example, for men with T2D, the denominator is 15,469 and for T2D controls with BMI ≥ 30 the denominator is 18,617.

Table 2: Type 2 Diabetes (T2D) with subcategorisation.

recorded diagnosis of Long COVID (Table 3). We did not find any relation between glycaemic control as measured by HbA1c and likelihood of developing Long COVID.

We also performed a logistic regression with just the demographic factors (age, sex, Townsend index and ethnicity—that is with BMI excluded) and whether a patient had T1D or T2D (Table 4). Here in addition to

	OR	LCL	UCL	p-value
(Intercept)	0.006	0.003	0.010	0.000
Age	0.994	0.989	0.999	0.016
Sex: Female	1.179	1.002	1.387	0.047
Ethnicity: Asian	0.822	0.616	1.097	0.184
Ethnicity: Black	0.924	0.547	1.560	0.766
Ethnicity: Mixed	2.022	1.179	3.467	0.010
Ethnicity: Other	0.655	0.460	0.933	0.019
Ethnicity: Unknown	1.031	0.593	1.792	0.914
Townsend Score	0.999	0.977	1.021	0.928
Latest BMI Value	1.013	1.001	1.026	0.041
HasT1D	0.671	0.357	1.261	0.216
HasT2D	0.947	0.779	1.151	0.584

LCL = lower 95% Confidence Limit (CI); UCL = upper 95% Confidence Limit (CI).

Table 3: Logistic regression results.

	OR	LCL	UCL	p-value
(Intercept)	0.007	0.005	0.009	0.000
Age	0.994	0.991	0.998	0.003
Sex: Female	1.269	1.126	1.431	0.000
Ethnicity: Asian	0.719	0.574	0.901	0.004
Ethnicity: Black	0.658	0.415	1.043	0.075
Ethnicity: Mixed	1.590	1.046	2.418	0.030
Ethnicity: Other	0.488	0.368	0.647	0.000
Ethnicity: Unknown	0.882	0.612	1.271	0.502
Townsend index	1.013	0.996	1.029	0.136
Has T1D	0.584	0.321	1.061	0.077
Has T2D	1.206	1.030	1.412	0.020

LCL = lower 95% Confidence Limit (CI); UCL = upper 95% Confidence Limit (CI).

Table 4: Logistic regression results.

younger vs older age, sex, and mixed ethnicity, individuals with T2D had an increased risk of being diagnosed to have developed Long COVID. People of Asian or “other” ethnicity had a reduced risk of being diagnosed with Long COVID. This regression made use of all observations except for 938 individuals for whom data were missing for either age, sex, ethnicity or Townsend index.

Extrapolation to the Greater Manchester population data base using a figure of 0.5% prevalence of Long COVID, there are approximately 1,900,000 individuals over the age of 25, giving an estimate of 9950 people who have been clinically diagnosed in primary care with Long COVID or referred for specialist assessment across Greater Manchester.

Discussion

Recorded Long COVID was more prevalent in men with T2D than in matched non-T2D controls with the opposite seen for T2D women, with recorded Long COVID rates being similar for T2D men and women. Specifically, for T2D the prevalence of Long COVID was markedly lower in matched controls at 0.46% vs 0.54% vs men without T2D. When considering the prevalence of Long COVID between females with T2D and their matched controls, the prevalence was markedly higher in matched controls at 0.61% vs 0.53% in women with T2D.

Younger age, female sex, mixed ethnicity, and higher BMI were all associated with an increased likelihood of developing Long COVID, with the diagnosis of T2D a predisposing factor when BMI was not included in the regression model. This can be seen in the context of our previous findings in acute COVID-19 that the risk factors for adverse consequences following an acute COVID-19 infection—defined as hospital admission or death within 28 days for T1D and T2D individuals—were not materially different from the general population.^{2,4,23}

A diagnosis of Long COVID is subject to an acute COVID-19 infection being coded in the GP record and then a suspected diagnosis of Long COVID and/or referral for assessment/treatment being made. We accept that not everyone will have undergone a COVID-19 test in relation to acute symptomatic episode. However in the absence of a COVID-19 positive test we cannot include individuals in the analysis, in order to retain methodological rigour. We acknowledge the bidirectional association between acute COVID-19 infection, Long COVID and T2D.²⁴

Long COVID diagnosis is subject to significant variability as previously reported.¹⁰ We accept that there will likely be under reporting of a positive test for acute COVID-19, but there is arguably no reason to suspect that this would affect diabetes and non-diabetes individuals differentially. The predisposing factors seen here in relation to a presentation with symptoms of Long COVID sufficiently severe to result in a GP coded diagnosis, is similar to that seen across the UK, where younger women under the age of 55 years, many of whom are overweight are the largest group seen in assessment and treatment services.²⁵

In relation to ethnicity, we found that being of non-white ethnicity altered the likelihood of being diagnosed with Long COVID. The factors underlying this are complex and are not necessarily primarily related to biological pre-determining factors but likely also associate with an individual’s likelihood of making contact with health care professionals in primary care regarding their post-acute COVID-19 symptoms. This is influenced by prevailing cultural factors,²⁶ such as the likelihood of undergoing a COVID-19 test in the context of acute symptoms or of consulting a doctor with potential symptoms of Long COVID. However more work is required better to understand the underlying factors.

While we found no difference between the T2D and non-T2D individuals in relation to Long COVID diagnosis rate, there was a distinct dyscongruity in relation to

sex difference in Long COVID diagnosis between T2D and non-T2D individuals, in other words little difference in Long COVID prevalence rate between sexes. This may relate to the fact that both men and women with T2D attend their general practices regularly in the UK for monitoring of their condition and so are potentially more likely to report symptoms including those of Long COVID, with the potential to increase the likelihood of Long COVID being spotted. Conversely in the general population young to middle years women are more likely to attend their GP practices than their male counterparts, for reasons often related to women's health.

The estimate of 0.5% of the adult population with Long COVID is much lower than the 3.1% of the population in private households in the UK who were reported as experiencing self-reported Long COVID (symptoms continuing for more than four weeks after the first confirmed or suspected coronavirus (COVID-19) infection that were not explained by something else) as of 2 January 2023 according to the United Kingdom (UK) Office of National Statistics.²⁷ However, the data that was analysed in our study is based on general practice (GP) coded diagnoses—these are likely to be significantly lower than self-reported diagnoses as described by the UK Office of National Statistics. Furthermore, we have chosen to include only patients with a confirmed acute COVID-19 infection as per the recording of a COVID-19 positive test result in the health record.

The strengths of this study are that our data are comprehensive and cover all general practices in the conurbation of Greater Manchester, UK where we were able to access a high-resolution primary care dataset. Diabetes diagnostic codes are known to be accurate owing to financially incentivised care under the United Kingdom Department of Health Quality Outcomes Framework (QOF). Furthermore, we covered the whole COVID-19 pandemic period up to mid-September 2023.

With regards to limitations this analysis is based on coded GP diagnoses and as our previous work in this area^{2–4,23} is subject to an acute COVID-19 infection being coded in the GP record (in the UK GP practice did not undertake COVID-19 testing themselves) and then a suspected diagnosis of Long COVID being made. We did not include the small number of people with other forms of diabetes such as diabetes secondary to pancreatitis or maturity onset diabetes of the young (MODY). Other limitations are that we utilised data collected in primary care, only coded diagnoses were included (thus we were not able to describe the symptoms associated with the Long COVID presentation) and we applied complete case analysis only. We accept that there is a lot of missing BMI data on non-diabetes individuals. However this is the case for all studies that create a comparison group of non-diabetes individuals derived from the general population. There is no reason to suspect that those with a missing BMI were any more

or less healthy than those non diabetes individuals with aa recorded BMI.

A strength of the paper is that the population in Greater Manchester is highly diverse in terms of both socioeconomic mix and racial diversity. Furthermore Stockport which forms part of the Greater Manchester conurbation, is considered to be highly representative of the population of England as a whole.²⁸

We accept that symptoms of Long COVID can potentially occur in the absence of a previous positive COVID-19 test. However the nature of Long COVID as a polysymptomatic condition means that caution needs to be exercised in ascribing the symptoms to Long COVID in the absence of a confirmed positive test. A person was deemed to have Long COVID on the basis of a GP coded diagnosis or GP coded referral to a Long COVID assessment/treatment service. We adhered rigorously to these criteria to ensure consistency of methodology. We accept that this will have underestimated the potential total number of Long COVID cases.

It should also be stated that we accept that our study is limited to individuals who survived the first and any subsequent COVID-19 infections. Therefore we cannot exclude a degree of survivor bias regarding the predisposing risk factors as defined.

Long COVID services in England are based on an assessment and treatment model as outlined in a recent online publication.²⁹ These post-acute COVID services, provide access to specialist diagnosis, treatment and rehabilitation. This paper is of relevance the focus of these services.

Recorded Long COVID was more prevalent in men with T2D than in matched non-T2D controls with the opposite seen for T2D women, with recorded Long COVID rates being similar for T2D men and women. Younger age, female sex, mixed ethnicity and higher BMI were all associated with a greater likelihood of developing Long COVID. There remains an imperative for continuing awareness of Long COVID as a differential diagnosis for multi-system symptomatic presentation in the context of a past acute COVID-19 infection.

Contributors

Adrian H Heald: Led on the writing of the paper and inputted to all sections of the paper.

Richard Williams: Analysed the data and provided all the tables.

David A Jenkins: Supervised the analysis and inputted to all sections of the paper.

Stuart Stewart: Provided conceptual overview and inputted to all sections of the paper.

Nawar Diar Bakerly: Provided conceptual overview and inputted to all sections of the paper.

Kevin Mccay: Supported data visualisation and inputted to all sections of the paper.

William Ollier: Provided senior overview and inputted to all sections of the paper.

All authors had access to and verified the underlying data and read and approved the final version of the manuscript.

Data sharing statement

A derivative data set will be available on application to the corresponding author.

Declaration of interests

No author has any conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.eclinm.2024.102607>.

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