MEDICINEINSIGHT

Report

The impact of COVID-19 on hydroxychloroquine and azithromycin prescribing patterns in general practice.

August 2020

2020 National Prescribing Service Limited, trading as NPS MedicineWise

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EXECUTIVE SUMMARY

Hydroxychloroquine is the active ingredient in medicines that for many years have been used to help prevent and treat malaria and to treat certain autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematous (SLE). Access to hydroxychloroquine has proved challenging during the COVID-19 pandemic, following media reports that the drug was being explored in clinical trials as a potential treatment for COVID-19. These reports led to a rapid increase in demand and anecdotal reports of stockpiling of the drug which meant that some people who need the drug to manage their chronic disease had difficulty filling their scripts.

The purpose of this report is to use data from the MedicineInsight general practice program to describe prescribing patterns of hydroxychloroquine and potentially inappropriate prescribing and co-prescribing with azithromycin during the COVID-19 pandemic. The MedicineInsight program is uniquely placed to provide information about patient conditions and the extent of private prescribing.

The impact of COVID-19 on prescribing trends

Based on information from 471 general practices across Australia that participate in the MedicineInsight program and 3.47 million patients who consulted one of these general practices at least once during the study time period (1 March 2018 to 31 May 2020):

- The prescribing rate for hydroxychloroquine in March 2020 was almost double the average monthly prescribing rate during the 2-year pre-COVID period (1.36 scripts versus 0.72 scripts per 1,000 encounters; risk ratio 1.9; $p < 0.0001$).
- The private (non-PBS subsidised) prescribing rate, while small, increased 20-fold in March compared with the pre-COVID period (0.06 scripts versus 0.003 scripts per 1,000 encounters; $p < 0.0001$).
- The weekly prescribing rate for hydroxychloroquine peaked between 16 March and 12 April 2020.

Appropriateness of prescribing during COVID-19

Based on information from 471 general practices across Australia that participate in the MedicineInsight program and 1.88 million regularly attending patients with at least three consultations at one of these general practices during the study time period (1 March 2018 to 31 May 2020)[1] we identified 2,464 patients (0.13%) who had a prescription for hydroxychloroquine recorded during the COVID-19 period (1 March 2020 to 31 May 2020).

- Of 2,464 patients who were prescribed hydroxychloroquine during the COVID-19 period, 80% had been prescribed hydroxychloroquine prior to the COVID period and 20% were new to therapy.
- Only half of the 500 patients who were new to hydroxychloroquine therapy during the COVID-19 period had a relevant condition recorded in their medical history that might explain the use of hydroxychloroquine for non-COVID reasons (ie, rheumatoid arthritis, SLE, sarcoidosis, Sjögrens syndrome, juvenile arthritis or malaria).
- 76% of patients with evidence of prior hydroxychloroquine use had a relevant condition recorded in their medical history.
- Compared to patients who were prescribed hydroxychloroquine prior to COVID-19, those who were new to therapy were more likely to be male (33% vs 21%), younger (30% of new users were aged 20–49 years vs 18% of prior users), reside in major cities (66% vs 54%) and in areas in the most socioeconomically advantaged quintile (34% vs 20%).
- 33 (1.3%) of the patients who were prescribed hydroxychloroquine during the COVID period were prescribed azithromycin on the same day, with 24% having a recorded relevant indication for hydroxychloroquine.

[1] Patients were also required to have at least one consultation on or before 1 May 2019 to increase the chance that included patients were being managed at the MedicineInsight for a sufficient period before COVID-19 to enable the opportunity for their medical history and prior therapy with hydroxychloroquine to be recorded.

Impact of regulatory actions

- The proportion of patients with potentially inappropriate prescribing of hydroxychloroquine during COVID-19, defined as no prescriptions for hydroxychloroquine recorded prior to COVID-19 and no relevant condition indicated for hydroxychloroquine in the patient's medical record, was highest before the TGA restrictions were implemented on 24 March 2020 at 14.2% and reduced to 7.2% between 24 March 2020 and 30 April 2020 and 3.7% between 1 May and 31 May 2020, after the PBS listing change on 1 May 2020.

Conclusions

This report confirms that prescribing of hydroxychloroquine increased substantially in general practices across Australia from March, with prescribing rates peaking between 16 March and 12 April 2020. Most of the patients who were prescribed hydroxychloroquine during the COVID-19 period had previously been prescribed hydroxychloroquine, which indicates that most of the increase in prescribing was due to stockpiling. However, one-fifth of patients were new to therapy and only half of the new users had a relevant indication for therapy recorded in their medical history. Significant reductions in the amount of potentially inappropriate prescribing were observed after the regulatory actions taken by the TGA and the PBAC restrictions were implemented.

BACKGROUND

Hydroxychloroquine

Hydroxychloroquine is the active ingredient in medicines that for many years have been used to help prevent and treat malaria and to treat certain autoimmune diseases such as rheumatoid arthritis and SLE. Another similar medicine, called chloroquine, is also used overseas but is not marketed in Australia.[1]

Access to hydroxychloroquine has proved challenging during the COVID-19 pandemic, following media reports[2-4] that the drug is being explored in clinical trials as a potential treatment for COVID-19. These reports have led to a rapid increase in demand and anecdotal reports of stockpiling of the drug which have meant that some people who need the drug to manage their rheumatoid arthritis, lupus or other relevant conditions have had difficulty filling their scripts.[2,5]

Like all medicines, hydroxychloroquine and chloroquine come with a risk of adverse effects. These effects are well understood when the medicines are used to prevent or treat malaria and autoimmune conditions, because of the long-term experience in these settings[6].

However, these medicines can have serious adverse effects if used incorrectly, at the wrong dose, combined with certain other medicines, or taken by people with other health conditions. Taking more than 4–5 grams of hydroxychloroquine or chloroquine in one dose is associated with severe poisoning.[7] They also pose well-known serious risks to patients, including irreversible eye damage, cardiac toxicity (potentially leading to sudden heart attacks) and severe depletion of blood sugar (potentially leading to coma).[6]

Currently there is no evidence to support the use of hydroxychloroquine as a treatment for COVID-19 outside of the clinical trial setting.[8] Information about the use of the medicine for people with COVID-19 who are in hospital is very limited. Multiple clinical trials are now underway to investigate if there is a role for hydroxychloroquine to treat or prevent COVID-19.[6,9]

Given the limited evidence for effect against COVID-19, as well as the risk of significant adverse effects, the TGA strongly discourages the use of hydroxychloroquine outside of its current indications other than in a clinical trial setting or in a controlled environment in the treatment of severely ill patients in hospital.[10]

Use of this medicine for the prevention or treatment of COVID-19 outside of clinical trial research is off-label and not recommended. New legislation has been created to limit the prescription of hydroxychloroquine, so that supply is available only for people who need it to manage chronic health conditions not related to COVID-19. The TGA is working with the pharmaceutical industry to help ensure the supply of hydroxychloroquine is maintained for patients who need it to treat their chronic conditions.[10]

TABLE 1 BRANDS OF HYDROXYCHLOROQUINE CURRENTLY AVAILABLE IN AUSTRALIA

Brand	Company
Plaquenil	Sanofi Australia
APO -hydroxychloroquine	Apotex Pty Ltd
Hequinel Hydroxychloroquine AN	Arrow Pharma Pty Ltd (owns both brands)
Hydroxychloroquine GH	Generic Health
Rusquen	Ipca Pharma

Box 1: TGA Product Information for hydroxychloroquine

Indications:

- Rheumatoid arthritis;
- Mild systemic and discoid lupus erythematosus;
- Suppression and treatment of malaria

Contraindications:

- Children < 6 years
- Pre-existing maculopathy
- Known hypersensitivity to hydroxychloroquine/chloroquine
- Long-term therapy in children

Adverse effects:

- Cardiac toxicity including fatal cardiomyopathy
- Severe hypoglycaemia (low blood sugar) with loss of consciousness
- QT interval prolongation
- Blurred vision, irreversible retinal damage
- Skin reactions including rash/itch
- GI disturbances including nausea/vomiting/abdominal cramps/diarrhoea
- Muscle weakness
- Headache
- Alopecia
- Blood dyscrasias, monitoring required for long-term treatment.

Potential off-label but relevant indications for hydroxychloroquine

- Juvenile arthritis
- Sarcoidosis
- Sjögrens syndrome

TGA restrictions on hydroxychloroquine – effective from 24 March 2020

To limit use of hydroxychloroquine to currently approved indications, new restrictions were placed on which health professionals can initiate patients on it. Only certain types of specialists are able to prescribe hydroxychloroquine to new patients – dermatology; intensive care medicine; paediatrics and child health; physicians; and emergency medicine. General practitioners and other medical practitioners (eg, hospital resident medical officers (RMOS) and doctors in training) can continue to prescribe repeats for hydroxychloroquine to patients in line with the registered indications for patients for whom the medication was prescribed prior to 24 March 2020. From 24 March 2020, general practitioners and doctors in postgraduate training can only prescribe these medicines for continued treatment of patients where initial treatment has been authorised by a specialist.[11]

PBS restrictions for hydroxychloroquine

To reflect the changes made by the TGA to the current scheduling of hydroxychloroquine, the Department of Health has adjusted the current PBS listing from general unrestricted PBS benefit to Authority Required (STREAMLINED). As of 1 May 2020, the current general unrestricted benefits listing of hydroxychloroquine on the PBS is split into separate initial and continuing treatment listings for the TGA-approved indications of malaria or autoimmune disorders. Both initial and continuing PBS listings will be Authority Required (STREAMLINED). Under the initial PBS listing, initial therapy must be authorised by a medical practitioner of one of the specialities defined in the clinical criteria.[12]

Azithromycin

Some early studies[13,14] suggested that the combination of hydroxychloroquine and azithromycin may reduce viral burden and shorten the duration of COVID-19 illness. However, to date, the evidence for benefit is not yet established. The combination of hydroxychloroquine and azithromycin is associated with cardiotoxicity, including a newly prolonged QTc interval of over 500 milliseconds in 10%–20% of trial participants.[15,16]

MedicineInsight program

MedicineInsight is a leading large-scale primary care dataset of longitudinal de-identified electronic health records (EHR) in Australia.[17] MedicineInsight was initially established by NPS MedicineWise in 2011, with core funding from the Australian Government Department of Health, to collect general practice data to support quality improvement in Australian primary care and post-market surveillance of medicines. The monthly collation of collected data can be analysed for the purposes of improving patient care, quality improvement and evaluation, performing population health analysis, research and developing health policy.

MedicineInsight utilises third-party data extraction tools which extract, de-identifies, encrypts and securely transmits whole of practice data from the GP clinical information systems of over 700 general practices. Patient level data are de-identified ‘at source’ meaning the patients’ personal identifiers such as name, complete date of birth and address are not extracted by the tool (although year of birth and postcode are extracted, enabling the calculation of age and Socio-Economic Indexes for Areas [SEIFA]). The data held in the MedicineInsight database are non-identifiable. However, each patient has a unique identifying number which allows all the records (clinical, prescription, referral etc) held in the database to be linked to the associated patient identifying number.

Representativeness

As of 1 July 2019, there were 5,074 active GPs participating in the MedicineInsight program representing 14% of the national GP workforce. MedicineInsight has national coverage across all states and territories, and all remoteness areas. Practices in South Australia are underrepresented and practices in Tasmania overrepresented but otherwise the proportion of MedicineInsight practices in each state is similar to the proportion of all practices in each state or territory. Compared to MBS data, patients within MedicineInsight are representative of the Australian patient population in terms of age, gender and indigenous status.

Further information is available in the MedicineInsight Data Resource Profile[17], the General Practice Insights Report 2017-18 and online: https://www.nps.org.au/medicine-insight

Ethics approval

In December 2017, NPS MedicineWise was granted ethics approval for the standard operations and uses of the MedicineInsight database by NPS MedicineWise. This 'umbrella' approval was given by the RACGP NREEC (NREEC 17-017). On 10 June 2020 the Independent MedicineInsight Data Governance Committee approved the application for NPS MedicineWise to use MedicineInsight data

for this study on hydroxychloroquine prescribing patterns before and during COVID-19 (application number: 2020-015).

AIMS AND METHODS

Study aims

The purpose of this report is to describe prescribing patterns for hydroxychloroquine and co-prescribing with azithromycin in Australian general practice, with a focus on prescribing outside of guidelines to patients without a relevant indication for therapy. MedicineInsight is also uniquely placed to provide information about the extent of private prescribing.

Specific objectives

TABLE 1: SPECIFIC OBJECTIVES AND RESEARCH QUESTIONS ABOUT HYDROXYCHLOROQUINE

Objectives	Questions
To describe the prescribing patterns for hydroxychloroquine during COVID compared with the past 2 years	1. What was the weekly prescribing rate of hydroxychloroquine in terms of issued scripts per 1,000 clinical encounters between 1 March 2018 and 30 May 2020, overall and by PBS / private status?
	2. What was the average prescribing rate of hydroxychloroquine during March 2020 compared with the pre-COVID period (1 March 2018 to 29 February 2020) in terms of: - issued scripts per 1,000 clinical encounters, overall and by PBS / private status - quantity prescribed (pack size and repeats) overall and by PBS / private status?
To describe the potential level of inappropriate prescribing of hydroxychloroquine during COVID-19	1. What number and proportion of patients were prescribed hydroxychloroquine during COVID-19, stratified by whether they had a relevant indication recorded, whether they had previously used hydroxychloroquine, whether azithromycin was co-prescribed on the same day?
	2. What were the sociodemographic characteristics of patients with a prescription for hydroxychloroquine during COVID-19, stratified by whether they had previously used hydroxychloroquine?
To describe the impact of the new TGA restrictions (24 March 2020) and new PBS restrictions (1 May 2020) on prescribing patterns	1. For the following time periods - 15 February 2020 to 23 March 2020 - 24 March to 30 April 2020 - 1 May to 31 May 2020 what number and proportion of patients were prescribed hydroxychloroquine, stratified by whether they had a relevant indication recorded (autoimmune condition or malaria) and whether they had previously used hydroxychloroquine?

Study type/design

This was a longitudinal descriptive analysis of data from patients attending MedicineInsight practices.

Study time period

The study time period covered 1 March 2018 to 31 May 2020, inclusive. Historical records outside of the study period were included when identifying patient demographics and diagnoses.

Study populations

To answer the first objective of the study about the prescribing patterns over the past 2 years, we included all patients who attended a practice at least once, in order to capture the full extent of GP prescribing.

Study population 1 included patients of all ages who met the following inclusion criteria:

- have visited a practice site that contributed data to MedicineInsight and meets specific MedicineInsight data quality requirements
- have valid information for age and sex
- had at least 1 clinical encounter during the study time period 1 March 2018 to 31 May 2020.

To answer the second and third objectives of the study about the appropriateness of therapy we selected a cohort of regularly attending ('regular') patients who were likely to be managed at the MedicineInsight practice and have their medical conditions and treatments recorded, reducing the impact of missing data on the study findings.

Study population 2 included patients of all ages who met the following inclusion criteria:

- have visited a practice site that contributed data to MedicineInsight and meets specific MedicineInsight data quality requirements
- have valid information for age and sex
- had at least 3 clinical encounters (consultations) at the general practice during the study time period 1 March 2018 to 31 May 2020
- had at least 1 encounter on or before 1 May 2019 (to increase the chance that included patients were being managed at the MedicineInsight for a sufficient period before COVID-19 to enable the opportunity for their medical history and prior therapy with hydroxychloroquine to be recorded).

Definitions

Clinical encounters

A clinical encounter, or any professional exchange between a patient and a healthcare professional, is defined as all encounters at the practice site with a GP or a nurse that are:

a. not identified as administrator entries nor encounters that have been transferred/imported from another practice and

b. are not identified by pre-defined 'administration-type' terms found in the 'reason for encounter' field such as 'administrative reasons', 'forms', and 'recall'.

Sociodemographics

Sociodemographics included in the analysis are age, gender, state, rurality and socio-economic status as described in Table 2.

TABLE 2: SOCIODEMOGRAPHIC CHARACTERISTICS DEFINITIONS

Characteristic	Definition
Age	Age was calculated at 1 July 2020 based on the patient's date of birth (defined as 1 July in the patient's year of birth) and presented as mean, 10-year age groups. Valid age was defined as 0–112 years.
Sex	As recorded in the clinical information system (CIS): Male, Female
State in Australia	State was assigned based on each patient's postcode of residence. If the patient's residence postcode was missing, the practice location postcode was used as a proxy.
Rurality	Rurality was assigned based on a mapping of each patient's postcode of residence using the Australian Bureau of Statistics (ABS) mapping of Postcode 2016 to the Australian Statistical Geography Standard (ASGS) Remoteness Areas 2011 data.[18]
Socioeconomic status (SEIFA)	SEIFA was assigned based on a mapping of each patient's postcode of residence using the Australian Bureau of Statistics (ABS) mapping of Postcode 2016 to the Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD).[19]

Prescriptions for hydroxychloroquine and azithromycin

Patients were defined as having had a prescription for hydroxychloroquine or azithromycin based on information from the 'medicine active ingredient' field of the Script Item table, which includes all scripts issued by the practice. A small number of patients had prescription(s) issued for chloroquine which were included under hydroxychloroquine.

Conditions

Patients are defined as having any of the conditions described in Table 5, if they had a relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields – diagnosis, reason for encounter or reason for prescription – recorded ever. 'Reason for prescription' is not a mandatory field in the clinical information system and is incomplete for roughly 70% of prescription records. Therefore, all relevant diagnosis fields are used to identify patients with a condition that might explain the prescription.

TABLE 3: CLINICAL DEFINITIONS USED TO IDENTIFY MEDICINEINSIGHT PATIENTS

Condition	Definition
Rheumatoid arthritis	Patients were defined as having rheumatoid arthritis, if they ever had a relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields. Relevant terms include: Rheumatoid arthritis, RA
Systemic lupus erythematosus (SLE)	Patients were defined as having SLE, if they ever had a relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields. Relevant terms include: Lupus, SLE, DLE
Sarcoidosis	Patients were defined as having sarcoidosis, if they ever had a relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields. Relevant terms include: Sarcoidosis
Sjögrens syndrome	Patients were defined as having Sjögrens syndrome, if they ever had a relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields. Relevant terms include: Sjogren
Malaria	Patients were defined as having malaria, if they ever had a relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields. Relevant terms include: Malaria
Juvenile arthritis	Patients were defined as having juvenile arthritis, if they ever had a relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields. Relevant terms include: Juvenile arthritis, JA, Stills disease

Data analysis plan

Analyses of the data were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA), including the use of the SURVEYFREQ procedure. Measures included descriptive statistics, frequencies and proportions as appropriate. To indicate the reliability of the estimates of prevalence and proportion, 95% confidence intervals were calculated using robust errors to adjust for clustering by practice site. Non-overlap of 95% CIs was used to determine if there were significant differences between time periods and patient characteristics between or groups when appropriate. The two-sample t-test was used to compare the prescribing rate during COVID-19 and the pre-COVID comparator periods. When assessing a difference between groups, a p-value < 0.05 was considered statistically significant.

If a particular result was only reported in 1–4 patients, this result has been reported as < 5 in order to preserve the privacy of individuals. If a particular result was not seen in any patient, the result has been reported using a dash (-) or as < 5 if required to preserve confidentiality.

PRESCRIBING TRENDS DURING COVID-19

- The prescribing rate for hydroxychloroquine in March 2020 was almost double the average monthly prescribing rate during the 2-year pre-COVID period (1.36 scripts versus 0.72 scripts per 1,000 encounters; risk ratio 1.9; $p < 0.0001$).
- The private (non-PBS subsidised) prescribing rate, while small, increased 20-fold in March compared with the pre-COVID period (0.06 scripts versus 0.003 scripts per 1,000 encounters; $p < 0.0001$).
- The weekly prescribing rate for hydroxychloroquine peaked between 16 March and 12 April 2020.

Study questions

1. What was the weekly prescribing rate of hydroxychloroquine in terms of issued scripts per 1,000 clinical encounters between 1 May 2018 and 30 May 2020, overall and by PBS / private status?
2. What was the average prescribing rate of hydroxychloroquine during March 2020 compared with the pre-COVID-19 period (1 March 2018 to 29 February 2020) in terms of:
    - issued scripts per 1,000 clinical encounters, overall and by PBS / private status
    - quantity prescribed (pack size and repeats) overall and by PBS / private status?

Methods

This analysis included data from 3,465,810 patients with at least 1 clinical encounter during the study time period (1 March 2018 to 31 May 2020), from 471 general practices that participate in the MedicineInsight program and met data quality criteria (study population 1).

The weekly number of clinical encounters at included MedicineInsight practices was used as the denominator for the weekly hydroxychloroquine prescribing rates. Importantly the weekly number of clinical encounters during the COVID-19 period was similar to the weekly number of clinical encounters in the same weeks of the previous two years. The weekly number of clinical encounters at MedicineInsight practices is included in Appendix 1.

Weekly prescribing rates from March 2018 to May 2020

Between 16 March and 12 April 2020, the average weekly prescribing rate for hydroxychloroquine roughly doubled, compared with the pre-COVID period. While the average weekly prescribing rate for hydroxychloroquine between 1 March 2018 and 15 March 2020 ranged from 0.6 to 1.0 HCQ scripts per 1,000 encounters, between 16 March and 12 April 2020 it ranged from 1.3 to 2.1 HCQ scripts per 1,000 clinical encounters. The bulk of hydroxychloroquine prescribing was recorded as PBS subsidised, however the prescribing rate for private prescriptions, while small, also increased around 16 March 2020, falling again by 30 March 2020. (Figure 1)

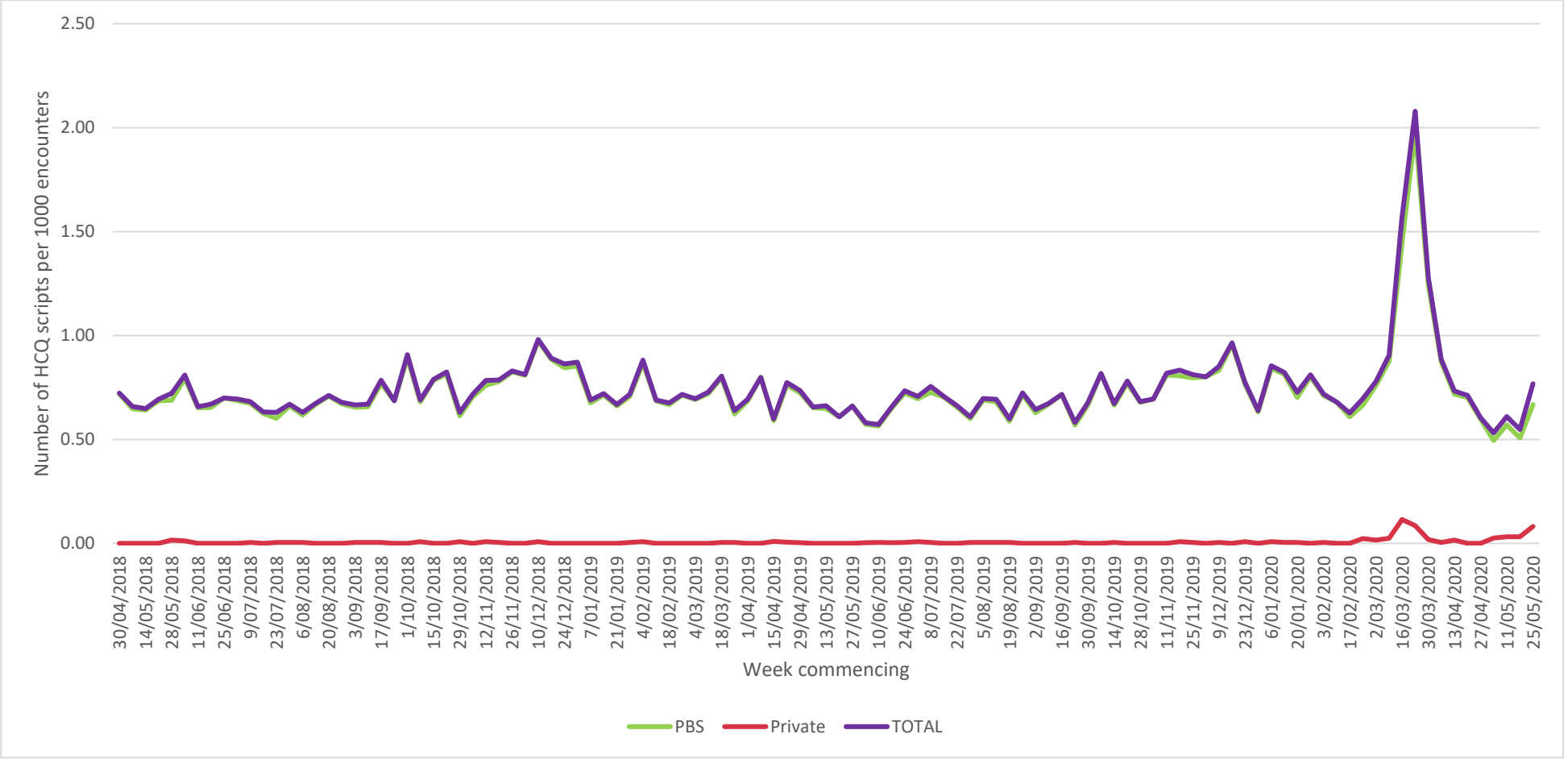


FIGURE 1: HYDROXYCHLOROQUINE WEEKLY PRESCRIBING RATE BETWEEN MAY 2018 AND MAY 2020; NUMBER OF ISSUED SCRIPTS PER 1,000 CLINICAL ENCOUNTERS, TOTAL AND BY PBS STATUS.

Comparison with pre-COVID-19 prescribing rates

The average prescribing rate for hydroxychloroquine in March 2020 almost doubled compared with the average monthly prescribing rate for hydroxychloroquine during the 2-year pre-COVID-19 period (1.36 scripts versus 0.72 scripts per 1,000 encounters; risk ratio 1.9; $p < 0.0001$). The private (non-PBS-subsidised) prescription rate, while small, increased 20-fold in March compared with the pre-COVID-19 period (0.06 scripts versus 0.003 scripts per 1,000 encounters; $p < 0.0001$). The results were similar when we compared the quantity of hydroxychloroquine tablets prescribed, based on the pack size and number of repeats. Overall, the number of tablets prescribed was 1.8 times higher in March compared with the average monthly quantity prescribed during the 2-year pre-COVID-19 period (263.0 tablets versus 142.7 tablets per 1,000 encounters; risk ratio 1.8; $p < 0.0001$). For private scripts only, the quantity of tablets prescribed increased 13-fold in March. (Table 4)

TABLE 4: MONTHLY MEAN AVERAGE NUMBER OF ISSUED SCRIPTS FOR HYDROXYCHLOROQUINE AND ISSUED TABLETS (BASED ON QUANTITY AND REPEATS) IN MARCH COMPARED WITH THE ENTIRE PRE-COVID-19 PERIOD (1 MARCH 2018 – 29 FEBRUARY 2020) PER 1,000 CLINICAL ENCOUNTERS

	March 2020 (1–30 March)	Pre-COVID period (1 March 2018 – 29 February 2020)	p-value [2-sample-t-test]
	Monthly mean average per 1,000 encounters	Monthly mean average per 1,000 encounters (95% CI)	
Issued scripts			
TOTAL	1.36	0.723 (0.697–0.749)	**< 0.0001**
PBS	1.30	0.713 (0.687–0.739)	**< 0.0001**
Private	0.06	0.003 (0.002–0.003)	**< 0.0001**
Issued tablets			
TOTAL	263.0	142.7 (137.7–147.7)	**< 0.0001**
PBS	250.0	140.3 (135.3–145.4)	**< 0.0001**
Private	11.4	0.9 (0.7–1.2)	**< 0.0001**

When we compared the full 3-month COVID-19 period (1 March 2020 to 31 May 2020) with the same comparator months in the previous two years (1 March 2018 to 31 May 2018 and 1 March 2019 to 31 May 2019) the hydroxychloroquine prescribing rate was about 50% higher than the pre-COVID-19 periods, but this was not statistically significant. See Table 5.

TABLE 5: MEAN NUMBER OF ISSUED SCRIPTS FOR HYDROXYCHLOROQUINE AND ISSUED TABLETS (BASED ON QUANTITY AND REPEATS) PER 1,000 CLINICAL ENCOUNTERS FOR THE FULL COVID PERIOD (1 MARCH – 31 MAY 2020) AND PRE-COVID COMPARATOR PERIODS (1 MARCH – 31 MAY 2018 AND 1 MARCH – 31 MAY 2019)

	COVID period (1 March –31 May 2020)	Pre-COVID comparator periods (11 March –31 May 2018 and 1 March –31 May 2019)	p-value [2-sample-t-test]
	Mean no. per 1,000 encounters (95% CI)	Mean no. per 1,000 encounters (95% CI)	
Issued scripts			
TOTAL	1.08 (0.51–1.65)	0.72 (0.71–0.72)	n.s.
PBS	1.04 (0.52–1.56)	0.71 (0.70–0.71)	n.s.
Private	0.032 (0.000–0.078)	0.004 (0.001–0.007)	n.s.
Issued tablets			
TOTAL	209.6 (103.2–316.0)	141.5 (139.2–143.8)	n.s.
PBS	201.4 (104.7–298.1)	139.3 (137.5–141.0)	n.s.
Private	6.6 (0.0–16.1)	1.0 (0.0–2.0)	n.s.

n.s.: Not significant at the $p < 0.05$ level

APPROPRIATENESS OF PRESCRIBING

- Of 2,464 patients who were prescribed hydroxychloroquine during the COVID-19 period, 80% had been prescribed hydroxychloroquine before the COVID-19 period and 20% were new to therapy.
- Only half of the patients who were new to hydroxychloroquine therapy had a relevant indication recorded in their medical history that might explain the use of hydroxychloroquine for non-COVID reasons (ie,. rheumatoid arthritis, SLE, sarcoidosis, Sjögrens syndrome, juvenile arthritis or malaria).
- 76% of patients with evidence of prior hydroxychloroquine use had a relevant indication recorded in their medical history.
- 1.3% of the patients who were prescribed hydroxychloroquine during the COVID-19 period were prescribed azithromycin on the same day.
- Compared to patients who were prescribed hydroxychloroquine prior to COVID-19, those who were new to therapy were more likely to be male (33% vs 21%), younger (30% of new users were aged 20–49 years vs 18% of prior users), reside in major cities (66% vs 54%) and live in areas in the most socioeconomically advantaged quintile (34% vs 20%).

Study questions

1. What number and proportion of patients were prescribed hydroxychloroquine during COVID-19, stratified by whether they had a relevant indication recorded, whether they had previously used hydroxychloroquine and whether azithromycin was co-prescribed on the same day?
2. What were the sociodemographic characteristics of patients with a prescription for hydroxychloroquine during COVID-19, with or without evidence of hydroxychloroquine use prior to COVID-19?

Methods

This analysis included data from 1,880,038 regularly attending patients with at least 3 clinical encounters during the study time period (1 March 2018 to 31 May 2020) and at least 1 encounter on or before 1 May 2019 from 471 general practices that participate in the MedicineInsight program and met data quality criteria (study population 2). Among these patients 2,464 (0.13%) had a prescription for hydroxychloroquine during the COVID-19 period (1 March 2020 to 31 May 2020).

Appropriateness of prescribing during COVID-19

Of 2,464 regular patients who were prescribed hydroxychloroquine during the COVID-19 period (1 March 2020 to 31 May 2020), 500 (20%) were new to therapy and 1,964 (80%) had been prescribed hydroxychloroquine prior to the COVID-19 period (Figure 2). Of the 1,964 patients with evidence of prior hydroxychloroquine use, 76% had a relevant indication recorded in their medical history that might explain the use of hydroxychloroquine (rheumatoid arthritis, SLE, sarcoidosis, Sjögrens syndrome, juvenile arthritis or malaria). Whereas, of the 500 patients who were new to therapy, only 50% had a relevant indication recorded in their medical history (Figure 3).

Of all patients who were prescribed hydroxychloroquine during the COVID-19 period, 715 (29%) did not have a relevant indication recorded. However, 65% of those patients (n = 463) were prescribed hydroxychloroquine prior to the COVID-19 period which indicates they may have a non-COVID-related reason for prescribing that wasn't recorded in fields available to MedicineInsight (Figure 4). For privacy reasons, MedicineInsight does not include data from GP progress notes which may contain further clinical information.

Azithromycin co-prescribing

During the COVID-19 period, 33 patients (1.3% of those prescribed hydroxychloroquine) were prescribed azithromycin on the same day as hydroxychloroquine, 24% of whom had a relevant indication for hydroxychloroquine recorded in their medical history.

FIGURE 2. PROPORTION OF REGULAR PATIENTS PRESCRIBED HYDROXYCHLOROQUINE DURING COVID-19 (1 MARCH 2020 TO 31 MAY 2020) WHO WERE NEW TO THERAPY OR HAD A PRESCRIPTION FOR HYDROXYCHLOROQUINE PRIOR TO 1 MARCH 2020

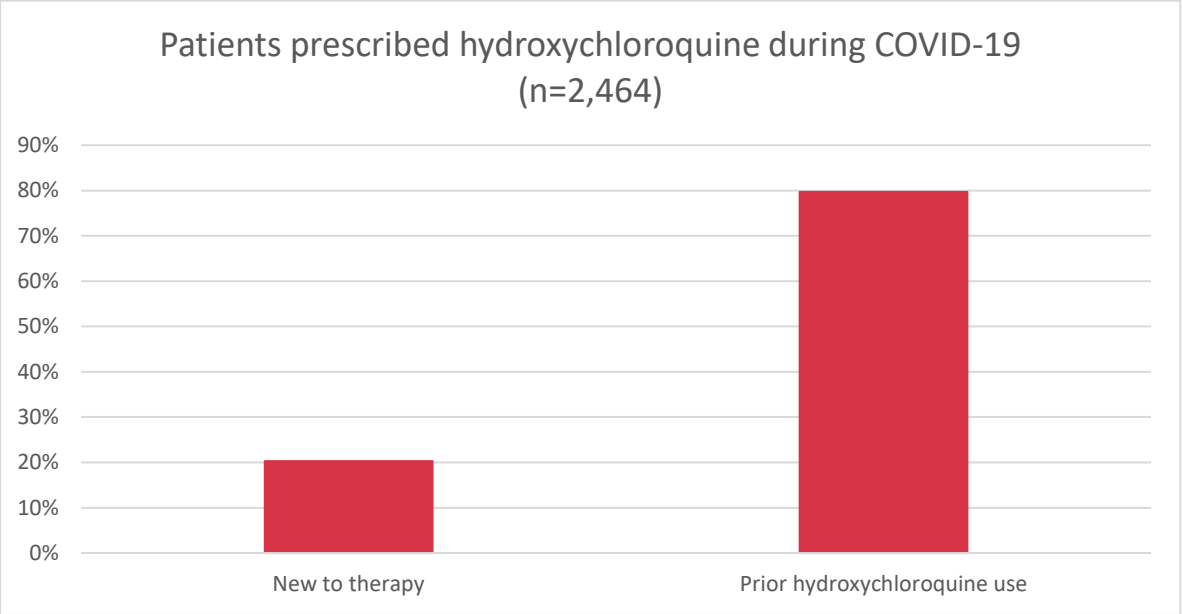


FIGURE 3. PROPORTION OF REGULAR PATIENTS PRESCRIBED HYDROXYCHLOROQUINE DURING COVID-19 (1 MARCH 2020 TO 31 MAY 2020) WITH OR WITHOUT A RELEVANT INDICATION RECORDED IN MEDICINEINSIGHT, BY PRIOR HYDROXYCHLOROQUINE USE

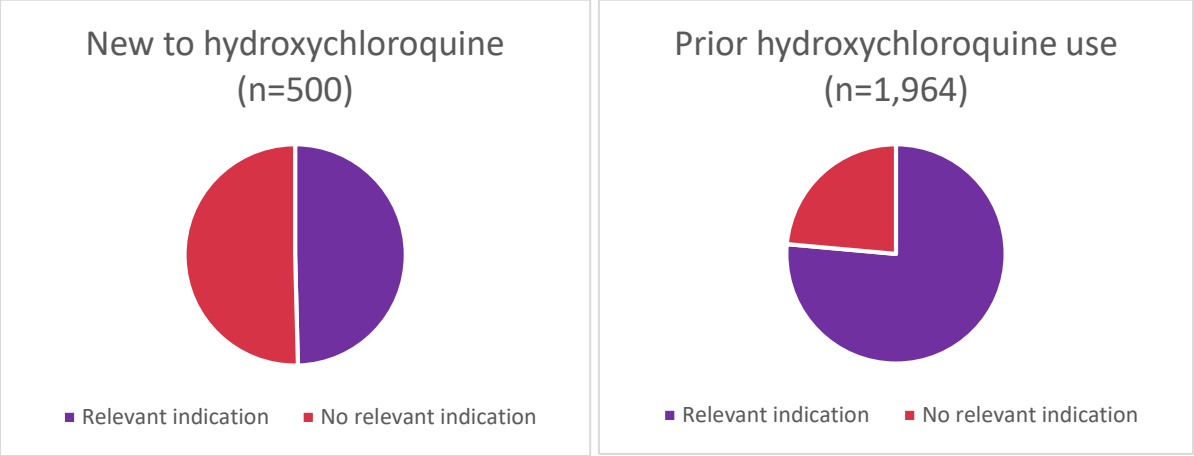
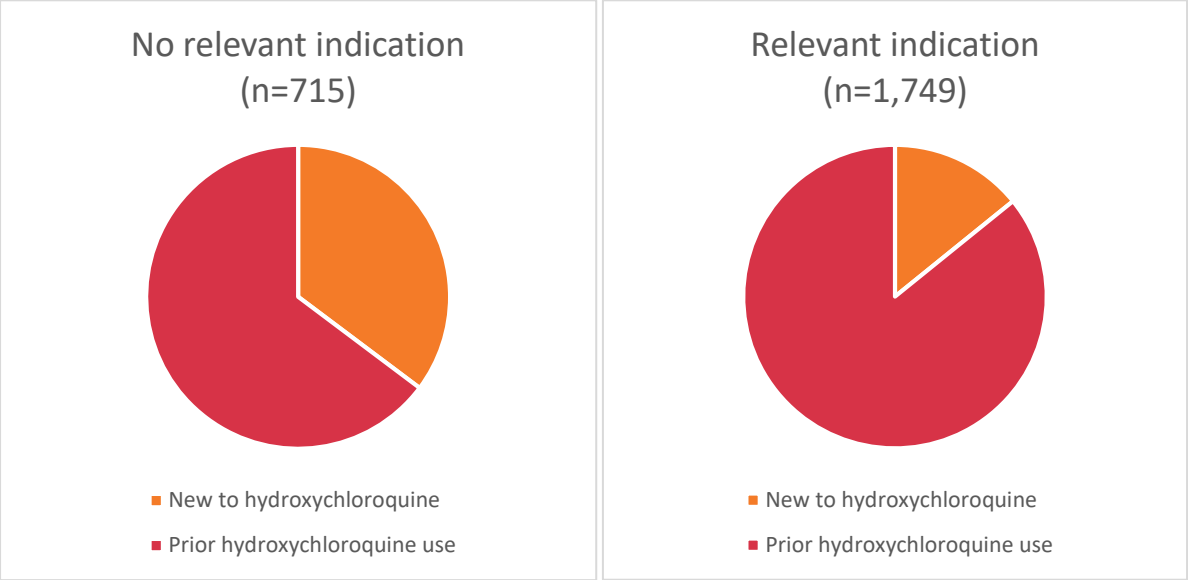


FIGURE 4 PROPORTION OF REGULAR PATIENTS PRESCRIBED HYDROXYCHLOROQUINE DURING COVID-19 (1 MARCH 2020 TO 31 MAY 2020) WHO WERE NEW TO THERAPY OR HAD A PRESCRIPTION FOR HYDROXYCHLOROQUINE PRIOR TO 1 MARCH 2020, BY WHETHER THEY HAD A RELEVANT INDICATION RECORDED IN MEDICINEINSIGHT



Patient characteristics

We compared the sociodemographic characteristics of patients prescribed hydroxychloroquine during the COVID-19 period (1 March 2020 to 31 May 2020) who were prescribed hydroxychloroquine prior to the COVID-19 period versus those patients who were new to therapy (Table 6). Compared to patients who were prescribed hydroxychloroquine prior to COVID-19, those who were new to therapy were more likely to be male (33% vs 21%), younger (30% of new users were aged 20–49 years vs 18% of prior users), reside in major cities (66% vs 54%) and reside in the most socioeconomically advantaged quintile (34% vs 20%). There was no significant difference by state.

TABLE 6: SOCIODEMOGRAPHIC CHARACTERISTICS OF REGULAR PATIENTS PRESCRIBED HYDROXYCHLOROQUINE FOR THE FIRST TIME DURING THE COVID-19 PERIOD 1 MARCH 2020 TO 31 MAY 2020 ('NEW TO THERAPY') AND THOSE WITH PRIOR USE OF HYDROXYCHLOROQUINE RECORDED

Characteristic		Prescribed hydroxychloroquine during COVID-19				General study population 2	
		Prior use pre-COVID-19		New to therapy			
		No.	% (95%CI)	No.	% (95%CI)	No.	% (95%CI)
Total		1,964		500		1,880,038	
Sex							
	Male	413	21.0 (19.0–23.1)	166	33.2 (29.0–37.4)	825,479	43.9 (43.5–44.3)
	Female	1,551	79.0 (76.9–81.0)	334	66.8 (62.6–71.0)	1,054,559	56.1 (55.7–56.5)
Age group (years)							
	0–9	< 5		< 5		210,962	11.2 (10.7–11.7)
	10–19	< 5		< 5		175,109	9.3 (9.0–9.6)
	20–29	29	1.5 (0.9–2.0)	19	3.8 (1.9–5.7)	209,818	11.2 (10.6–11.7)
	30–39	104	5.3 (4.2–6.4)	49	9.8 (6.8–12.8)	249,891	13.3 (12.7–13.9)
	40–49	213	10.8 (9.4–12.3)	84	16.8 (13.4–20.2)	241,294	12.8 (12.6–13.1)
	50–59	371	18.9 (17.2–20.6)	102	20.4 (16.8–24.0)	243,605	13.0 (12.7–13.2)
	60–69	548	27.9 (26.0–29.8)	131	26.2 (21.9–30.5)	234,102	12.5 (12.0–12.9)
	70–79	488	24.8 (22.7–27.0)	76	15.2 (12.0–18.4)	189,366	10.1 (9.5–10.6)
	80–89	194	9.9 (8.2–11.5)	29	5.8 (3.9–7.7)	95,248	5.1 (4.7–5.4)
	90+	16	0.8 (0.4–1.2)	8	1.6 (0.4–2.8)	30,643	1.6 (1.5–1.8)
State/Territory							
	ACT	70	3.6 (0.1–7.1)	15	3.0 (0.5–5.6)	41,876	2.2 (0.4–4.1)
	NSW	548	28.0 (22.5–33.4)	151	30.4 (23.6–37.2)	661,213	35.2 (29.5–41.0)
	NT	25	1.3 (0.3–2.3)	< 5		32,285	1.7 (0.5–2.9)
	QLD	315	16.1 (11.8–20.4)	84	16.9 (11.6–22.2)	304,475	16.2 (12.3–20.2)
	SA	104	5.3 (2.0–8.6)	11	2.2 (0.4–4.0)	52,577	2.8 (1.2–4.4)
	TAS	258	13.2 (7.6–18.7)	34	6.8 (2.0–11.7)	151,339	8.1 (4.6–11.5)
	VIC	476	24.3 (18.1–30.5)	139	28.0 (19.9–36.0)	419,914	22.4 (17.0–27.7)
	WA	163	8.3 (5.2–11.5)	59	11.9 (6.9–16.8)	212,195	11.3 (7.6–15.1)
	Missing	8		8		4,164	
Rurality							
	Major city	1,045	53.5 (46.9–60.1)	329	66.2 (59.2–73.2)	1,164,824	62.3 (56.9–67.6)
	Inner regional	568	29.1 (23.4–34.8)	118	23.7 (17.5–30.0)	456,413	24.4 (19.9–28.9)
	Outer regional	308	15.8 (11.3–20.2)	45	9.1 (5.9–12.2)	219,489	11.7 (8.6–14.9)
	Remote/very remote	33	1.7 (0.6–2.7)	5	1.0 (0.0–2.1)	29,542	1.6 (0.7–2.4)
	Missing	13		13		9,770	
SEIFA quintile (IRSAD)							
	1 (least advantaged)	429	22.0 (17.9–26.0)	58	11.7 (8.2–15.1)	332,663	17.8 (14.6–21.0)
	2	405	20.7 (17.0–24.4)	87	17.5 (12.7–22.3)	332,192	17.8 (14.9–20.6)
	3	411	21.0 (17.3–24.8)	84	16.9 (13.1–20.7)	411,641	22.0 (18.8–25.3)
	4	319	16.3 (13.0–19.6)	101	20.3 (15.9–24.7)	367,003	19.6 (16.7–22.6)
	5 (most advantaged)	390	20.0 (15.2–24.7)	167	33.6 (26.4–40.8)	426,760	22.8 (19.0–26.7)
	Missing	13		13		9,779	

IMPACT OF POLICY CHANGES

- The proportion of patients with potentially inappropriate prescribing of hydroxychloroquine during COVID-19 was highest before the TGA restrictions was implemented, at 14.2%, and reduced to 7.2% between 24 March 2020 and 30 April 2020, and 3.7% from 1 to 31 May 2020.

Study questions

1. What number and proportion of patients were prescribed hydroxychloroquine during COVID-19 but before the TGA restriction effective from 24 March 2020 (ie, 15 February 2020 to 23 March 2020), between the TGA restriction and the PBS listing change (ie, 24 March to 30 April) and since the PBS listing change (1 May to 31 May), stratified by whether they had a relevant indication recorded (autoimmune condition or malaria) and whether they had previously used hydroxychloroquine?

Methods

This analysis included data from 1,880,038 regularly attending patients with at least 3 clinical encounters during the study time period (1 March 2018 to 31 May 2020) and at least 1 encounter on or before 1 May 2019, from 471 general practices that participate in the MedicineInsight program and met data quality criteria (study population 2).

To compare the proportion of patients with potentially inappropriate prescribing of hydroxychloroquine before and after regulatory changes made by the TGA and the PBAC, three comparable periods for assessment included:

- before the TGA restriction effective from 24 March 2020 (ie, 38 days between 15 February 2020 and 23 March 2020)
- between the TGA restriction and the PBS listing change (ie, 38 days between 24 March 2020 and 30 April 2020); and
- since the PBS listing change (1 May to 31 May, or latest available data for May at the practice).

The third time period is shorter than the first two time periods and resulted in a smaller sample size with less reliable estimates.

We defined potentially inappropriate prescribing of hydroxychloroquine during COVID-19 as having

- no evidence of hydroxychloroquine prescribing prior to COVID-19 and
- no relevant indication for hydroxychloroquine in the medical record.

Impact of policy changes on prescribing to guidelines

Table 7 describes the patients prescribed hydroxychloroquine in each of the three time periods.

- 1,164 patients were prescribed hydroxychloroquine in the first time period before the TGA restriction (15 February 2020 – 23 March 2020)
- 1,326 patients were prescribed hydroxychloroquine in the second time period between the TGA restriction and the PBS listing change (24 March 2020 – 30 April 2020)
- 433 patients were prescribed hydroxychloroquine in the third time period after the PBS listing change (1 May to 31 May, or latest available data for May at the practice).

The proportion of patients with potentially inappropriate prescribing of hydroxychloroquine (ie, no evidence of hydroxychloroquine prescribing recorded in MedicineInsight prior to COVID-19 and no relevant indication for hydroxychloroquine in the medical record) was highest before the TGA restriction was implemented at 14.2% and decreased to 7.2% of patients prescribed

hydroxychloroquine between 24 March 2020 and 30 April 2020, and 3.7% of patients prescribed hydroxychloroquine from 1 to 31 May 2020. (Figure 5)

FIGURE 5: PROPORTION OF REGULAR PATIENTS WHO WERE NEW TO HYDROXYCHLOROQUINE THERAPY AND HAD NO RELEVANT INDICATION BEFORE THE TGA RESTRICTION (15 FEBRUARY 2020 TO 23 MARCH 2020, N=1164), BETWEEN THE TGA RESTRICTION AND THE PBS LISTING CHANGE (24 MARCH TO 30 APRIL N=1326)) AND SINCE THE PBS LISTING CHANGE (1 MAY TO 31 MAY; N-433)

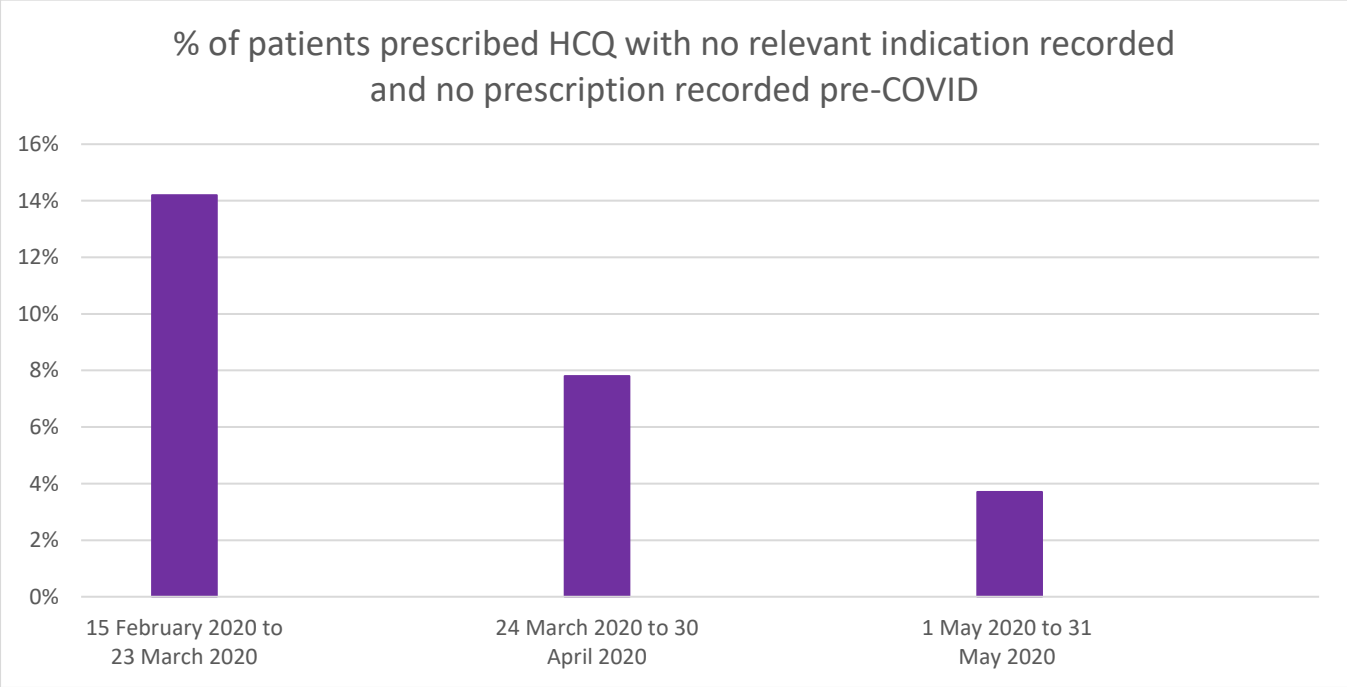


TABLE 7: NUMBER AND PROPORTION OF PATIENTS PRESCRIBED HYDROXYCHLOROQUINE SINCE COVID-19 BUT BEFORE THE TGA RESTRICTION, BETWEEN THE TGA RESTRICTION AND THE PBS LISTING CHANGE AND SINCE THE PBS LISTING CHANGE, STRATIFIED BY WHETHER THEY HAD A RELEVANT INDICATION RECORDED (AUTOIMMUNE CONDITION OR MALARIA) AND WHETHER THEY HAD PREVIOUSLY USED HYDROXYCHLOROQUINE PRIOR TO COVID-19

	15 February 2020 to 23 March 2020		24 March 2020 to 30 April 2020		1 May 2020 to 31 May 2020	
	No.	% (95%CI)	No.	% (95%CI)	No.	% (95%CI)
Relevant indication and prior HCQ use	705	60.6 (57.2–64.0)	827	62.4 (59.4–65.3)	284	65.6 (60.7–70.5)
Relevant indication and no prior HCQ use	106	9.1 (7.5–10.8)	143	10.8 (9.0–12.6)	37	8.5 (5.8–11.3)
No relevant indication and prior HCQ use	188	16.2 (13.8–18.5)	253	19.1 (16.5–21.7)	96	22.2 (17.8–26.5)
No relevant indication and no prior HCQ use	165	14.2 (11.1–17.3)	103	7.8 (6.3–9.3)	16	3.7 (1.8–5.6)
TOTAL	1,164	100.0	1,326	100.0	433	100.0

HCQ: hydroxychloroquine

Strengths and limitations

The MedicineInsight database provides national coverage of general practices, and the included patients are broadly representative of the Australian population in terms of age, gender and Indigenous status. MedicineInsight captures PBS/RPBS subsidised and private prescriptions. Unlike other national prescription datasets, MedicineInsight contains diagnoses recorded in general practice.

Because MedicineInsight is an open cohort and patients in Australia can visit multiple general practices, we included patients who had regular (three or more) encounters with general practices during the study period, who were likely to be receiving most of their care at a MedicineInsight practice, in order to improve data quality. Prevalence estimates of several chronic conditions have been shown to be similar in the MedicineInsight population to those reported in other Australian sources.[17,20,21] The importance of high-quality patient records in general practice is increasingly recognised, with the data being used across the health care system by multiple practitioners and for research, policy and education.[22]

When interpreting the information presented in this report, readers should note the following caveats and/or assumptions related to the MedicineInsight data.

- MedicineInsight data are dependent on the accuracy and completeness of data recorded in, and available for extraction from, the general practice clinical systems.
- Identification of conditions is dependent on GPs recording these items in their clinical software systems. Conditions may be underreported in MedicineInsight data depending on GPs' recording practices.
- The reason or indication for prescribing was not commonly recorded, and thus we could not directly link conditions with hydroxychloroquine prescribing. We relied on other fields such as medical history and reason for encounter, and we identified conditions recorded at any time in the patients' medical histories to maximise the chance of identifying relevant diagnoses. This approach was necessary as autoimmune conditions are typically chronic, lasting for years, and clinicians may record the diagnosis in the medical history only once at initial diagnosis, even if it is managed for years.
- Medicines prescribed at non-MedicineInsight practices or by specialists will not routinely be available to MedicineInsight and may lead to an underestimate of hydroxychloroquine prescribing.
- Medications reflect what has been prescribed, not what has been dispensed or taken.
- We can't rule out the possibility that some patients identified as first-time users of hydroxychloroquine in this report may have been misclassified if they were prescribed hydroxychloroquine previously at a non-MedicineInsight practices or by a specialist.
- It is also possible that patients with a relevant condition were misclassified if their diagnosis was not recorded in fields available to MedicineInsight or if their autoimmune condition wasn't included in our search strategy.
- Due to confidentiality issues we do not have access to progress notes, which may contain further information on diagnoses.
- Patients are free to visit multiple other practices. We do not have data on patients from non-MedicineInsight clinics. Currently we cannot identify patients who have attended multiple MedicineInsight practices. However, based on patient loyalty data from the Australian Department of Health, which provides information on the average number of different GPs seen annually, and the proportional national coverage of MedicineInsight practices, we expect that less than 4% of MedicineInsight patients are duplicates.

REFERENCES

1. Zhou D, Dai SM, Tong Q. COVID-19: a recommendation to examine the effect of hydroxychloroquine in preventing infection and progression. J Antimicrob Chemother 2020;75:1667-70. https://www.ncbi.nlm.nih.gov/pubmed/32196083.
2. Business Insider Australia. Australians are buying hydroxychloroquine after Trump called it a 'very powerful' treatment for COVID-19 – a claim which remains unproven Australia: Pedestrian, 2020. https://www.businessinsider.com.au/coronavirus-hydroxychloroquine-covid19-australia-prescriptions-trump-death-2020-3 (accessed 15 June 2020).
3. Trump D. Hydroxychloroquine and azithrmoycin taken together, have a real chance to be one of the biggest game changers in the history of medicine. Twitter, 2020. https://twitter.com/realDonaldTrump/status/1241367239900778501 (accessed 7 July 2020).
4. SBS. Clive Palmer has bought 30 million doses of an anti-malaria drug to fight COVID-19. But experts warn this may not be the cure-all. New South Wales: SBS, 2020. https://www.sbs.com.au/news/the-feed/clive-palmer-has-bought-30-million-doses-of-an-anti-malaria-drug-to-fight-covid-19-but-experts-warn-this-may-not-be-the-cure-all (accessed 5/8/2020).
5. Coombes I, Markwell A, Kubler P, et al. Principles of ethical prescribing for self and others: hydroxychloroquine in the COVID 19 pandemic. . Australian Prescriber 2020;43:76-7. https://www.nps.org.au/australian-prescriber/articles/principles-of-ethical-prescribing-for-self-and-others-hydroxychloroquine-in-the-covid-19-pandemic.
6. NPS MedicineWise. Can hydroxychloroquine be used to treat or prevent COVID-19? Sydney: NPS MedicineWise, 2020. https://www.nps.org.au/covid-19-and-medicines-faqs#can-hydroxychloroquine-be-used-to-treat-or-prevent-covid-19? (accessed 07/07/2020).
7. Isbister GK, Dawson A, Whyte IM. Hydroxychloroquine overdose: a prospective case series. Am J Emerg Med 2002;20:377-8. https://www.ncbi.nlm.nih.gov/pubmed/12098196.
8. The National COVID-19 Clinical Evidence Task Force. Australian guidelines for the clinical care of people with COVID-19. Melbourne: The National COVID-19 Clinical Evidence Task Force, https://covid19evidence.net.au/ (accessed 15 June 2020).
9. US National Library of Medicine. Clinical Trials. United States: United States Department of Health and Human Services, 2020. https://clinicaltrials.gov/ct2/results?term=Hydroxychloroquine&cond=COVID-19 (accessed 28 April 2020).
10. Therapeutics Goods Administration. TGA Safety Alert: New restrictions on prescribing hydroxychloroquine for COVID-19 Canberra: TGA, 2020. https://www.tga.gov.au/alert/new-restrictions-prescribing-hydroxychloroquine-covid-19 (accessed 15 June 2020).
11. Therapeutics Goods Administration. Notice of an amendment to the current Poisons Standard under paragraph 52D(2)(a) of the Therapeutic Goods Act 1989: Amendment related to hydroxychloroquine Canberra: TGA, 2020. https://www.tga.gov.au/scheduling-decision-final/notice-amendment-current-poisons-standard-under-paragraph-52d2a-therapeutic-goods-act-1989#hydroxy (accessed 17 May 2020).
12. The Pharmaceutical Benefit Scheme (PBS). Revised hydroxychloroquine PBS listings for the treatment of autoimmune disorders and malaria from 1 May 2020 Canberra: PBS, 2020. https://www.pbs.gov.au/info/news/2020/05/revised-hydroxychloroquine-pbs-listings-for-the-treatment (accessed 15 June 2020).
13. Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents 2020:105949. https://www.ncbi.nlm.nih.gov/pubmed/32205204.
14. Gautret P, Lagier JC, Parola P, et al. Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: A pilot observational study. Travel Med Infect Dis 2020;34:101663. https://www.ncbi.nlm.nih.gov/pubmed/32289548.
15. Chorin E, Dai M, Shulman E, et al. The QT interval in patients with COVID-19 treated with hydroxychloroquine and azithromycin. Nat Med 2020;26:808-9. https://www.ncbi.nlm.nih.gov/pubmed/32488217.
16. Mercuro NJ, Yen CF, Shim DJ, et al. Risk of QT interval prolongation associated with use of hydroxychloroquine with or without concomitant azithromycin among hospitalized patients testing

positive for coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020. https://www.ncbi.nlm.nih.gov/pubmed/32356863.

17. Busingye D, Gianacas C, Pollack A, et al. Data Resource Profile: MedicineInsight, an Australian national primary health care database. Int J Epidemiol 2019;48:1741-h. https://www.ncbi.nlm.nih.gov/pubmed/31292616.

18. Australian Bureau of Statistics. The Australian Statistical Geography Standard (ASGS) remoteness structure. Canberra: ABS, 2018. https://www.abs.gov.au/websitedbs/D3310114.nsf/home/remoteness+structure (accessed 23 March 2020).

19. Australian Bureau of Statistics. Socio-Economic Indexes for Areas. Canberra: ABS, 2018. http://www.abs.gov.au/websitedbs/censushome.nsf/home/seifa (accessed 7 November 2019).

20. NPS MedicineWise. General Practice Insights Report July 2017–June 2018. Sydney: NPS MedicineWise, 2019. https://www.nps.org.au/assets/NPS/pdf/General-Practice-Insights-Report_2017-18.pdf (accessed 24 June 2020).

21. Australian Bureau of Statistics. National Health Survey: First Results, 2017-18 (Catalogue No. 4364.0.55.001). Canberra: ABS, 2018. https://www.abs.gov.au/ausstats/abs@.nsf/mf/4364.0.55.001 (accessed 5 June 2020).

22. Royal Australian College of General Practitioners. Improving health record quality in general practice: How to create and maintain health records that are fit for purpose. East Melbourne: RACGP, 2018. https://www.racgp.org.au/getattachment/73857c48-42ea-4712-8d64-a5feede6afc2/Improving-health-record-quality-in-general-practice.aspx (accessed 30 June 2020).

APPENDIX 1

FIGURE A1: WEEKLY NUMBER OF CLINICAL ENCOUNTERS AT MEDICINEINSIGHT PRACTICES BETWEEN MARCH 2018 AND MAY 2020 (N=471 PRACTICES AND 3.47 MILLION PATIENTS).