Choppy waters: The importance of accounting for shifting drug utilization during the COVID-19 pandemic in future observational drug-related studies

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1 | INTRODUCTION

The 2019 novel coronavirus (COVID-19) pandemic caused a large shift in the delivery of health care globally, including prescription drugs. Media reports of drug stockpiling, anecdotal reports of an uptick in commonly used medications and off-label use of medications to treat COVID-19 have led to rapidly changing drug utilization trends.1 We have observed shifting drug utilization trends in a number of our ongoing projects globally. These shifting drug utilization trends should be of consideration for anyone conducting future observational drug-related studies—we write this Reflective Piece, Hot Topic as a word of caution to our colleagues.

2 | WHAT WE HAVE OBSERVED

Through a number of recent studies, our group has characterized the impact of COVID-19 on drug utilization, locally in Ontario, Canada, and also globally across 76 countries.2–6 Our research team developed a COVID-19 Ontario Prescription Drug Utilization Tool to provide provincial data on drug utilization during the COVID-19 pandemic.2 This tool reports weekly trends on the number and rate of individuals who were dispensed a prescription drug using claims data for all controlled substance and publicly funded prescriptions in the province. Through this initiative, we observed a rise in total prescription volumes, increased use of particular medications and excessive accumulation of various medications associated with COVID-19 for later use across the province of Ontario (ie stockpiling).

We observed three major changes that shifted the use of medications during this time period. Firstly, there was more frequent dispensing of chronic medications (eg drugs used to treat high blood pressure and diabetes). This trend was symptomatic of policies limiting the size of prescriptions to mitigate the pressure on the drug supply during a pandemic and has reversed since restrictions have eased. For example, in order to protect drug supply and ensure that sufficient medication would be available throughout the pandemic, the Ontario Ministry of Health, similar to other jurisdictions around the world, recommended that pharmacies dispense no more than a 30 days’ supply compared with the usual 90 days for many chronic drugs.7 Secondly, news about proposed COVID-19 treatments impacted the way people used medications. Global drug trends showed initial signs of increased use and stockpiling of hydroxychloroquine (HCQ) when it was initially suggested as a potential COVID-19 treatment.8
However, studies have since demonstrated that HCQ is likely ineffective in treating the virus and the use of the HCQ appears to have declined. Thirdly, there was a concern among people with chronic diseases that they might not be able to access their essential medications. As expected, we observed stockpiling across all jurisdictions of important drugs such as short-acting beta agonist (SABA) inhalers and insulin.

3 | CONSIDERATIONS FOR OBSERVATIONAL DRUG-RELATED STUDIES

Rapid changes in drug utilization and dispensing patterns, and how people use drugs will directly impact observational drug studies and have implications for future research. These changes should be considered when examining drug utilization trends, defining medication adherence and determining medication exposure in drug safety and effectiveness studies.

3.1 | Drug utilization trends

Drug utilization studies overall should account for the COVID-19 pandemic if they aim to measure the impact of changing policy or prescribing that overlaps with the pandemic. As highlighted, pandemic-related shifts across broad classes of drugs may impact trends which could be erroneously attributed to other interventions. For example, if a study was exploring opioid prescribing in 2020, they would likely find a rapid reduction in opioid prescribing. However, it is unlikely that this would be attributable to an opioid-specific change in policy or clinical practice, but instead would be due to fewer surgeries and dental procedures being completed during the pandemic, major indications for opioid prescribing. We suggest to either account for these changes by comparing to historical controls or when contextualizing drug utilization shifts during this time period, interpreting that it could be due to the COVID-19 pandemic.

3.2 | Adherence and continuous use definitions

The COVID-19 pandemic brought forward new challenges to measure adherence. Patient treatment compliance may have been impacted by media reports and studies that suggested increased mortality and morbidity of COVID-19 with a number of drugs. For example, angiotensin-converting enzyme (ACE) inhibitors and angiotensin II type 1 receptor blockers (ARBs) were initially suggested to worsen outcomes in COVID-19, possibly leading patients to reduce or discontinue use of their medications. These greater drops in adherence during this time period should be accounted by study design changes or adherence definition shifts. We also encourage consideration of future studies of guideline adherence/prescribing indicators at a population level that may be influenced by alterations in prescribing that occurred during the pandemic. For example, patients with hypertension might not have been prescribed ACE/ARBs due to suggestions that they may worsen outcomes among patients infected with COVID-19. Secondly, many international jurisdictions observed signs of patients stockpiling medications. This means some patients were dispensed more drugs than needed or may have extended time until next refill and it is important to account for these changes in our adherence measures (eg medication possession ratios). We suggest longer look forward windows with extended periods of observation to account for larger volumes held by patients.

3.3 | Study designs examining safety/effectiveness of medications

The shifting patterns of drug use during the COVID-19 pandemic may require adjusting of study design methods to correctly examine drug safety and effectiveness. As cited previously, adherence to medications may have shifted which can introduce gaps in therapy during the pandemic, thus impacting exposure definitions. Additionally, evidence in a variety of settings and indications suggests that some patients may see a rise in medication use (eg rising medication use in long-term care homes) or higher use of off-label medication (eg increased use of HCQ as COVID-19 prophylaxis). This can lead to protopathic bias where the background rates of drug utilization have increased leading to higher probability of exposure during the pandemic. For example, as the utilization of HCQ increases quickly over time, the likelihood of patients using it in the future is increased as a function of this rising use. Therefore, taking into account what is happening in the “background” of drug dispensing for future drug safety studies is imperative since this could also be associated with shifting outcome patterns (eg adverse drug events) on a population level.

4 | CONCLUSION

There are unique drug use patterns that transpired during the COVID-19 pandemic that need to be accounted for in future observational drug studies. We highlight the impact that these shifts may have on measuring patterns in drug utilization, medication adherence and the associated impact on studies that aim to examine drug safety and effectiveness. Potential solutions may vary by study design and question; however overall, observational drug-related studies must account for the changing drug utilization patterns that took place during
the COVID-19 pandemic. Lastly, although this Reflective Piece, Hot Topic uses Ontario, Canada, as a case example, we recommend future work to account for what happened in their specific jurisdiction as trends may differ. We suggest accounting for jurisdiction-specific policy changes and examining the local drug utilization patterns.

CONFLICT OF INTEREST
The authors declare that no potential conflicts of interest exist with respect to the research, authorship and/or publication of this article.

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