

## Critique of FIN11 Study: What Role Do Antipsychotics Have in Increasing Mortality in Schizophrenia?

The following is an extract of:

De Hert M, Correll CU, Cohen D. Do antipsychotic medications reduce or increase mortality in schizophrenia? A critical appraisal of the FIN-11 study. *Schizophrenia Research* 2010,117:68-74.

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### Bottom Line:

- The FIN11 study found lower mortality among consumers treated with antipsychotics. Those on clozapine had lower all-cause mortality and death from suicide, and no increased death from cardiovascular causes.
- De Hert and colleagues argue that methods and analysis used in the FIN11 study may have obscured the potential cardiovascular contribution to mortality that other researchers have found.

### FIN11 Background

The FIN11 study, published in *The Lancet* in 2009, looked at consumers with a diagnosis of schizophrenia. This study had a number of outcomes, some of which were controversial and at odds with other studies, particularly the absence of increased mortality due to cardiovascular disease for high risk drugs. De Hert et al, wrote a response in which they discuss several analytical and methodological issues that could explain the results of the FIN11 study.

### Conceptual and Methodological Aspects

The authors present concerns about the data and its analysis, along with a “wish list” for additional analyses that would be of interest to researchers and clinicians. Concerns include: 1) need for a table with demographic data, more data on illness duration and treatment, and data on the distribution of antipsychotics used in polypharmacy, which would provide a more complete understanding of potential confounding variables; 2) the impact of factors such as age and illness duration on the differential use of first vs. second generation antipsychotics; 3) overestimation of the mortality benefit of clozapine due to its use later in the course of treatment when suicide risk is lower. De Hert et al observe that the mortality rates for clozapine in the FIN11 study are considerably lower than those found in other studies, and note that it is unclear whether methodological issues contributed to this lower mortality rate. Other issues include: 1) failure to provide additional analysis of the polypharmacy group, which represents 40% of the person years studied in FIN11; 2) restriction of mortality data to those who died outside the hospital or in the first 2 days of hospitalization, potentially excluding people who died due to cardiovascular disease during prolonged hospital stays; 3) absence of increased mortality in people taking medications with the highest cardiometabolic risk (clozapine and olanzapine), which would be expected in light of past studies.

### Discussion and Conclusions

De Hert et al note the importance of the FIN11 findings, namely that those with schizophrenia and who are not taking antipsychotics have an increased risk of dying, and that these people need closer monitoring and improved treatment. The authors note that methodological flaws may explain the discrepant results between FIN11 and other studies, specifically the role of certain antipsychotics in contributing to cardiovascular disease and death.

Drs De Hert, Correll and Cohen report receiving honoraria, being consultants for or receiving grant/research support from various pharmaceutical companies