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CYP2C19 Genetic Polymorphisms and Response to Proton Pump Inhibitors

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INTRODUCTION

Proton pump inhibitors (PPIs) undergo metabolism primarily by the CYP2C19 enzyme. Genetic polymorphisms in the CYP2C19 enzyme may affect response to PPI therapy, possibly leading to efficacy and tolerability issues.[1]

AIMS

To appraise evidence on the clinical relevance of CYP2C19 genetic variation and response to PPI therapy and identify priority patient groups for pharmacogenetics (PGx)-guided PPI therapy

METHOD

- **A literature appraisal covering a ten-year period (2012-2022) was conducted using PubMed® and ProQuest® using the search terms (proton pump inhibitor) AND ((pharmacogenetic) OR (pharmacogenomic) OR (CYP2C19)).**
- **Articles included were peer-reviewed, in English and available as free-full text. PRISMA was used as a reporting tool.**
- **The research was registered with the University of Malta Faculty of Medicine and Surgery Research Ethics Committee.**

RESULTS

- **The primary search identified 4,006 records, of which 108 articles were included in the review (Figure 1).**
- **86% of the articles focused on CYP2C19 genetic polymorphisms in relation to effectiveness of PPIs and 14% focused on side-effects.**
- **An association between CYP2C19 genetic polymorphisms and PPI therapy response was mostly reported in *Helicobacter pylori* infection (37%), with highest eradication rate in poor metabolisers (PMs).**
- **Other patient groups were paediatrics (22%), patients experiencing side-effects (15%), oesophagitis (12%), peptic ulcer disease/gastro-intestinal bleeding (12%), gastro-oesophageal reflux disease (10%).**
- **More persistent symptoms were reported in CYP2C19 rapid metabolisers (RMs) and normal metabolisers (NMs) and higher efficacy was reported in PMs.**
- **With respect to side-effects, worsening asthma control and increased risk of upper respiratory tract infections were reported in paediatric PMs on lansoprazole.**
- **In adults, PMs had increased risk of chronic migraines compared to NMs and RMs.**

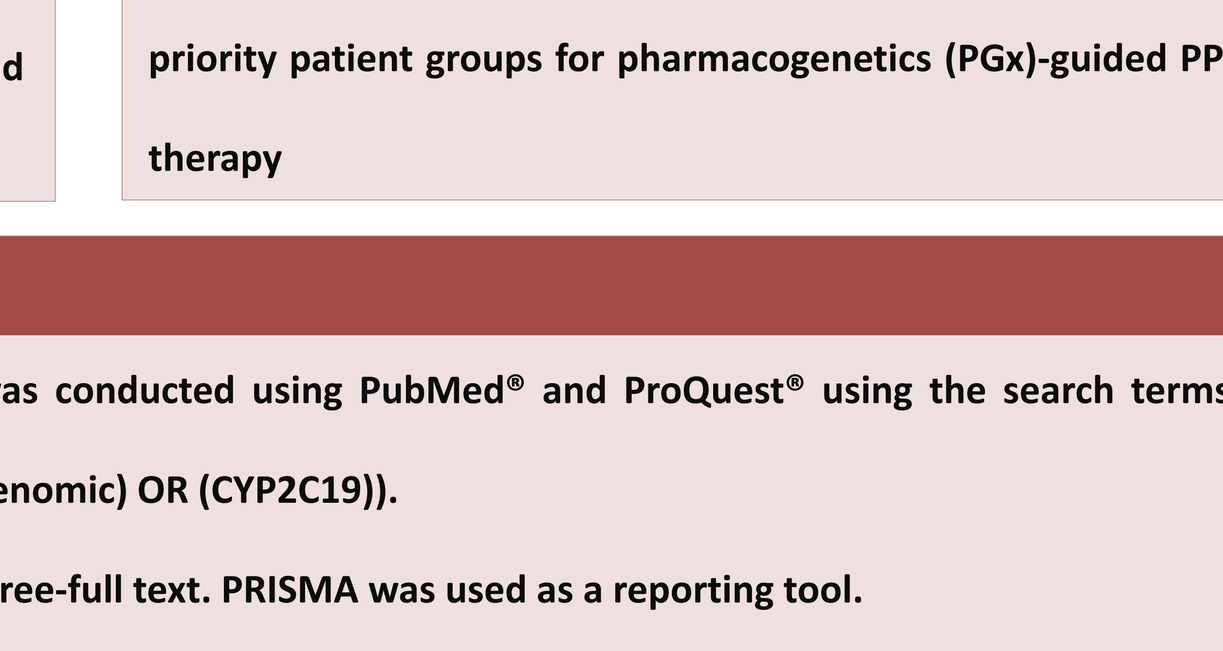

Figure 1: PRISMA flow diagram

- **Genotype-guided PPI therapy to improve outcomes was recommended in 15% of the articles.**
- **PGx testing for PPIs is being implemented successfully in paediatrics in the United States (US) in a prescriber-led setting, where genotype-guided dosing led to less upper respiratory side-effects.[2]**
- **Implementation is reported to have started in other areas of the US and in The Netherlands in patients experiencing side-effects and non-response to various medications including PPIs, where pharmacist and general practitioner-led genotyping are being piloted.[3-5]**

CONCLUSION

This literature appraisal described the application of PGx testing for the use of PPIs and identified patient groups where genotype may influence PPI therapy outcomes, hence supporting prioritisation for PGx-guided PPI therapy.

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