

Factors associated with general practitioner-led diagnosis of long COVID: an observational study using electronic general practice data from Victoria and New South Wales, Australia

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The known: Long COVID is a growing concern worldwide. Research outside Australia has identified demographic factors and pre-existing conditions as potential risk factors for long COVID.

The new: In an Australian population, patients who were female, aged 40–59 years or of high socio-economic status, and those who had a pre-existing mental health condition, respiratory condition, cancer or musculoskeletal condition, had an increased risk of general practitioner-led diagnosis of long COVID.

The implications: Identification of predisposing risk factors is essential to inform early intervention and management strategies for those at greatest risk of long COVID and to help alleviate the burden of long COVID on the health care system.

Despite Australia having recorded over 11.5 million confirmed coronavirus disease 2019 (COVID-19) cases, as of August 2023, research into the impact of long COVID (the emergence and persistence of longer term sequelae after COVID-19) is still challenged by definitional disparity and data limitations.¹ The unique pandemic context in Australia, where exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was mostly after vaccination and predominantly involved the Omicron variant, suggests that Australia may have a lower long COVID burden than other countries. However, the true frequency and factors associated with long COVID in Australia are poorly understood, which impedes the use of evidence-based interventions, management strategies and service planning.

A systematic review and meta-analysis of current international evidence indicated that factors associated with long COVID include demographic characteristics, pre-existing comorbidities and severity of the initial SARS-CoV-2 infection.² This analysis was largely based on studies conducted in European countries, predominantly involving hospitalised patients, and did not include any Australian studies. Yet, most individuals who are diagnosed with COVID-19 or experience post-acute symptoms do not require hospitalisation.³ Thus, general practice data are key to identifying factors associated with long COVID and increasing our understanding of long COVID in Australia.

In this study, we aimed to investigate whether sociodemographic factors and pre-existing comorbidities are associated with a general practitioner-led diagnosis of long COVID in general practice patients in Victoria and New South Wales, Australia.

Abstract

Objectives: To investigate associations between sociodemographic factors, pre-existing chronic comorbidities, and general practitioner-led diagnosis of long COVID.

Design, setting, patients: We conducted a retrospective observational case-control study using de-identified electronic general practice data, recorded between January 2020 and March 2023, from 869 general practice clinics across four primary health networks in Victoria and New South Wales.

Main outcome measures: Sociodemographic factors and pre-existing chronic comorbidities associated with general practitioner-led diagnosis of long COVID.

Results: A total of 1588 patients had a recorded general practitioner-led long COVID diagnosis. Females exhibited a higher likelihood of general practitioner-led long COVID diagnosis (adjusted odds ratio [aOR], 1.58; adjusted confidence interval [aCI], 1.35–1.85) compared with males. Patients aged 40–59 years had a higher likelihood of general practitioner-led long COVID diagnosis (aOR, 1.68; aCI, 1.40–2.03) compared with patients aged 20–39 years. The diagnosis was more likely in patients of high socio-economic status (aOR, 1.37; aCI, 1.05–1.79) compared with those of mid socio-economic status. Mental health conditions (aOR, 2.69; aCI, 2.25–3.21), respiratory conditions (aOR, 2.25; aCI, 1.85–2.75), cancer (aOR, 1.64; aCI, 1.15–2.33) and musculoskeletal conditions (aOR, 1.50; aCI, 1.20–1.88) were all significantly associated with general practitioner-led long COVID diagnosis.

Conclusions: Female sex, middle age, high socio-economic status and pre-existing comorbidities, including mental health conditions, respiratory conditions, cancer and musculoskeletal conditions, were associated with general practitioner-led long COVID diagnosis among general practice patients. These factors largely parallel the emerging international evidence on long COVID and highlight the patient characteristics that practitioners should be cognisant of when patients present with symptoms of long COVID.

Methods

We undertook a retrospective observational case-control study using de-identified electronic general practice data for the period March 2018 to March 2023, provided via Outcome Health's Population Level Analysis and Reporting (POLAR) platform.⁴ The de-identified dataset included clinical information (eg, diagnoses and comorbidities as SNOMED CT [Systematized Nomenclature of Medicine – Clinical Terms] codes,⁵ medications, pathology test results) and demographic information (eg, five-year age group, sex, state of residence, local government area).

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Study population

General practice clinics from four primary health networks (PHNs) — two in Victoria and two in New South Wales — were included in our dataset. For this study, we isolated a general practitioner-led long COVID diagnosis cohort by identifying all records within the dataset that had a long COVID diagnosis documented by a general practitioner; this was determined using SNOMED CT code 1119304009, “symptoms related to COVID-19 that persist for more than 12 weeks following onset”.^{5,6}

We formed a comparison cohort comprising all records for the period January 2020 to March 2023 that had no documented history of COVID-19 or general practitioner-led long COVID diagnosis. Records that had no documentation of COVID-19 but had documentation of COVID-19 antiviral medication (molnupiravir or nirmatrelvir/ritonavir) being prescribed were also excluded from this comparison cohort.

Chronic comorbidities were classified as binary variables; these included alcohol- and drug-related conditions, cancer, cardiovascular conditions, chronic kidney disease, dementia, diabetes, disability, mental health conditions, musculoskeletal conditions, and respiratory conditions. For the general practitioner-led long COVID diagnosis cohort, only chronic conditions recorded before the general practitioner-led long COVID diagnosis were included to ensure that only pre-existing comorbidities were captured. Socio-economic status was determined using the Index of Relative Socio-economic Advantage and Disadvantage (IRSAD)⁷ deciles, which encapsulate the socio-economic diversity of the Australian population, and categorised into five groups (low, low-mid, mid, mid-high, high). Each patient’s socio-economic status was then assessed by assigning them to one of these groups based on their respective local government area.

Statistical analysis

We summarised data for continuous variables as medians with interquartile ranges (IQRs), and categorical variables as counts and proportions. We used χ^2 tests to assess differences between the general practitioner-led long COVID diagnosis and comparison cohorts. We developed a univariate logistic regression model to identify independent factors potentially associated with a general practitioner-led diagnosis of long COVID. Candidate variables included sex, age group, socio-economic status, state of residence, and comorbidities. A mixed-effects multivariate logistic regression model was derived with covariates significant at the univariate level. In addition, state of residence (Victoria, NSW, other) was incorporated as a random effect variable in the model to account for variations in state lockdown measures. The likelihood ratio test was used to verify that there was enough variability between the states to favour a mixed-effects multivariate logistic regression over multivariate logistic regression without random effects. Univariate logistic regression yielded crude odds ratios (ORs) and mixed-effects multivariate logistic regression models yielded adjusted odds ratios (aORs), for the independent variables, along with 95% confidence intervals (CIs), and we used an alpha level of 0.05 to indicate significance.

To account for the increased risk of false positives due to multiple comparisons, we applied a Bonferroni correction to the alpha level, resulting in the adjusted significance level. A result was considered statistically significant if the *P* value was less than the Bonferroni-adjusted alpha level: $0.05 \div N$, where *N* is the number of hypotheses tested. In addition, we estimated the

adjusted confidence intervals (aCIs) using the following formula: $(1 - (0.05/N))$. All analyses were performed using Python 3.7 (Python Software Foundation) and Stata MP15.1 (StataCorp).

Ethics approval

Outcome Health received ethics approval from the Royal Australian College of General Practitioners (NREEC 17-008 POLAR GP data warehouse). The Macquarie University Human Research Ethics Committee Medical Sciences Committee granted approval for the project (Project ID: 6756). Reporting of this study followed the STROBE guidelines.

Results

A total of 869 general practice clinics were included in our dataset, which contained more than 7 million patient records. These covered about 60% of the Victorian population ($n = 4\,018\,396$) and 43% of the NSW population ($n = 3\,554\,096$), plus a small number of patients from other states and territories. We note that the dataset primarily consisted of patients in local government areas with a relatively high socio-economic status compared with the overall Australian population, resulting in a skew towards higher IRSAD scores.

Long COVID cohort characteristics

During the period January 2020 to March 2023, 1588 patients in the dataset had a general practitioner-led diagnosis of long COVID and 5065803 patients met the inclusion criteria for the comparison cohort. Among the general practitioner-led long COVID diagnosis cohort, 656 patients (41.3%) had a previously documented COVID-19 diagnosis. The first general practitioner-led diagnosis of long COVID in the dataset was on 26 July 2020; 74 patients (4.7%) were diagnosed with long COVID in 2021, 1309 patients (82.4%) were diagnosed in 2022, and 197 patients (12.4%) were diagnosed between January 2023 and March 2023. The median interval between a recorded COVID-19 diagnosis and a general practitioner-led long COVID diagnosis was 82 days (IQR, 32–160 days).

Demographic factors

The general practitioner-led long COVID diagnosis cohort had a higher proportion of females (1034; 65.1%) compared with the comparison cohort (2632155; 52.0%) (Box). The largest proportion of general practitioner-led long COVID diagnosis patients were in the age range 40–59 years (646; 40.7%), while the largest proportion of comparison cohort patients were in the age range 20–39 years (1656112; 32.7%). Both cohorts had a notable number of individuals from high socio-economic status backgrounds (1020 [64.2%] in the general practitioner-led long COVID diagnosis cohort, and 2978774 [58.8%] in the comparison cohort). A higher proportion of general practitioner-led long COVID diagnosis patients were from Victoria (988; 62.2%), while the comparison cohort was more evenly distributed between Victoria (2794692; 55.2%) and NSW (2209302; 43.6%).

Univariate analysis showed that females had an increased likelihood of general practitioner-led long COVID diagnosis compared with males (OR, 1.73; 95% CI, 1.56–1.91) (Box). Patients aged 40–59 years (OR, 1.88; 95% CI, 1.66–2.11) and 60–79 years (OR, 1.66; 95% CI, 1.45–1.91) had a higher likelihood of general practitioner-led long COVID diagnosis, while patients aged 0–19 years (OR, 0.25; 95% CI, 0.19–0.31) had a significantly lower likelihood of general practitioner-led long COVID diagnosis

Sociodemographic characteristics of general practice patients and their association with a general practitioner-led long COVID diagnosis

	General practitioner-led long COVID cohort (n = 1588)*	Comparison cohort (n = 5 065 803)	P	Crude OR (95% CI), univariate analysis	Adjusted OR (95% aCI), multivariate analysis
Sex					
Male	554 (34.9%)	2 433 648 (48.0%)	< 0.001	1.00 (Ref)	1.00 (Ref)
Female	1 034 (65.1%)	2 632 155 (52.0%)		1.73 (1.56–1.91)	1.58 (1.35–1.85)
Age (years)					
0–19	76 (4.8%)	1 137 796 (22.5%)	< 0.001	0.25 (0.19–0.31)	0.28 (0.20–0.41)
20–39	449 (28.3%)	1 656 112 (32.7%)		1.00 (Ref)	1.00 (Ref)
40–59	646 (40.7%)	1 269 472 (25.1%)		1.88 (1.66–2.11)	1.68 (1.40–2.03)
60–79	364 (22.9%)	805 777 (15.9%)		1.66 (1.45–1.91)	1.24 (0.98–1.57)
≥ 80	53 (3.3%)	196 646 (3.9%)		0.99 (0.74–1.32)	0.60 (0.38–0.96)
Socio-economic status					
Low	64 (4.0%)	273 318 (5.4%)	< 0.001	1.05 (0.79–1.40)	1.01 (0.66–1.58)
Low–mid	< 25	39 170 (0.8%)		1.14 (0.61–2.17)	0.87 (0.33–2.31)
Mid	173 (10.9%)	778 230 (15.4%)		1.00 (Ref)	1.00 (Ref)
Mid–high	287 (18.1%)	868 526 (17.1%)		1.48 (1.23–1.80)	1.21 (0.88–1.69)
High	1 020 (64.2%)	2 978 774 (58.8%)		1.54 (1.31–1.81)	1.37 (1.05–1.79)
Not specified	34 (2.1%)	127 785 (2.5%)		1.19 (0.83–1.73)	1.24 (0.71–2.18)
State or territory					
Victoria	988 (62.2%)	2 794 692 (55.2%)	< 0.001	1.33 (1.21–1.48)	–
New South Wales	583 (36.7%)	2 209 302 (43.6%)		1.00 (Ref)	–
Other	< 25	61 809 (1.2%)		1.04 (0.64–1.69)	–
Chronic condition					
Alcohol and drug related	< 25	26 989 (0.5%)	0.17	1.90 (1.16–3.11)	0.70 (0.33–1.50)
Cancer	81 (5.1%)	97 163 (1.9%)	< 0.001	2.75 (2.20–3.44)	1.64 (1.15–2.33)
Cardiovascular	281 (17.7%)	512 227 (10.1%)	< 0.001	1.91 (1.68–2.17)	1.06 (0.84–1.34)
Chronic kidney disease	< 25	13 682 (0.3%)	> 0.999	1.16 (0.48–2.81)	–
Dementia	< 25	14 690 (0.3%)	> 0.999	0.65 (0.21–2.02)	–
Diabetes (type 1 or 2)	103 (6.5%)	190 777 (3.8%)	< 0.001	1.77 (1.45–2.16)	1.05 (0.76–1.45)
Disability	33 (2.1%)	69 815 (1.4%)	0.02	1.51 (1.08–2.14)	1.21 (0.65–1.89)
Mental health	462 (29.1%)	465 301 (9.2%)	< 0.001	4.05 (3.64–4.52)	2.69 (2.25–3.21)
Musculoskeletal	283 (17.8%)	370 627 (7.3%)	< 0.001	2.75 (2.41–3.12)	1.50 (1.20–1.88)
Respiratory	317 (20.0%)	363 448 (7.2%)	< 0.001	3.22 (2.85–3.65)	2.25 (1.85–2.75)

aCI = adjusted confidence interval; CI = confidence interval; COVID = coronavirus disease; OR = odds ratio; Ref = reference group. * Due to ethics requirements, exact patient counts under 25 cannot be reported. ♦

(compared with patients aged 20–39 years) (Box). High socio-economic status (OR, 1.54; 95% CI, 1.31–1.81) and mid–high socio-economic status (OR, 1.48; 95% CI, 1.23–1.80) were both associated with a significantly higher likelihood of general practitioner-led long COVID diagnosis (compared with mid socio-economic status). Patients from Victoria also had an increased likelihood of general practitioner-led long COVID diagnosis compared with those from NSW (OR, 1.33; 95% CI, 1.21–1.48).

In the more conservative mixed-effects multivariate analysis, females again had a higher likelihood of general practitioner-led long COVID diagnosis compared with males (aOR, 1.58; 99% aCI, 1.35–1.85) (Box). Patients aged 40–59 years maintained a higher

likelihood of general practitioner-led long COVID diagnosis compared with individuals aged 20–39 (aOR, 1.68; 99% aCI, 1.40–2.03), while patients aged 0–19 years or ≥ 80 years had a lower likelihood of general practitioner-led long COVID diagnosis compared with patients aged 20–39 years). Those of high socio-economic status again had a higher likelihood of general practitioner-led long COVID diagnosis compared with those of mid socio-economic status (aOR, 1.37; 99% aCI, 1.05–1.79).

Pre-existing chronic comorbidities

Patients who received a general practitioner-led long COVID diagnosis were more likely to have pre-existing chronic

comorbidities (871; 54.8%) compared with the comparison cohort (1342461; 26.5%). Among the general practitioner-led long COVID diagnosis cohort, 435 patients (27.4%) had one pre-existing chronic comorbidity and 436 patients (27.5%) had multiple pre-existing chronic comorbidities. In the comparison cohort, 827988 patients (16.3%) had one pre-existing chronic comorbidity and 514473 patients (10.2%) had multiple pre-existing chronic comorbidities.

Mental health conditions were the most prevalent pre-existing chronic comorbidity in the general practitioner-led long COVID diagnosis cohort (462 patients; 29.1%), followed by respiratory conditions (317 patients; 20.0%) and musculoskeletal conditions (283 patients; 17.8%) (Box). In the comparison cohort, cardiovascular conditions were most prevalent (512227 patients; 10.1%), followed by mental health conditions (465301 patients; 9.2%) and musculoskeletal conditions (370627 patients; 7.3%).

The univariate analysis identified several pre-existing chronic comorbidities as possible risk factors for a general practitioner-led long COVID diagnosis, including mental health conditions (OR, 4.05; 95% CI, 3.64–4.52), respiratory conditions (OR, 3.22; 95% CI, 2.85–3.65), cancer (OR, 2.75; 95% CI, 2.20–3.44), musculoskeletal conditions (OR, 2.75; 95% CI, 2.41–3.12), cardiovascular conditions (OR, 1.91; 95% CI, 1.68–2.17), alcohol- and drug-related conditions (OR, 1.90; 95% CI, 1.16–3.11), diabetes (OR, 1.77; 95% CI, 1.45–2.16), and disability (OR, 1.51; 95% CI, 1.08–2.14). In the more conservative mixed-effects multivariate analysis, mental health conditions (aOR, 2.69; aCI, 2.25–3.21), respiratory conditions (aOR, 2.25; aCI, 1.85–2.75), cancer (aOR, 1.64; aCI, 1.15–2.33), and musculoskeletal conditions (aOR, 1.50; aCI, 1.20–1.88) remained statistically significant risk factors for a general practitioner-led long COVID diagnosis (Box).

Discussion

For general practice patients in Victoria and NSW, sociodemographic factors that we found to be associated with a general practitioner-led diagnosis of long COVID included being female, aged 40–59 years and of high socio-economic status. Victorians were also significantly more likely to have a documented general practitioner-led long COVID diagnosis than NSW patients. The pre-existing chronic comorbidities found to be most prominently associated with a general practitioner-led long COVID diagnosis were mental health conditions, cancer, respiratory conditions, and musculoskeletal conditions.

Understanding of long COVID and its associated risk factors is in its early stages. However, there is growing international evidence that risk factors associated with long COVID include female sex, middle age and pre-existing comorbidities, particularly mental health conditions (eg, anxiety, depression) and respiratory conditions (eg, asthma, chronic obstructive pulmonary disease).^{2,8–11} Our findings largely align with this emerging international evidence and closely parallel survey findings from the Victorian Department of Health, which identified female sex, age 40–49 years, chronic illness, and pre-existing anxiety or depression as factors that increase the risk of a long COVID diagnosis.¹² Similarly, survey findings from the Western Australian Department of Health identified female sex, age 50–69 years, and pre-existing conditions as key risk factors for long COVID.¹³ This congruency among study findings suggests that there is a substantial degree of universal commonality in the factors associated with a diagnosis of long COVID.

We observed an association between high socio-economic status and a general practitioner-led long COVID diagnosis, while others have reported low socio-economic status or patients with low education as being at greater risk of long COVID.^{9,14} This may be a result of study populations, with the majority of patients in our study classified as being of high socio-economic status. In addition, individuals with lower socio-economic status may encounter barriers when trying to access primary care,¹⁵ which could explain some of the observed differences.

Currently, there is no clear consensus on the number of individuals that will develop long COVID following an acute case of COVID-19. In a systematic review, a substantial range in prevalence estimates and an overall global pooled prevalence of 43% were reported.¹⁶ Australian estimates are on the conservative end of the spectrum, with the Australian Institute of Health and Welfare suggesting that between 5% and 10% of people who have had COVID-19 will develop long COVID.¹⁷ Even at the lower estimate, the burden of long COVID on the health system and economy will be significant. We echo calls from other researchers who have advocated the need to generate evidence from robust large scale quantitative studies, plus qualitative studies that capture the voices and experiences of patients and practitioners, to help establish health strategies and plan effective care.¹⁸ Furthermore, with the management of long COVID largely falling onto primary care, assessing the increasing burden of disease through large general practice datasets and providing rapidly updated evidence-based guidelines to primary care providers is essential.

A limitation of our study is that we relied on electronic general practice data to identify patients who had had COVID-19 and those who had received a long COVID diagnosis. Recording of acute COVID-19 is often contingent on patients reporting the infection and subsequent documentation by the general practitioner. We identified almost 49 000 records of prescriptions for antivirals that are used to treat COVID-19 without corresponding documentation of a confirmed COVID-19 infection, indicating the possibility of additional acute COVID-19 cases in the comparison cohort. For long COVID, there remain challenges to understanding how general practitioners attribute persistent symptoms to a long COVID diagnosis in the context of other sequelae (eg, postural orthostatic tachycardia syndrome) and when they subsequently record this. Further, the sensitivity and specificity of the SNOMED CT code 1119303003 for true long COVID are not well established. However, given that long COVID is a diagnosis of exclusion, and that a diagnosis cannot be confirmed by clinical investigations, we relied on the expertise of general practitioners diagnosing long COVID and the POLAR platform for coding long COVID. Based on prevalence estimates, we anticipated a far greater number of long COVID cases in our dataset, thus long COVID was almost certainly under-represented in our results. However, this is an international challenge as practitioners still encounter uncertainty in making and documenting a definitive long COVID diagnosis while evidence on the condition is still emerging. This challenge likely reflects the low occurrence of general practitioner-led diagnosis of long COVID in our study, thus emphasising that our study cannot be used to identify the prevalence of long COVID in patients presenting to Australian general practices. In addition, owing to the number of identified general practitioner-led long COVID diagnoses, we could only undertake analysis on categories of chronic conditions (eg, respiratory conditions as a group rather than asthma). Furthermore, we did not have data on severity of acute COVID-19, and documentation of COVID-19 vaccination status was too variable to be used because COVID-19

vaccines are available via several avenues. Thus, we were unable to assess whether associations between severity and vaccination and long COVID exist in general practice patients.

In conclusion, female sex, middle age, high socio-economic status and pre-existing comorbidities — including mental health conditions, respiratory conditions, cancer and musculoskeletal conditions — were found to be associated with a general practitioner-led long COVID diagnosis among general practice patients in Victoria and NSW. Identification of predisposing risk factors is essential to inform early intervention and management strategies for those at greatest risk of long COVID and to help alleviate the burden of long COVID on the health care system.

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