Supplementary Table 14. Ethnopsychopharmacology relevant for patients of East Asian ancestry

East Asians need lower doses of diazepam: well described in the literature
• In typical doses, diazepam is mainly metabolized by CYP2C19 but at higher diazepam doses, the relative contribution of CYP3A4 ↑.[52] In CYP2C19 PMs it is metabolized by CYP3A4.[52]
• CYP2C19 PMs are frequent in East Asia with an average prevalence of 13% (versus 2% in Europeans)[180] and they have twice the serum concentrations of normal metabolizers.[181]
• As CYP2C19 PMs appear to have longer diazepam half-life and may have a higher risk of diazepam-induced sedation,[182] physicians from East Asian countries have empirically prescribed lower doses in East Asian populations than those recommended in the West.[183] In a meta-analysis of Japanese diazepam studies for anxiety, the maximum effective doses were 12−18 mg/day,[184] lower than those recommended in Western countries.
Some but not all East Asians may have greater risk for carbamazepine SJS/TEN: well described in the literature
• HLA-B*15:02 is strongly associated with carbamazepine-induced SJS/TEN.[185]
• HLA-B*15:02 throughout South and East Asian populations ranges from 22% in the Philippines to 1.5% in South Korea.[185] Therefore, in these countries genotyping for HLA-B*15:02 in all patients before starting carbamazepine is recommended as cost-effective,[186] since this drug should not be prescribed in patients with this allele.
• Japan is the exception with <0.1% HLA-B*15:02.[185] HLA variants in the Japanese population may differ from other East Asian populations due to differences in the genetic footprints of prehistoric migrations. A mix with some archaic humans (Denisovan) may be absent in the Japanese, but may influence the HLA genes of other East Asians.[187]
East Asians may need lower doses of olanzapine: not well described in the literature
• Olanzapine is also mainly metabolized by CYP1A2. As with clozapine dosing, olanzapine dosing may also be influenced by three levels of complexity: 1) ancestry groups, 2) sex-smoking subgroups and 3) presence/absence of PM status.[21,131] Olanzapine does not appear to be prone to cause inflammation or myocarditis;[157] a personalized olanzapine dosing guideline does not need to include CRP measures or worry about rapid titration causing inflammation.[21]
• Olanzapine has a wide therapeutic index of 4 (80/20=4).[25]
• The abstract of a single-dose study in 12 male Caucasians and 12 male Chinese in Singapore by the marketer,[188] stated that "the pharmacokinetics of olanzapine are similar in both Chinese and Caucasian racial groups." Based on the study data,[a] the author estimates the plasma/serum concentrations are the same for males of East Asian ancestry vs males of European ancestry when taking 1) 8 vs. 10 mg/day, or 2) 24 vs. 30 mg/day.
East Asians may need lower doses of haloperidol: not well described in the literature
• Western articles usually state that haloperidol is metabolized by CYP3A4 and that CYP2D6 PMs may need lower haloperidol doses.[24,64] Japanese articles disagree. In 1999, Kudo and Ishizaki[189] proposed that the greatest proportion of haloperidol metabolism is by UGT enzymes. In 2012, in an in vitro study, Kato et al.[190] reported that haloperidol glucuronidation is explained by several UGTs, but UGT2B7 is the most important.
• In a recent review of haloperidol pharmacokinetics,[61] the author commented that some patients of African-American ancestry may have longer elimination half-lives possibly due to differences in UGTs, but there was little understanding of the functional effects and racial variations of the UGT2B7 allele. Unfortunately, he was not aware of differences for East Asians.
• In a 2022 review of antipsychotics focused on differences for patients of East Asian ancestry, Lin[191] explained that haloperidol is among the antipsychotics that, under similar dosing, provides patients of East Asian ancestry with higher plasma concentrations than in Western studies.

[a]Table 1 from that article[188] indicates that a 10-mg single dose produced a significant difference (using only one dose and not repeated dosing) in a very small sample of only 12 male patients of both ancestries. CYP1A2, cytochrome P450 1A2; CYP2C19, cytochrome P450 2C19; CYP2D6, cytochrome P450 2D6; CYP3A4, cytochrome P450 3A4; CRP, c-reactive protein; HLA, human leukocyte antigen; PM, poor metabolizer; SJS/TEN, Stevens-Johnson syndrome/toxic epidermal necrolysis; UGT, UDP-glucuronosyltransferase enzymes; UGT2B7, UDP-glucuronosyltransferase 2B7