

Supplementary Table 12. Detailed analysis of accumulated clozapine dosage in Australian protocols

Ronaldson et al.⁹⁶ defined rapid doses based on accumulated dosage by day 9

- One of the official Australian protocols recommends 612.5 mg.
 - The other protocol recommends 812.5 mg.
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Data from Ronaldson et al.⁹⁶ indicate these accumulated dosages are not always followed

- 15% of 401 titrations were more aggressive and reached ≥ 920 mg/day on day 9.⁹⁶
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The official Australian protocols are too aggressive for PMs of European ancestry

- The international guideline²⁸ proposed for non-PM patients of European ancestry an accumulated dosage on day 9 around 700 mg/day (roughly between both Australian protocols).
 - On the other hand, for PM patients of European ancestry it proposed an accumulated dosage around 262 mg/day, which is much lower. If the international guideline is correct, Australian patients of European ancestry be at risk of clozapine-induced myocarditis, including patients:
 - taking valproate,
 - taking oral contraceptives,
 - with any systemic inflammation or
 - perhaps those with obesity.
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These Australian dosages are inappropriate for patients of Asian ancestry

- The international guideline²⁸ recommends much lower accumulated dosages at day 9 for patients of Asian ancestry around:
 - 287.5 mg for non-PMs and
 - 187.5 mg for PMs.
 - The Australian titrations are likely to be very rapid for Asians.
 - No Australian study of clozapine-induced myocarditis has been published with data on the ancestry of the patients.
 - In the past, the majority of Australians were of European ancestry but Australia is fast becoming a diverse nation with recent census data estimating that one-third of the population was born outside of Australia. According to a 2019 article, since 2011, the proportion of Australian citizens born in China had increased from 6% to 8.3%.¹⁵⁸
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PM, poor metabolizers