Supplementary Table 2. Basic concepts in pharmacokinetics

Concepts
• The term pharmacokinetics was first introduced in 1953.[16]
• The idea that different people may need different drug doses led to the development of a new science called pharmacogenetics.[17] Pharmacogenetic differences in pharmacokinetic genes are crucial in understanding differences in drug dosing.[14]
Genetic PMs and UMs
• Psychiatrists may not be aware that studies in the Karolinska Institute in Sweden on the TCAs have a major role in developing pharmacogenetics as a science.[17] First, some Swedish patients were found to have very high serum concentrations when given average doses and will respond to much lower doses; they were called PMs and this difference appeared to have a genetic basis.[18] Later on, these genetic PMs were found not to have the main metabolic enzyme for TCAs. These TCA PMs had two CYP2D6 alleles with no activity associated with CYP2D6 in their bodies. Third, in a couple of Swedish families, they found patients who had undetectable concentrations and were called UMs. TCA UMs had three or more active CYP2D6 alleles and synthesized too much CYP2D6.[19]
Non-genetic PMs and UMs
• Non-genetic PM/UM status can be caused by personal or environmental factors,[14] as long as they are present. Pharmacologists call this phenoconversion.[20] PM/UM causes, genetic vs non-genetic (phenoconversion), vary according to the metabolic pathways of the drugs, thus, across antipsychotics.[21]

CYP2D6, cytochrome P450 2D6; PM, poor metabolizer; TCAs, tricyclic antidepressants; UM, ultrarapid metabolizer