BMJ Public Health

Evaluating the utilisation patterns of pharmacological therapy in COVID-19 patients: an ecological study in Italy

Maria Lucia Marino ,[1] Aurora Di Filippo,[1] Graziano Onder,[2,3] Davide Eleuteri,[4] Francesco Trotta[1]

To cite: Marino ML, Di Filippo A, Onder G, *et al*. Evaluating the utilisation patterns of pharmacological therapy in COVID-19 patients: an ecological study in Italy. *BMJ Public Health* 2025;**3**:e001767. doi:10.1136/bmjph-2024-001767

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjph-2024-001767).

Received 18 July 2024
Accepted 29 January 2025

[1]Italian Medicines Agency, Rome, Italy
[2]Fondazione Policlinico Gemelli IRCCS, Rome, Italy
[3]Università Cattolica del Sacro Cuore, Rome, Italy
[4]Department of Emergency, Intensive Care Medicine and Anesthesia, Fondazione Policlinico Universitario A Gemelli IRCCS, Rome, Italy

Correspondence to
Dr Maria Lucia Marino;
ml.marino@aifa.gov.it

ABSTRACT

Backgound The drug central monitoring system set up in Italy to evaluate the real-time trends of medicines used in hospital and primary care settings contributed to inform drug supplies, avoided stockpiling and allowed to monitor adherence to clinical practice guidelines for the treatment of COVID-19 patients. The primary objective of the study is to understand how and to what extent the drug utilisation tracked the evolution of COVID-19 pandemic and evaluate the different pharmacological approaches adopted in hospital and primary care settings.

Methods A national ecological study correlating the drug utilisation of specific categories of drugs related to SARS-CoV-2 with the number of SARS-CoV-2 hospitalised or positive subjects. The correlation is estimated by using linear regression models and reporting the angular coefficients (slope) with relative p value.

Results Overall, 15 drug categories are identified: 7 categories are available in both settings, 6 categories are prevalent in hospital setting and 2 categories are used in primary care. As for drugs common to both settings, a statistically significant positive association between the number of SARS-CoV-2-positive subjects and drug consumption is found only for low-molecular-weight heparin, oxygen, azithromycin and steroids. As regards drugs used exclusively in hospital, a significant correlation is observed for cardiac stimulants, general anaesthetics, hypnotics and sedatives as well as muscle relaxant drugs. Among drugs used exclusively in primary care, the study has shown a positive correlation only for vitamin D. Finally, the adoption in clinical practice of the recommendations issued by the competent authorities was assessed: at hospital level, the use of drugs with a negative recommendation (such as hydroxychloroquine and azithromycin) was promptly stopped.

Conclusions Study findings show a positive correlation between the use of specific drug categories used during the pandemic and the number of COVID-19-positive and hospitalised patients, suggesting the relevant role of evaluating drug utilisation patterns in tracking the evolution of pandemics and guideline adherence in clinical practice.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The studies conducted about the use of drugs during pandemic showed altered and inappropriate prescription for hydroxychloroquine, azithromycin, antiviral and steroids in hospital or primary care settings.

WHAT THIS STUDY ADDS

⇒ Our study provides comprehensive information on prescribing patterns of 15 categories of drugs for COVID-19 patients treated both in hospital and primary care at national level, as well as compliance with recommendations issued by competent authorities.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study shows that monitoring drug utilisation patterns for COVID-19 patients treated both in hospital and primary care could provide insights into the progress of the pandemic from different aspects and verify adherence to guidelines and influence prescribing in clinical practice.

INTRODUCTION

The first phase of COVID-19 pandemic was characterised by high level of uncertainty in the treatment of SARS-CoV-2 infection; the evidence on effective treatments was limited and the therapeutic approaches were based on studies providing in vitro data on antiviral activity, poor quality clinical studies or compassionate/off-label use of drugs that in most cases proved to be unsuccessful.[1] Moreover, during the early phase of pandemic, it was observed an increased and unexpected demand for several medicines by hospitals, both for COVID-19 treatment (recommended and off-label) and supportive therapies.[2] Moreover, the primary care setting faced abnormal behaviours in medicines purchase, which sometimes resulted in shortages of hydroxychloroquine and oxygen.[3–5] A drug central monitoring system was set up in Italy to evaluate the real-time trends of medicines used in hospital and primary care settings; this system contributed to inform on

drug supplies, avoiding (inappropriate) stockpiling, and it also allowed to monitor the adherence to clinical practice guidelines for the treatment of COVID-19 patients.[6 7]

The uncertainties on COVID-19 treatments altered prescription pattern and purchasing behaviour in several countries. Different studies conducted in ambulatory setting (community pharmacy) confirmed this phenomenon highlighting an altered prescription, especially for hydroxychloroquine and azithromycin, when compared with background period.[8–11] An increased use of antiviral, antibiotics, steroids and hydroxychloroquine was also observed among hospitalised patients.[12–14]

There is a lack of studies, conducted throughout all phases of the pandemic, evaluating prescription patterns and purchasing behaviours on principal therapeutic classes of drugs used both in hospital and primary care settings. Moreover, no study attempted to link altered prescribing patterns with the number of COVID-19 patients by attempting to correlate pandemic severity with peak drug demand trends.

The pandemic period, as defined by the WHO from 11 March 2020 to 31 March 2022,[15] was characterised by the rapid change in the prevalent viral variant and disease severity, as well as by the evolution of different pharmacological approaches. In fact, as new evidence became available, the guidelines were continuously updated. The global vaccination campaign represented a key breakthrough in tackling the pandemic; moreover, it reduced pressure on the healthcare system in terms of hospital access and intensive care unit admission.[16]

Therefore, analyses of national drug consumption in various settings may provide important information about the severity of COVID-19 pandemic, the change in treatments over time and their appropriateness of use.

The primary objective of the study is to understand how and to what extent the drug utilisation tracked the evolution of the COVID-19 pandemic and evaluate the different pharmacological approaches adopted in different settings (non-hospitalised and hospitalised patients). A further objective of the study is to investigate the adoption in clinical practice of the recommendations issued by the Italian Medicines Agency (AIFA) periodically updated on the basis of newly available evidences.

METHODS

Data source

The data source used is the so-called 'traceability' system (Decree of the Minister of Health 15 July 2004) aimed at the tracking movements of medicines with Marketing Authorisation in Italy. This is a nationwide information system tracking drug movements generated by pharmaceutical companies, including all packages sent (sell-in) to healthcare facilities of the Italian National Health System or to community pharmacies. Sell-in data were considered a proxy for drug utilisation and were aggregated on a monthly basis.

Data on cases of SARS-CoV-2-positive individuals and hospitalisations related to COVID-19 were retrieved through daily monitoring by the Italian Ministry of Health.[17]

Study design

This study is a national ecological study that correlated the use of specific categories of drugs related to SARS-CoV-2 with the number of subjects testing positive for SARS-CoV-2. In the primary care setting, monthly drug utilisation trends were compared with the SARS-CoV-2-positive patients (non-inpatients), while at the hospital level, SARS-CoV-2 patients undergoing hospitalisation were used as a comparison.

The specific demand for the selected drugs was compared nationwide over four different phases: (1) the pre-COVID period (January 2019–February 2020), (2) the first pandemic phase (first waves) before mass vaccination (March 2020–January 2021), (3) the second pandemic phase (second waves) after the start of vaccination (February 2021–November 2021) and (4) the third pandemic phase (third waves), during which the booster dose was administered (December 2021–December 2022).

The selected drug categories were those frequently used and available during all phases of the pandemic (ie, from February 2020 to the end of the study), regardless of their specific indication for the treatment of SARS-CoV-2. Depending on the prevalent setting (hospital or primary care), the drugs were divided into drugs available in both settings (group 1), those for hospital use (group 2) and those for primary care (group 3). The complete list of drugs (by the Anatomical Therapeutic Chemical classification (ATC) level V and therapeutic class) included in each group is available in online supplemental tables 1–3. For the hospital setting, the injectable formulation of the drugs selected (if available) was considered, and for primary care the oral formulations.

Drug utilisation, in terms of number of packs, in both hospital and primary care settings was evaluated. The comparison was made in graphical terms by superimposing the monthly consumption curves and those of SARS-CoV-2-positive subjects for the entire time span from pre-COVID phase to phase 4, that is, following mass vaccination; the pre-COVID phase was considered as a baseline to assess subsequent changes. All time series were smoothed using five-period moving averages; the correlation between the drug sell-in and the number of patients testing positive for SARS-CoV-2 was then estimated for each phase using linear regression models; the angular coefficients (slope) and associated p-values were then reported to test the significance of the relationship using Student's t-test. The slope should be interpreted as the variation observed in drug utilisation (in a given phase) corresponding to the unit increase in a SARS-CoV-2-positive subject (hospitalised or not depending on the reference category); an angular coefficient (slope) significantly > of 0 means that an increase in the number

of individuals positive or hospitalised for COVID-19 (according to the category considered) resulted in an increase in drug utilisation equal to that coefficient.

To respond to the second objective of the study, monthly sell-in time series was evaluated against the time references of specific AIFA and Ministry of Health recommendations. The focus was on azithromycin, hydroxychloroquine and vitamin D, for which the regulatory authorities have issued negative opinions.

Ethics committee approval was not required according to Italian legislation because the study was a descriptive analysis of aggregated data. Analyses were performed with SAS, version 9.4 (SAS Institute).

RESULTS

Overall, 15 drug categories are identified, including 82 active ingredients, 7 drug categories are available in both settings (group 1), 6 are prevalent in hospital setting (group 2), while 2 categories are mainly used in primary care use (group 3) (online supplemental tables 1–3).

Drugs commonly used in both hospital and primary care settings

As for drugs commonly used in both settings, drug utilisation patterns seem to follow the trends of patients hospitalised for SARS-CoV-2 or SARS-CoV-2-positive cases (supplementary material S-Figure1); however, a statistically significant positive correlation is observed only for low-molecular-weight heparins (LMWHs), oxygen, azithromycin and steroids, as showed in section 1 of table 1 and figure 1.

In particular, a strong positive association is found between the number of SARS-CoV-2-positive subjects and drug consumption of LMWH during vaccination phase, both in hospital and primary care (section 1 of table 1). Specifically, in the primary care setting, an increase in LMWH sell-in is observed both in the vaccination phase and the subsequent booster phase (slope=0.13 and 0.24, respectively). This may suggest that such reversal could be driven by the lower severity of the disease and new treatment approaches (including the arrival of vaccines), which have shifted COVID-19 patients from the hospital to home treatment, as also confirmed by positive patient data over time (figure 1A,B and section 1 of table 1).

As for oxygen, the correlation between drug sales and positive patients is observed, in particular, in the hospital setting for the entire observation period, whereas this association is observed only in the prevaccination and vaccination phases in primary care setting. In numerical terms, the increase observed for oxygen is +14.43 units per SARS-CoV-2-positive subjects in the prevaccination phase, +23.32 units in the vaccination phase and +20.33 in the booster phase. The peak is, therefore, reached in the very early phase of the pandemic, before mass vaccination has been implemented and when the most serious cases and the highest number of deaths due to COVID-19 are observed (figure 1C and section 1 of table 1).

The association between sell-in and SARS-CoV-2-positive subjects is also positive in the primary care setting, although with significantly lower slopes (+0.13 in the prevaccination phase and +0.24 in the vaccination phase); however, no association has been found between SARS-CoV-2-positive subjects and oxygen in the booster phase in this setting (figure 1D and section 1 of table 1).

With regards to azithromycin, the correlation with patient hospitalised for COVID-19 is observed only in the hospital setting showing a reduction of sell-in from the prevaccination phase to the vaccination phase; in the primary care setting, however, a significant increase in sell-in is observed, especially in the prevaccination phase, which, however, is not associated with the trend of SARS-CoV-2-positive subjects (figure 1E,F and section 1 of table 1).

Finally, for corticosteroids, we observed a significant positive slope in the prevaccination and vaccination phases only for the hospital setting; in the booster phase, however, we do not observe an increase in sell-in as cases increase (figure 1G,H and section 1 of table 1).

Drugs used in hospital setting

Regarding drugs used exclusively in hospital setting, a significant correlation is observed with respect to patients hospitalised for COVID-19 during prevaccination and vaccination phases for cardiac stimulants, general anaesthetics and hypnotics and sedatives. As for muscle relaxant drugs, however, it is observed that the intensity of the correlation is approximately the same in all phases (slope between 0.12 and 0.14) and, thus, the correlation with hospitalised patients remains statistically significant even in the booster phase.

While for general anaesthetics, hypnotics and sedatives and peripheral muscle relaxants, reductions in sell-in trends are observed between the prevaccine phase and the booster phase consistent with the trend in the number of hospitalisations for COVID-19; for cardiac stimulants, the sell-in continues to grow even in the booster phase despite the reduction in cases. In fact, it can be seen from the graph that, for all these categories, sell-in levels in the booster phase are similar to those in the prepandemic phase with the exception of cardiac stimulants, whose sales levels continue to be higher than prepandemic levels (figure 2A–D and section 2 of table 1).

This trend is consistent with the trend of the pandemic, which has been characterised by greater uncertainty in the early phase, during which a greater use of intensive and subintensive therapies is observed and greater pressure on hospitals is recorded.

Drugs used in primary care

With regards to drugs used exclusively in primary care, only for vitamin D, a positive and significant correlation has emerged between consumption and SARS-CoV-2-positive subjects during all pandemic phases considered (figure 3 and section 3 of table 1). In particular, the strength of the correlation has grown progressively from

Table 1 Linear regression for the relationship between the COVID-19 patients and drugs used in hospital and primary care settings, in each phase of the pandemic

		Hospital setting			Primary care setting		
Category	Phase	Slope of the regression line	SD	Probt (significance)	Slope of the regression line	SD	Probt (significance)
Section 1: Common drugs in hospital and primary care settings							
LMWH	prevaccine phase	0.25	0.16	0.1540	0.15	0.11	0.2083
	vaccination phase	0.31	0.07	0.0011 (*)	0.24	0.03	0.0000 (†)
	booster phase	0.18	0.28	0.5426	0.32	0.14	0.0468 (*)
Oxygen	prevaccine phase	16.43	3.28	0.0007 (†)	0.13	0.05	0.0290 (*)
	vaccination phase	23.32	1.72	0.0000 (†)	0.24	0.03	0.0000 (†)
	booster phase	20.33	5.22	0.0025 (*)	0.42	0.28	0.1602
Azithromycin	prevaccine phase	0.16	0.10	0.1208	0.67	0.38	0.1099
	vaccination phase	0.08	0.02	0.0054 (*)	0.00	0.29	0.9941
	booster phase	0.05	0.04	0.2029	0.93	0.56	0.1258
Corticosteroids for systemic use	prevaccine phase	0.38	0.15	0.0317 (*)	0.48	0.50	0.3560
	vaccination phase	0.38	0.09	0.0032 (*)	−0.37	0.27	0.2044
	booster phase	0.20	0.13	0.1427	0.03	0.94	0.9784
Section 2: Drugs used exclusively in hospital setting							
Cardiac stimulants	prevaccine phase	0.32	0.09	0.01 (*)			
	vaccination phase	0.21	0.08	0.0230 (*)			
	booster phase	0.18	0.20	0.3904			
General anaesthetics	prevaccine phase	0.32	0.11	0.0162 (*)			
	vaccination phase	0.28	0.04	0.0000 (†)			
	booster phase	0.09	0.05	0.0868			
Hypnotics and sedatives	prevaccine phase	0.14	0.05	0.0236 (*)			
	vaccination phase	0.12	0.02	0.0001 (†)			
	booster phase	0.08	0.04	0.0806			
Peripheral muscle relaxant	prevaccine phase	0.14	0.05	0.0230 (*)			
	vaccination phase	0.12	0.02	0.0001 (†)			
	booster phase	0.14	0.04	0.0019 (*)			
Section 3: Drugs used in primary care setting							
Vitamin D	prevaccine phase				1.10	0.30	0.0048 (*)
	vaccination phase				1.46	0.33	0.0018 (*)
	booster phase				3.10	1.33	0.0390 (*)

*p value<0.05.
†p value<0.01.
LMWH, low-molecular-weight heparin.

the prevaccination phase to the booster phase: the slope has increased from 1.10 to 3.10, meaning that, as a single SARS-CoV-2-positive subject increases, vitamin D sell-in increases by 3.10 packs during the booster phase.

Again, however, the increase in vitamin D sell-in peaks, in absolute terms, in the vaccination phase, regardless of the prevalence of SARS-CoV-2-positive cases. Therefore, the maximum correlation is reached in the booster phase, a phase in which SARS-CoV-2-positive cases also increase (figure 3 and section 3 of table 1).

Adoption in clinical practice of national recommendations

The analysis of drug sales trends to evaluate how and whether the (negative) recommendations provided by the competent national agencies have been implemented in clinical practice is shown in figure 4A–F.

For azithromycin, the Italian Medicines Agency (AIFA) has released a recommendation (updated May 2020)[18] against its use alone or in association outside of overlapping bacterial infection. As a result of such recommendation, it can be observed that hospital use has decreased

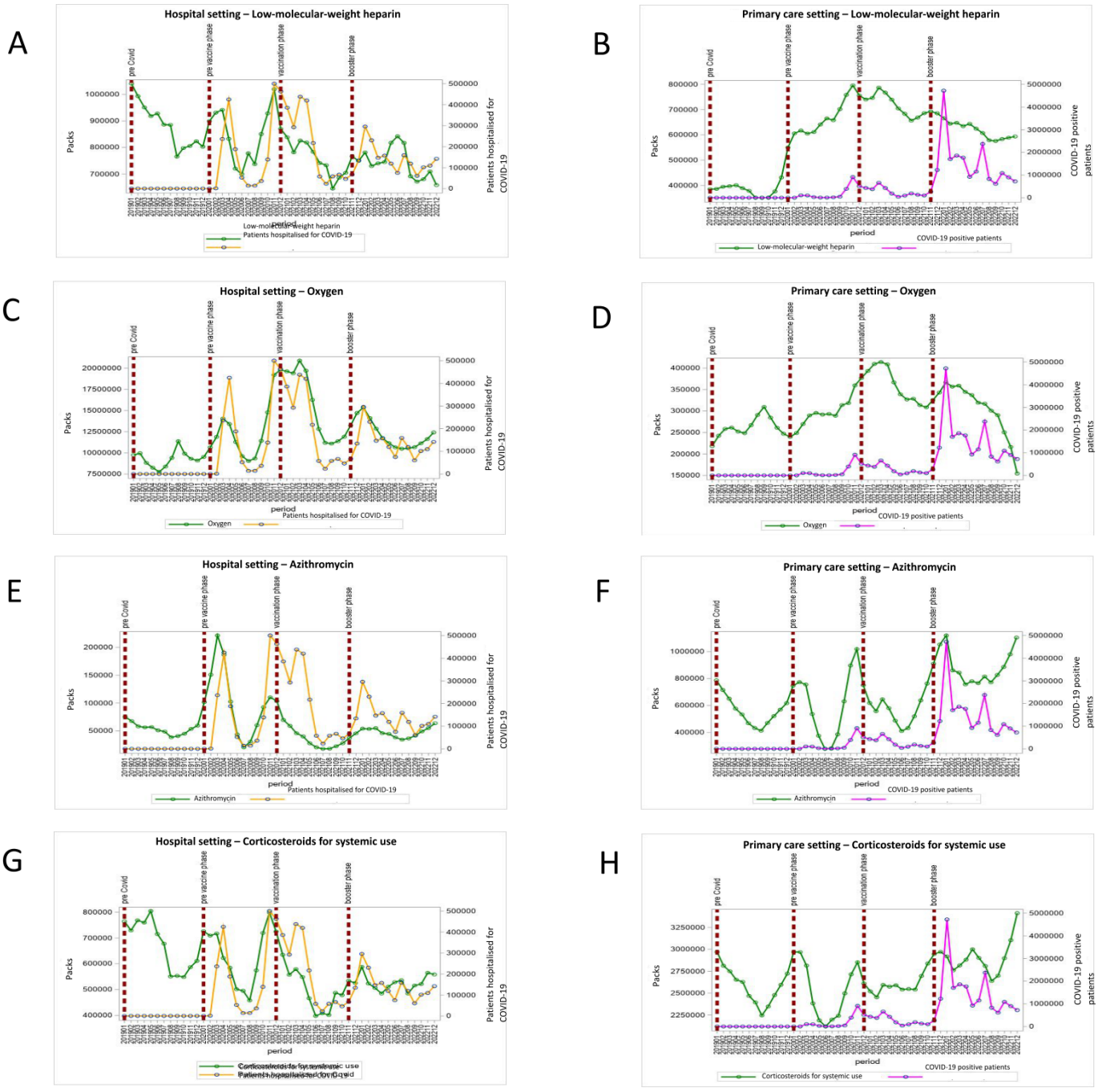

Figure 1 Time series of drugs used in both hospital and primary care settings and COVID-19 patients by settings for each of the four pandemic phases.

since November 2020, although lagging behind the agency's indication. In contrast, in primary care, increasing and continuous use is observed over time, despite the negative recommendation (figure 4A,B).

AIFA issued a recommendation against the use of hydroxychloroquine (April 2020)[19] in both hospital and primary care settings. Subsequent updates to the indication were released in May, July and November 2020. Following AIFA's negative recommendation, the use of hydroxychloroquine was immediately abandoned by hospitals. A strong reduction has also been observed at the primary care level after the initial negative recommendation, although stable use of the drug remained (averaging 150.000 packs/month) at a higher level than prepandemic, suggesting weaker uptake than in the hospital setting (figure 4C,D).

Although the Italian Ministry of Health released a recommendation[20] to reiterate that the efficacy of vitamin supplements, including vitamin D, is not proven for the treatment of COVID-19 patients, consistent use has been observed in both hospital and primary care settings during all phases of the pandemic (figure 4E,F).

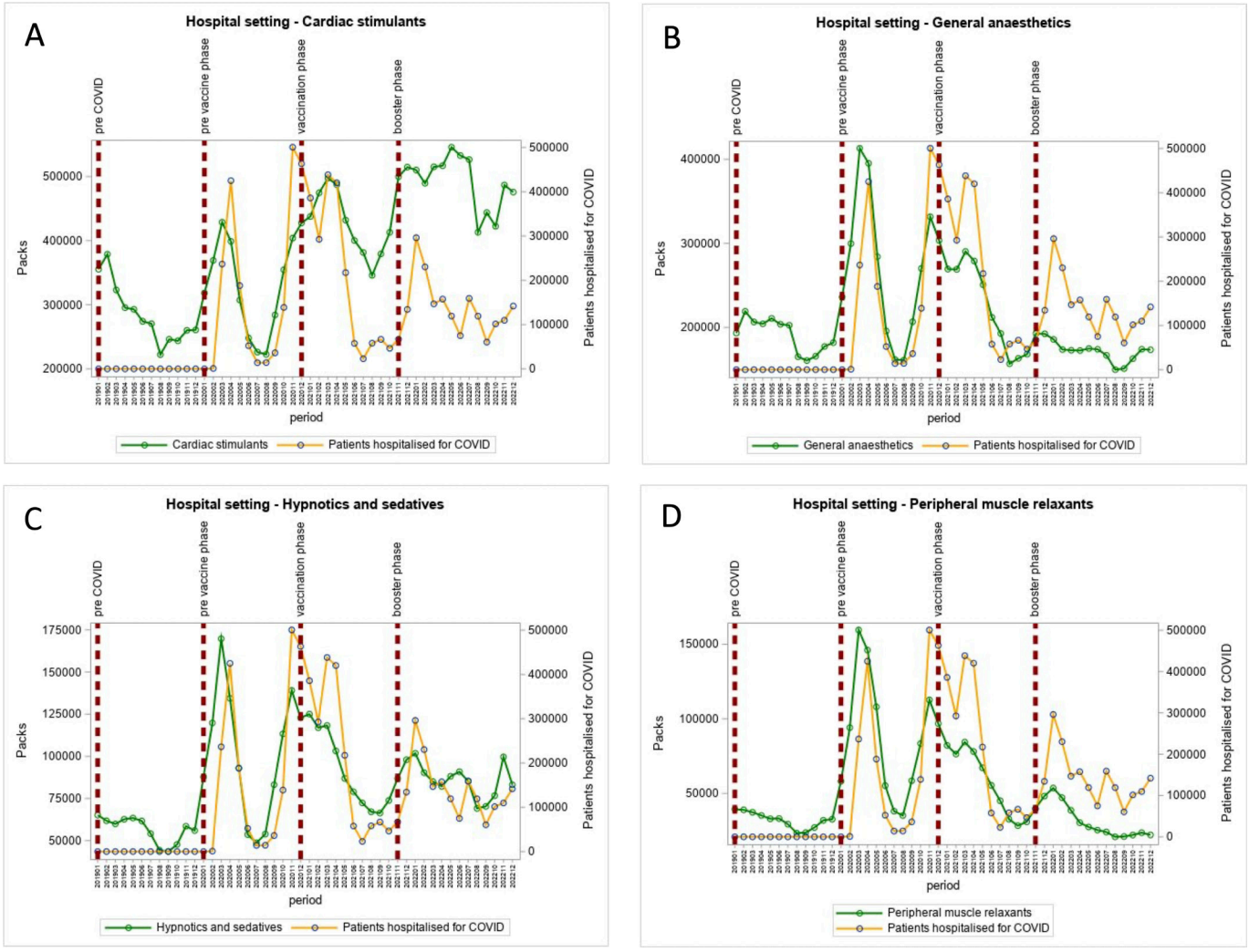

Figure 2 Time series of drugs used in hospital setting and COVID-19 patients for each of the four pandemic phases.

DISCUSSION

This is the first study to analyse the real-world use of drugs widely used during the COVID-19 pandemic in both hospital and primary care settings with national coverage. Furthermore, it represents the first attempt to monitor the translation of national recommendations on medicines used for COVID-19 into clinical practice. The results of the study show a positive correlation between the use of specific categories of drugs widely used during the pandemic and the number of COVID-19-positive and hospitalised patients, suggesting the relevant role of assessing drug utilisation patterns in tracking the evolution of pandemics. Such experience confirms that the interpretation of drug utilisation patterns allows to understand the 'burden' of disease and its severity (eg, the effect of the introduction of vaccination and the spread of virus variants) through peak claims in different settings, time periods and geographic areas, as well as to consistently grasp the appropriateness of drug treatment use through its modification over time.

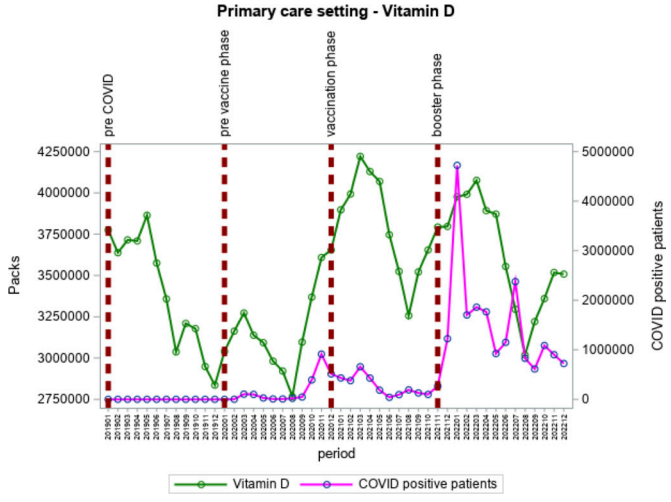

Figure 3 Time series of drugs used in primary care and COVID-19 patients for each of the four pandemic phases.

In fact, it has been found that specific drug categories, such as oxygen, LMWH and corticosteroids, correlated significantly with the number of patients hospitalised for COVID-19; furthermore, even for these categories, a reduction in use (particularly in the hospital setting) was observed starting from 2021 following the arrival of vaccination campaign and monoclonal antibodies,

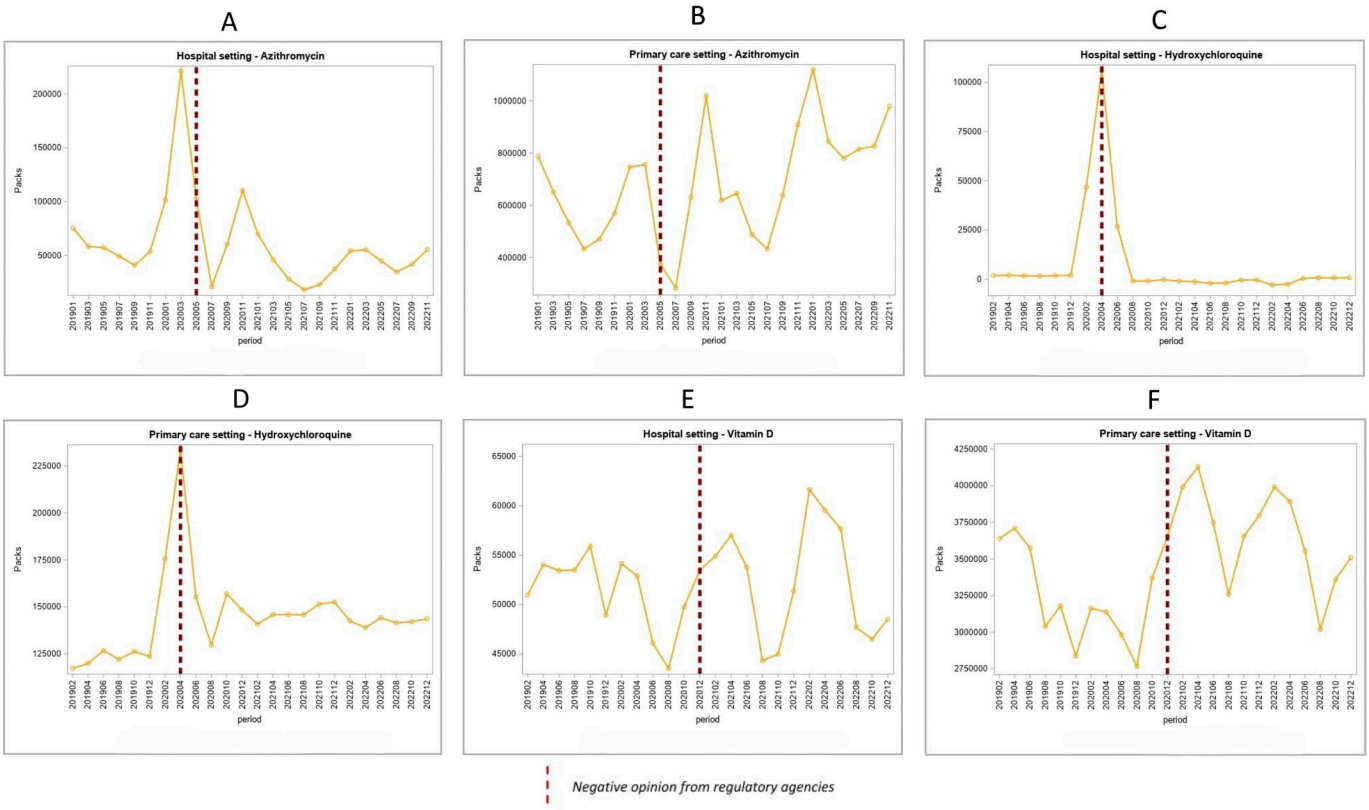

Figure 4 Time series of utilisation patterns of drugs for which regulatory agencies issued negative recommendation (dotted red line).

when the disease had a less dangerous course and consequently fewer patients needed intensive care. The more benign course of COVID-19 infections also seems to be demonstrated by an observed correlation for oxygen and LMWH, compared with COVID-19-positive subjects, in the primary care setting: in fact, the highest correlation between these categories of drugs and the number of positive subjects treated in the primary care setting occurs precisely in the vaccination phase. These trends probably indicate that more positive patients could be treated at home because they did not require hospitalisation. As reported by the Health Ministry circular of 26 April 2021, for COVID-19 patients with oxygen saturation values ≤92% who do not require hospitalisation, home oxygen therapy may be prescribed by the general practitioner.[21] The correlation between the use of supportive therapies for critically ill hospitalised patients (see injectable drugs, such as cardiac stimulants, general anaesthetics, and hypnotics and sedatives) and hospitalised patients also points in the same direction. The use of supportive therapies was higher in the phases preceding the vaccination campaign.

Evaluating how and which drugs were used to treat COVID patients in hospital and community settings provides important information about the progress of the pandemic, clinical management by health authorities as well as the ability of clinical practice to act in situations of uncertainty and adapt to rapidly changing evidence. In this regard, studies have been conducted to assess prescribing profiles for hospitalised COVID patients[12 22] or COVID outpatients,[23 24] but never, before our study, had the treatment of COVID patients as a whole been studied simultaneously in both settings. As reported by Alvarez *et al*,[12] during the first weeks of the pandemic in Spain, more than 70% of patients hospitalised with COVID infection had received hydroxychloroquine, lopinavir/ritonavir or azithromycin mostly in combination. A study describing the drug utilisation patterns over time in patients hospitalised with COVID-19 in the USA during 2021 showed that most common treatment regimens are represented by corticosteroids in monotherapy and by association of steroids/remdesivir, its use follows the hospitalisation trend and the treatment regimens evaluated are consistent with NIH guidelines.[22] The study conducted in the outpatient setting showed that, for COVID-19 outpatients, in some Italian regions, the most prescribed therapies were based on the antibiotic agent (mostly azithromycin) combined with corticosteroid,[23 24] also combined with antithrombotic[23] or vitamin D.[24] The prescription of hydroxychloroquine was limited to the first months.[23] Unlike ours, these studies are able to observe drugs directly dispensed to COVID patients, but they focus on only one of the two settings, hospital or primary care.

The uncertainty that characterised the early stages of the pandemic led to the use of drugs with little evidence of efficacy exposing patients to both the potential ineffectiveness of treatments and the risk of serious adverse

events. In the early phase of the pandemic (first half of 2020), a high sell-in of azithromycin, hydroxychloroquine, antivirals (darunavir–cobicistat and lopinavir–ritonavir) and immunosuppressants (tocilizumab, anakinra, baricitinib and sarilumab) was observed, but muscle relaxants and general anaesthetics were also used as supportive therapy in hospitalised patient requiring mechanical ventilation.[25] Some of these drugs, including azithromycin, hydroxychloroquine and the antiviral association lopinavir/ritonavir or darunavir/cobicistat, proved ineffective in clinical trials completed after the first epidemic phase.[26 27] As new evidence has emerged from clinical trials, therapies have become increasingly appropriate and effective, raising the need for further investigation into the prescribing profiles and therapies used to treat COVID-19 patients,[12 22–24] as well as how the pandemic has impacted prescribing profiles in chronic conditions or for primary care outpatients[10 11 28 29] or in certain patient populations, such as the elderly,[30] showing the impact of the COVID pandemic on both prescribing patterns and drug consumption for common chronic diseases.

This study has also assessed whether the use of drugs was consistent with the recommendations provided by health authorities. At the hospital level, it can be said that the use of drugs with a negative recommendation was promptly dropped; this is the case with hydroxychloroquine and azithromycin. The situation in primary care was different: azithromycin continued to be massively used (misused) even after the regulatory agency's negative opinion, as did vitamin D.

Thus, there appears to be a clear need to improve the dissemination of scientific information, also in order to promptly identify any obstacles to proper adherence to recommendations. In addition, timely monitoring made it possible to capture real-time prescribing trends and prevent any hoarding and/or shortages.

The strength of this study, although descriptive in nature, is represented by the overall population at risk in the country, the types of drugs overall distributed in different clinical settings and a long study period covering the prepandemic, pandemic and postpandemic periods.

Our study has some limitations. The irst limitation is represented by the use of aggregate data that do not allow to establish an individual link between COVID-19-positive patients (hospitalised or treated at home) and their actual drug consumption. Although in the limitation of aggregate data, they can provide useful information for very large phenomena with a dynamic trend, such as the coronavirus pandemic COVID-19. Moreover, it should be considered that the sell-in data used do not guarantee the actual use of drugs, but rather the purchase by hospitals (in the hospital setting) and community pharmacies (in the primary care setting). Finally, another limitation is that the private purchases of medicines by citizens have not been taken into account.

In conclusion, our study underlines the importance of drug monitoring systems, which through real-time assessment can provide important information on drug use. At an aggregate level, correlations between drug use and COVID patients could provide information on the evolution of the pandemic and the severity of the disease, as well as on the evolution of patients' pharmacological management. Indeed, assessing how and which drugs have been used to treat COVID patients in hospital and community settings provides important information on clinical management by health authorities, adherence to clinical practice guidelines for the treatment of COVID-19 patients, the ability to capture prescribing trends in real time and prevent possible hoarding and/or shortages and the ability of clinical practice to act in situations of uncertainty and adapt to rapidly changing evidence.

Acknowledgements Thanks to Linda Pierattini for the linguistic revision.

Contributors FT, ADF and MLM conceptualised and designed the study; ADF was in charge of the methodology and analysed the data; MLM, ADF, FT and GO prepared the original draft; MLM, ADF, FT, GO and DE reviewed, edited and approved the final manuscript for submission and accepted public access; FT supervised study design, data collection, data analysis, data interpretation and writing of the manuscript. All authors had full access to all the data in the study, take full responsibility for the finished work and the conduct of the study and the corresponding author had final responsibility for the decision to submit for publication. MLM is responsible for the overall content as the guarantor. All authors have read and approved the published version of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

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

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

ORCID iD

Maria Lucia Marino http://orcid.org/0009-0004-6255-4022

REFERENCES

1 Kalil AC. Treating COVID-19-Off-Label Drug Use, Compassionate Use, and Randomized Clinical Trials During Pandemics. *JAMA* 2020;323:1897–8.
2 Ammassari A, Di Filippo A, Trotta MP, *et al*. Comparison of Demand for Drugs Used for COVID-19 Treatment and Other Drugs During the

Early Phase of the COVID-19 Pandemic in Italy. *JAMA Netw Open* 2021;4:e2037060.
3 Available: https://www.quotidianosanita.it/scienza-e-farmaci/articolo.php?articolo_id=83695
4 Available: https://www.federfarma.it/Edicola/Comunicati-stampa/16-11-2020-12-48-09.aspx
5 Available: https://www.medicair.it/news/allarme-carenza-bombole-di-ossigeno-lappello-di-medicair-per-la-restituzione-dei-recipienti-vuoti-e-dei-contenitori-criogenici
6 Filippo A, Ambrosino F, Gallinella F, *et al*. L'uso dei farmaci durante la pandemia di covid-19 in Italia. Drug use during the covid-19 pandemic in Italy. *Recenti Prog Med* 2021;112:338–42.
7 Available: https://www.aifa.gov.it/en/monitoraggio-uso-farmaci-durante-epidemia-covid-19
8 Enners S, Gradl G, Kieble M, *et al*. Utilization of drugs with reports on potential efficacy or harm on COVID-19 before, during, and after the first pandemic wave. *Pharmacoepidemiol Drug Saf* 2021;30:1493–503.
9 Vaduganathan M, van Meijgaard J, Mehra MR, *et al*. Prescription Fill Patterns for Commonly Used Drugs During the COVID-19 Pandemic in the United States. *JAMA* 2020;323:2524–6.
10 Mian M, Sreedharan S, Giles S. Increased dispensing of prescription medications in Australia early in the COVID-19 pandemic. *Med J Aust* 2021;214:428–9.
11 Selke Krulichová I, Selke GW, Bennie M, *et al*. Comparison of drug prescribing before and during the COVID-19 pandemic: A cross-national European study. *Pharmacoepidemiol Drug Saf* 2022;31:1046–55.
12 Alvarez A, Cabia L, Trigo C, *et al*. Prescription profile in patients with SARS-CoV-2 infection hospitalised in Aragon, Spain. *Eur J Hosp Pharm* 2022;29:287–9.
13 Rosenberg ES, Dufort EM, Udo T, *et al*. Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State. *JAMA* 2020;323:2493–502.
14 Fajgenbaum DC, Khor JS, Gorzewski A, *et al*. Treatments Administered to the First 9152 Reported Cases of COVID-19: A Systematic Review. *Infect Dis Ther* 2020;9:435–49.
15 Available: https://www.who.int/europe/emergencies/situations/covid-19
16 Marcellusi A, Fabiano G, Sciattella P, *et al*. The Impact of COVID-19 Vaccination on the Italian Healthcare System: A Scenario Analysis. *Clin Drug Investig* 2022;42:237–42.
17 Available: https://github.com/pcm-dpc/COVID-19
18 Available: https://www.aifa.gov.it/documents/20142/1123276/azitromicina_05.05.2020.pdf
19 Available: https://www.aifa.gov.it/documents/20142/1123276/idrossiclorochina%20update05_22.12.2020.pdf
20 Available: https://www.salute.gov.it/portale/nuovocoronavirus/archivioFakeNewsNuovoCoronavirus.jsp?lingua=italiano&tagId=1314
21 Available: https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2021&codLeg=80056&parte=1%20&serie=null
22 Vititoe SE, Govil P, Baglivo A, *et al*. A Descriptive Cohort Study of Drug Utilization Patterns Among Patients Hospitalized With Coronavirus Disease 2019 in the United States, January 2021–February 2022. *Open Forum Infect Dis* 2023;10:fad339.
23 Belleudi V, Finocchietti M, Fortinguerra F, *et al*. Drug Prescriptions in the Outpatient Management of COVID-19: Evidence-Based Recommendations Versus Real Practice. *Front Pharmacol* 2022;13:825479.
24 Crisafulli S, Ientile V, L'Abbate L, *et al*. COVID-19 Patient Management in Outpatient Setting: A Population-Based Study from Southern Italy. *J Clin Med* 2021;11:51.
25 Filippo A, Cas R, Trotta F, *et al*. Cambiamenti nella domanda farmaceutica durante i primi mesi dell'epidemia. Changes in the demand for pharmaceuticals during the first semester of COVID-19 epidemic in Italy. *Epidemiol Prev* 2020;44:424–5.
26 Arabi YM, Gordon AC, Derde LPG, *et al*. Lopinavir-ritonavir and hydroxychloroquine for critically ill patients with COVID-19: REMAP-CAP randomized controlled trial. *Intensive Care Med* 2021;47:867–86.
27 Available: https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19
28 Aboulatta L, Peymani P, Vaccaro C, *et al*. Drug utilization patterns before and during COVID-19 pandemic in Manitoba, Canada: A population-based study. *PLoS One* 2022;17:e0278072.
29 Le-Dang MA, Nguyen-Thi HY, Dinh LP, *et al*. Impact of COVID-19 on patterns of drug utilization: A case study at national hospital. *PLoS One* 2024;19:e0297187.
30 Marengoni A, Cangini A, Pierantozzi A, *et al*. Impact of COVID-19 pandemic on medication use in the older Italian population. *Aging Clin Exp Res* 2023;35:443–53.