Impact of the COVID-19 Pandemic on Global Anticoagulant Sales: A Cross-Sectional Analysis Across 39 Countries

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The coronavirus disease 2019 (COVID-19) pandemic has been associated with important changes in the use of anticoagulants, including (1) the recommendation of low-molecular-weight heparin (LMWH) or fondaparinux to prevent thrombotic complications associated with COVID [1–3], and the increased use of direct oral anticoagulants (DOACs) in atrial fibrillation to prevent exposure to healthcare facilities for blood monitoring required with warfarin.

We quantified the change in global sales of anticoagulant agents after the COVID-19 pandemic declaration in March 2020.

MIDAS[®] data for August 2014–August 2020 were obtained from IQVIA [4], which contains retail and hospital drug purchase data for 39 countries. We extracted records for anticoagulants, including injectable anticoagulants (heparins and LMWH), vitamin K antagonists, and DOACs.

For each month and country, we calculated the number of units sold per 1000 population, and we conducted interrupted time-series analyses to examine changes in the trend of sales after the pandemic declaration in March 2020. Regression models included a continuous variable for month, an indicator variable for the period after March 2020, the interaction between them, and an indicator variable

for developing countries. To quantify country-level variation, we calculated the proportion change in the number of units sold in March–August 2020 versus March–August 2019. Due to the instability of estimates for smaller countries, we constrained these analyses of variation in units for March–August 2020 versus March–August 2019 to countries with a population of at least 20 million ($n = 17$ countries).

Before 2020, sales of anticoagulants increased by an annual average of 6%, driven by an annual average increase in sales of DOACs of 26%. Sales of vitamin K antagonists decreased by an annual average of 8%, and sales of injectable anticoagulants remained constant (Fig. 1). After the pandemic declaration in March 2020, there was a significant increase in sales of all anticoagulant products (p -value for level change = 0.006) and DOACs (p -value for level change = 0.019). Global sales of injectable products remained constant, while sales of vitamin K antagonists increased after the pandemic declaration, but the change was not significant ($p = 0.133$).

On average, countries purchased 11% more anticoagulant units in March–August 2020 than in March–August 2019 (Fig. 2). Russia and Mexico had the largest increases in sales of anticoagulant products, with increases of 39% and 40%, respectively. The UK was the only country with a decrease in sales of anticoagulant products (– 2%). Country-level variation in changes in anticoagulant sales was particularly large for injectable products. While global sales of injectable anticoagulants were lower in March–August 2020 than in March–August 2019, five countries increased their demand, most remarkably Australia (55%), Russia (42%), and Mexico (34%). Russia and Mexico also presented the greatest increases in purchases of DOACs (73% and 43%, respectively), while the US had the largest decrease in purchases of injectable anticoagulants (– 22%).

Our paper is subject to four main limitations. First, we did not include fondaparinux in analyses because of missing data for some countries. Second, because we did not have access to drug utilization data, it is possible that changes in

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Fig. 1 Trends in anticoagulant sales, August 2014–August 2020

purchases of anticoagulants did not translate into changes in their clinical use. Additionally, it is unclear what indications anticoagulants were used for. Third, we used March 2020 as the start of the pandemic period, even though the pandemic

peak did not happen simultaneously for all countries. Fourth, our analyses included countries with widely different health-care systems, where changes in purchases of anticoagulants may not similarly translate into changes in their use.

Nevertheless, our study is an important contribution to the literature on the impact of COVID on the demand for medications. Sales of DOACs presented a significant increase in March 2020, which could reflect patients' tendency to hoard medications in the early months of the COVID-19 pandemic for chronic indications of anticoagulants or switches from warfarin to DOACs to avoid exposing patients to health-care facilities for blood testing. Although injectable anticoagulants have been recommended to prevent thrombotic complications in hospitalized COVID-19 patients since May 2020, global sales remained constant through August 2020. Only a few countries increased demand for these agents, most remarkably Australia, Russia, and Mexico. Interestingly, the US presented the strongest decrease in purchases of injectable anticoagulants. This could reflect the marked decrease in non-COVID-19 hospital admissions observed in the US following the pandemic outbreak [5], or the long periods with postponed elective procedures, for which injectable anticoagulants are often recommended. Additionally, country-level variation in purchases of injectable anticoagulants could be due to variability in national and institutional stockpile reserves and in the implementation of policies in response to COVID. For example, in January

Fig. 2 Country-level variation in change in units March–August 2020 versus March–August 2019. The figure represents the proportion change between the number of units sold per 1000 in March–August 2020 and March–August 2019 at the country level. The lines represent median and interquartile range. Analyses were performed for the subset of countries with a population of at least 20 million ($n = 17$), including China, India, US, Brazil, Russia, Japan, Mexico, the Phil-

ippines, Germany, Turkey, the UK, France, Italy, Spain, Poland, Australia, and Canada. Countries excluded, with a population of < 20 million included Austria, Belarus, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Finland, Hungary, Kazakhstan, Lithuania, The Netherlands, New Zealand, Norway, Portugal, Romania, Slovakia, Sweden, Switzerland and Tunisia. DOACs direct oral anticoagulants

2020, Russia released special rules for the import, pricing, and distribution of pharmaceutical products [6], which could partially explain the high increase in anticoagulant purchases observed. Finally, international variability in purchases of anticoagulants could represent differential speed in the uptake of new scientific evidence and guideline recommendations on COVID-19 treatments. Future research using patient-level data should examine to what extent the decrease in purchases of injectable anticoagulants observed in the US was due to the decrease in demand for inpatient care for non-COVID-19 conditions versus a delay in the use of oral anticoagulants to prevent thrombotic complications associated with COVID-19.

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Declarations

Conflicts of interest Inmaculada Hernandez has received consulting fees from Pfizer and Bristol Myers Squibb, outside of the submitted work, and has served on an advisory board for Bristol Myers Squibb. Mina Tadrous, Jared W. Magnani, Jingchuan Guo, and Katie J. Suda have no conflicts of interest to declare.

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Consent for publication Not applicable.

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