Objection Hearsay, Objection Overruled
Overriding Paxlovid Drug Interactions

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BACKGROUND

Paxlovid (nirmatrelvir/ritonavir) is 89% effective in patients at risk of serious illness due to Coronavirus Disease-19 (COVID-19). When considering the appropriateness of Paxlovid, prescribers must consider the potential CYP3A4 drug interactions and exercise clinical judgement in assessing the appropriateness. The University of Liverpool "COVID-19 Drug Interactions" reference is a resource commonly referred to by Australian clinicians which classifies interactions to support clinical judgement.

AIM

To understand the extent of prescriber clinical discretion when overriding severities of CYP3A4 drug interactions when prescribing Paxlovid.

METHODS

A retrospective, observational, scoping study reviewed patients charted Paxlovid between 1 January and 31 July 2022. To assess CYP3A4 drug interactions, patients with a Best Possible Medication History (BPMH) conducted by a pharmacist were included for analysis. All medications included in the BPMH were entered into the University of Liverpool "COVID-19 Drug Interactions" reference and classified as *Do Not Coadminister*, *Potential Interaction*, *Potential Weak Interaction* and *No Interaction Expected*.

RESULTS

209 drug interactions were assessed among 23 patients with a total of 39 overridden interactions with Paxlovid. On average, patients were on 9.1 medications, aged 78.7 years old [61-96] and the male to female ratio was 10:13. 28.2% (n=11) were classified as *Do Not Coadminister*, 38.5% (n=15) were *Potential Interaction* and 33.3% (n=13) *Potential Weak Interaction*. The average number of drug interactions per patient was 1.7. The most commonly implicated drugs were rosuvastatin (12.8%) and mirtazapine (10.3%). Of the top six medications with the most interactions, three were *Do Not Coadminister* medications – simvastatin, tamsulosin and apixaban.

DISCUSSION

This review confirms prescribers were most likely to exercise clinical discretion when overriding CYP3A4 drug interactions with a classification of *Potential Interaction* or *Potential Weak interactions*. Comparatively, there were lower numbers of *Do Not Coadminister* interactions. A greater sample size is required to improve the study's power.

Interaction Classification % of drug interactions assessed n=209

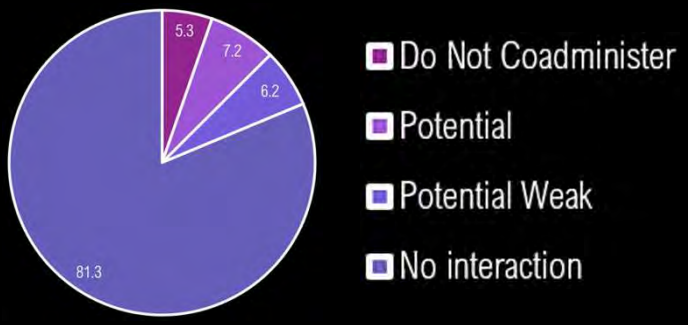

Figure 1: Classification of drug interactions as a percentage.

Interaction Classification % of overridden interactions n=39

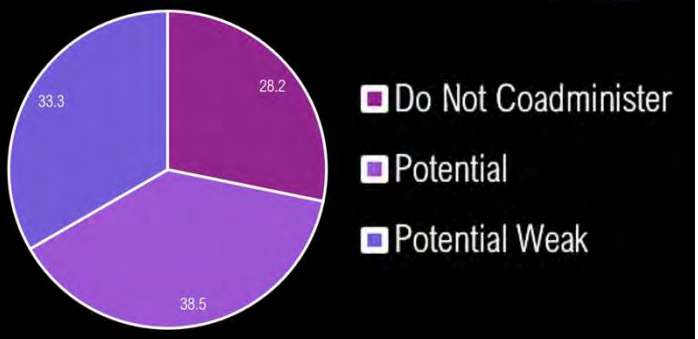

Figure 2: Classification of overridden interactions as a percentage.

Top 6 interactions n=39

rosuvastatin	12.8%
mirtazapine	10.3%
simvastatin	7.7%
atorvastatin	7.7%
tamsulosin	5.1%
apixaban	5.1%

Figure 3: Most commonly drug interactions.