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Influence of CYP2C19 and CYP2D6 on Side Effects of Aripiprazole and Risperidone: A Systematic Review

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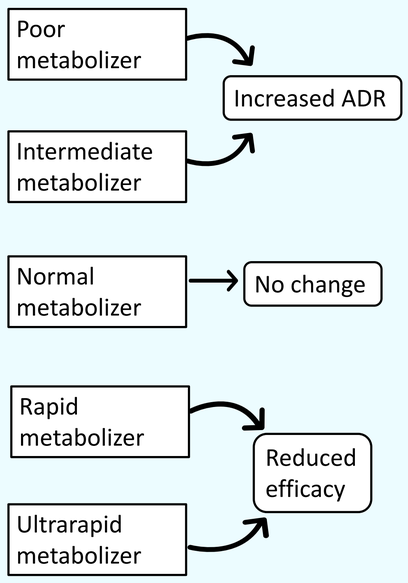
Background

Adapting medication choice and dose to interindividual differences in genetic variation encoding for hepatic cytochrome P450 (CYP) enzymes responsible for the metabolism of medications may improve treatment outcome [1]. In psychiatry, the CYP enzymes CYP2C19 and CYP2D6 have been of interest for this purpose [2][3]. Patients may be at increased risk of side-effects (in case of decreased metabolism) or inefficacy (in case of increased metabolism). In March 2023, the Dutch Pharmacogenetics Working Group released pharmacogenetic guidelines for antipsychotics based on previous pharmacogenetic studies, advising to reduce the dose of both aripiprazole and risperidone for poor metabolisers [4].



Objective

A summary of pharmacogenetic studies on the effect of CYP2C19 and CYP2D6 metabolizer status on side-effects and tolerability experienced by users.

Methods

On October 20th, 2022, a search was performed of the Pubmed, PsychInfo, Embase, Central, and Web of Science databases. On October 25th, 2022, Google Scholar was searched. After removal of duplicates, 1143 papers were scanned for inclusion. 34 papers were included.

Side-effects were categorized as "adverse reactions not otherwise specified" (ADR), extrapyramidal symptoms (EPS), prolactin, weight gain, QTc interval changes, and measures not falling in these previous categories.

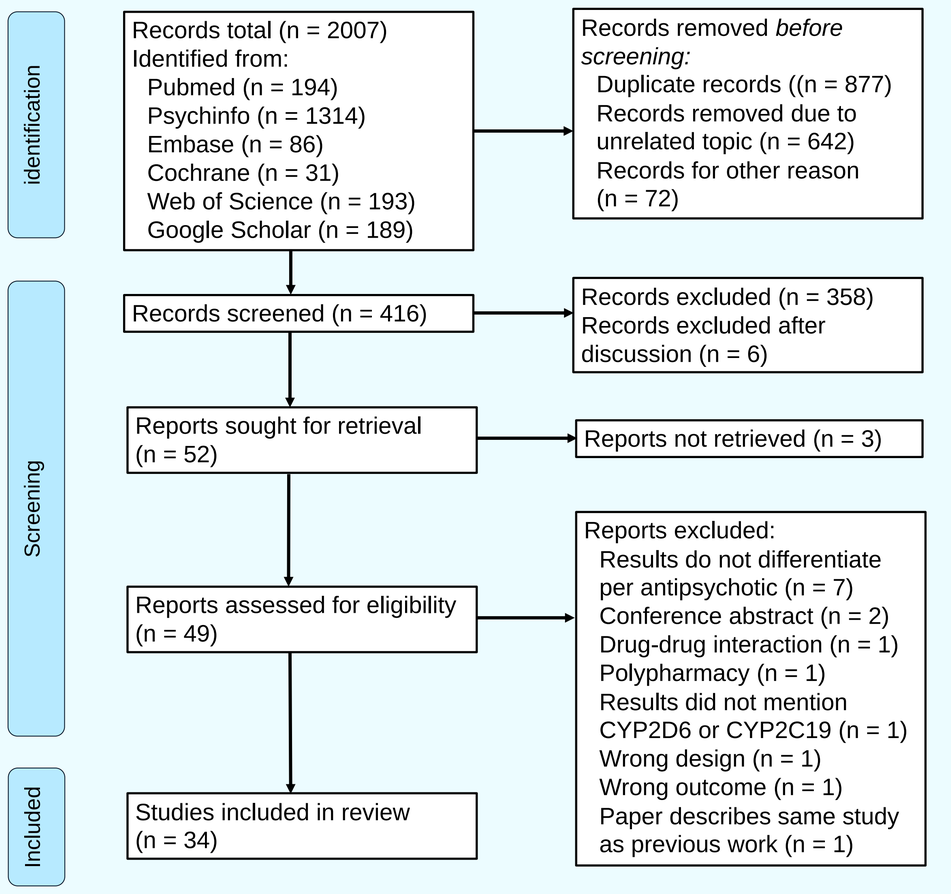


Figure 1: PRISMA flowchart

Results - Aripiprazole

- Four out of eight studies used an adult population, three of which healthy volunteers.
- None examined CYP2C19.
- Two studies in healthy adults reported increased prolactin or higher frequency of reported side-effects.
- One pediatric study found an association with CYP2D6 poor metabolizer status and BMI percentile change.

Results - Risperidone

- 2/3rd of 27 studies examined adults.
- One study examined CYP2C19 on ADR in adults and found a significant association with neurological side-effects.
- Six adult studies found a significant association with CYP2D6 and side-effects, where decreased CYP2D6 activity was associated with increased risk or report of side-effects

Conclusion

The results remain mixed and available evidence is insufficient. Some contributing factors may be considered:

- Heterogeneity between studies in methodology and sample.
- Lack of randomized clinical trials and control groups.
- Inability to account for confounding factors common in naturalistic designs.

This review demonstrates the need to establish a consensus regarding methodology and highlights the gap of studies examining CYP2C19.

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This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 945151.

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