

Comment on Firth et al.: Lack of evidence that antipsychotics reduce the mortality risk

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We applaud Firth et al.¹ for addressing physical health in people with mental health problems and for proposing intervention and prevention targets. We were surprised, however, that the authors state, several times, that antipsychotics reduce mortality risk in people with psychotic disorders. A comprehensive review of the scientific evidence does not support this claim.

The authors cite only two observational studies to support this claim, both co-authored by Dr. Tiihonen, who has multiple ties to manufacturers of antipsychotics (e.g. he was lecturer/speaker, consultant, and/or advisory board member for Janssen-Cilag, Eli Lilly, Pfizer, GlaxoSmithKline, AstraZeneca, Bristol-Myers Squibb, and others; see his declaration here: <https://academic.oup.com/schizophreniabulletin/article/41/3/656/2375074>).

Observational studies have major limitations, including inadequate control for important confounders, and incomplete data on mortality and drug prescriptions.^{2,3}

The evidence from observational studies is inconsistent. Contrary to the two favourable studies selectively cited by Firth et al.,¹ there are epidemiologic studies suggesting that mortality risk is increased with antipsychotics.³

Randomised placebo-controlled trials don't indicate that antipsychotics reduce the mortality risk.⁴ Indeed, if meta-analysis is restricted to the elderly and dementia patients, mortality risk is increased relative to placebo.⁴

Firth et al. are correct that there is a compelling body of evidence that antipsychotics have adverse cardiometabolic effects.¹ A meta-analysis of randomised placebo-controlled trials confirms that most antipsychotics are cardiotoxic, and cause weight gain, and endocrine dysfunction.⁵ These side effects are major risk factors for death due to cardiometabolic disease.¹

In view of these conflicting lines of evidence it is not correct to claim that antipsychotics reduce the mortality risk in people with psychotic disorders and we should remain mindful of the possibility that they may increase this risk.

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