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Invited Letter Rejoinder

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Rejoinder to rejoinder to commentary

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First, we agree that the mortality gap is observed in people with severe mental illness, including schizophrenia, and driven in large part by cardiovascular deaths (Correll et al., 2017), and needs to be reduced, including by use of the least cardiometabolically problematic medications possible (Pillinger et al., 2020). Similarly, the insufficient recovery rates in schizophrenia (Jääskeläinen et al., 2013) need to be increased, and the treatment paradigm that focuses mostly on pharmacologic management needs to be expanded to include sufficient medical and psychosocial care. In fact, integrating psychosocial with pharmacological management was found to increase recovery rates by as much as 24% in early phase patients compared to usual care (Correll et al., 2018). However, while clearly remaining far too low, it is not true that recovery rates have dropped significantly over the past 50 years. Instead, they have remained unchanged (likely affected also by higher demands on people in education and at work), as indicated in the meta-analysis cited by Whitaker (Jääskeläinen et al., 2013) which reported an overall median recovery rate of 13.5%, without finding a significant time effect ($p = 0.70$). Moreover, a recent study following 98 first-episode patients treated with long-acting injectable antipsychotics for 24 months reported a recovery rate defined by concurrent symptomatic and functional remission of 44%, dropping to 29% when good overall quality of life was also required (Phahladira et al., 2020).

Concerning the detailed discussion on the meta-analysis of randomized trials by Khan, Faucett, Morrison, and Brown (2013), it is incorrect that raw mortality rates are more accurate than those adjusted for follow up since discounting duration of follow up obviously inflates raw mortality events in the group followed for a longer period of time during which more events can occur. Moreover, a more recent meta-analysis focusing only on the short-term treatment phase (excluding open extension phase data in antipsychotic treated patients, thereby, eliminating the use of person-years criticized by Whitaker) confirmed that there was no increased mortality risk with antipsychotics, reporting a non-significantly 31% lower mortality risk among patients with schizophrenia randomized to antipsychotics *v.* placebo (Schneider-Thoma et al., 2018).

Concerning the big-picture question, a recent nation-wide cohort study showed a large reduction in the standardized mortality (SMR) rate for suicide and a slight increase in the SMRs for cardiovascular illness and cancer. Overall, the all-cause SMR of patients with schizophrenia remained similar during the last 30 years (i.e. from 1984 to 2014), and both patients with schizophrenia and the general population live nowadays about 10 years longer (Tanskanen, Tiihonen, & Taipale, 2018). Nevertheless, we agree with Whitaker that much remains to be done to decrease the mortality gap and increase recovery rates, yet, we believe that the data indicate that antipsychotic maintenance treatment should be part of these efforts and is not counterproductive.

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