

Assessing the importance of gender and age-related influences of CYP enzyme activity; the next step into personalized medicine

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Background

- The cytochrome P450 (CYP450) system is a group of enzymes found in the liver, crucial for the breakdown and elimination of drugs from the body.
- Drug response is highly variable, 40-70% of patients experience ineffectiveness or adverse drug reactions (ADRs) [1]
- Psychiatric medications are frequently metabolized by CYP450 enzymes, and variations in enzyme activity can significantly impact their effectiveness and safety, and this can aid in selecting personalized medication [2].

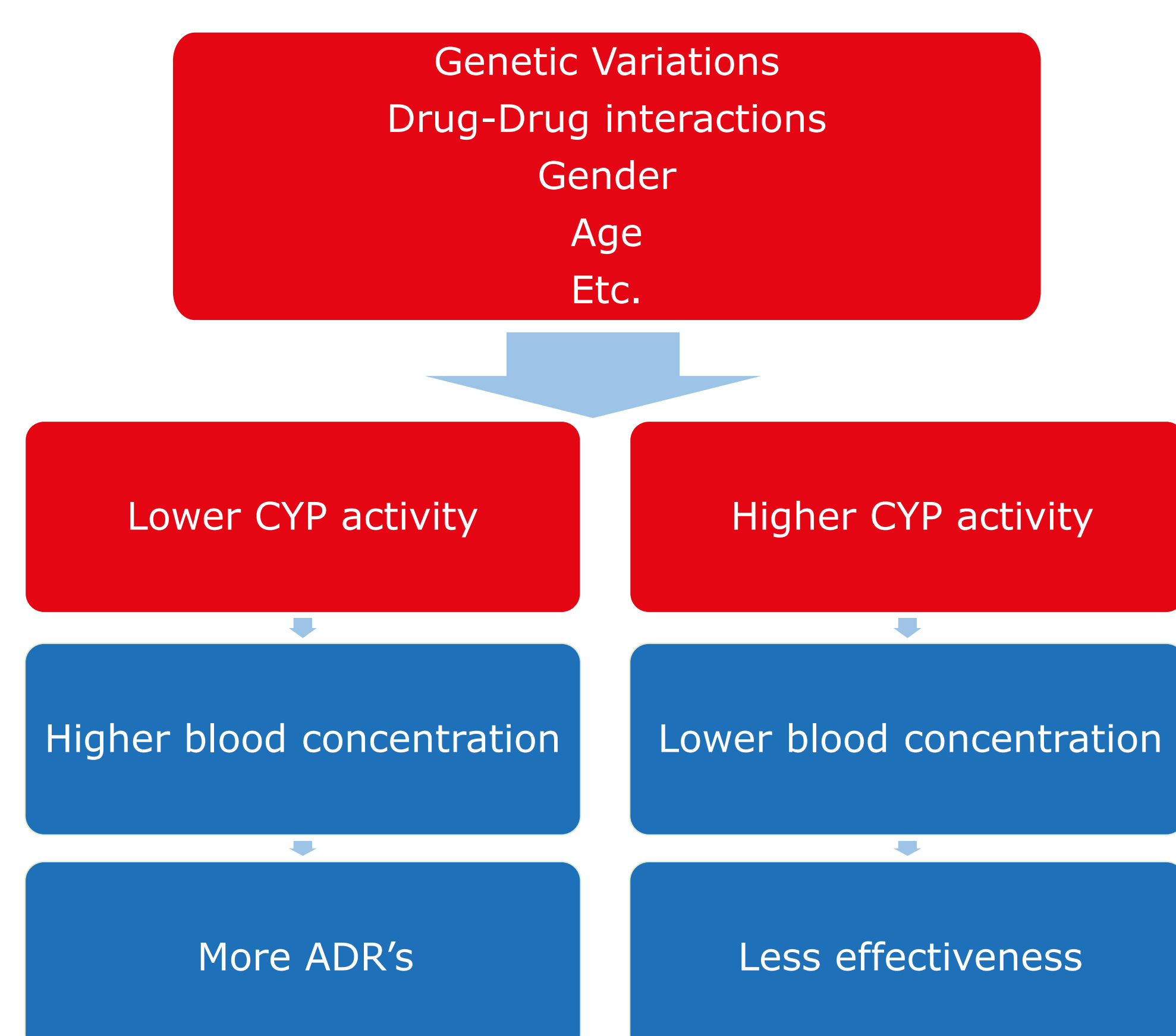


Figure 1. Visualisation of variability in cytochrome P450 enzymes and its effects on drug safety

- Research suggests that a significant proportion of ADRs and ineffective treatments can be attributed to genetic polymorphisms, with estimates ranging from 15% to 30%. [3]
- Observations have been made that indicate some gender and age differences in the activity of the CYP450 enzymes. However, the effects seem to be small.
- No recent reviews on the effects of gender or age on CYP mediated metabolism.
- Findings in this review could contribute to the field of personalized medicine and could help lower the burden of ADRs and might increase the effectiveness of available pharmacotherapy.

Methods

- A systematic search has been performed in Medline, Embase, PsycINFO, clinicaltrials.gov and The Cochrane Library to look for peer reviewed articles reporting on the human in-vivo original data on the influence of age or gender on the activity of five CYP enzymes with the help of the Ovid app interface.

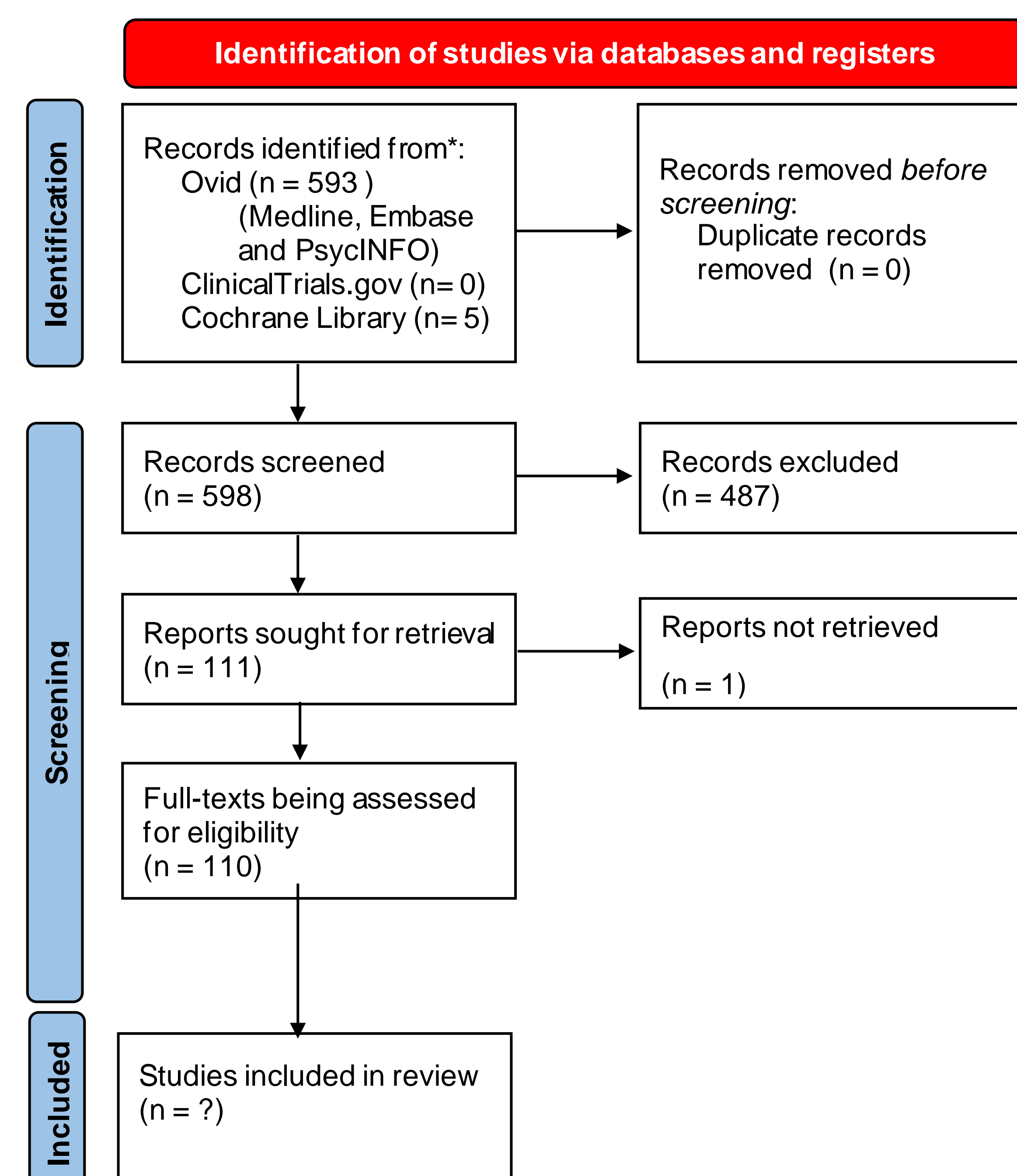


Figure 2. PRISMA flowchart

Results

- A first search yielded close to $n = 2200$ articles. After narrowing search terms, $n = 593$ articles were left. With 5 more articles found in the Cochrane library.
- These articles were screened with the help of screening app Rayyan, $n = 487$ articles were excluded, and $n = 111$ articles were sought for retrieval.
- Full-text articles are currently being assessed for eligibility

Preliminary findings

Some findings when looking at past reviews and current literature:

- Not all studies assessing P450 activity managed to genotype their subjects, opening their results up for a big confounding effect
- A first search yielded some results, indicating that;
 - Some articles suggest a marginal difference in CYP2C19 and CYP1A2 activity between genders [4, 5], while others CYPs seem to be unaffected [6].
 - There is an effect of age on CYP3A4 and CYP2C19 activity [5].
 - CYP2D6 activity seems to be largely unaffected by age or gender [7]

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