Although a good selection of antidepressants is available nowadays, the pharmacotherapy of depression still represents a challenge for psychiatrists worldwide. International guidelines and textbooks advise monotherapy with a selective serotonin reuptake inhibitor as treatment of first choice in depression. However, still one third of the depressive patients do not respond to the first antidepressant treatment implicated. Furthermore, approximately 20%-30% of them prove to be treatment resistant for two different antidepressants with different mechanisms of action. For these treatment resistant patients (TRD) augmentation and combination strategies are advised.

According to AMSP surveillance data (European international pharmacovigilance program, named AMSP: Arzneimittelsicherheit für Psychiatrie) from 2007 (obtained in 54 psychiatric institutions), 1829 depressive inpatients were recorded on the two reference days. 1674 inpatients received an antidepressant medication and among them 875 were concomitantly treated with an antipsychotic medication. Although the majority of inpatients were treated with one antidepressant (72%); 28% received two or more antidepressants. The most common combination of antidepressants was Venlafaxine with Mirtazapine (5.6%) being followed from Citalopram with Mirtazapine (2.7%). Interestingly similar findings have been recently reported from an US database.

Polypharmacy, although needed in treatment resistant cases, has a greater risk for adverse drug reactions and most augmentation strategies have not been tested regarding their long term safety. A combination of antidepressants seems only to be useful if they engage different mechanisms of action. Further clinical studies addressing combination strategies are needed in order to evaluate their benefit against monotherapy.