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**Title:**

SCHIZOPHRENIA TREATMENT WITH SECOND-GENERATION ANTIPSYCHOTICS: A MULTI-COUNTRY EVALUATION OF THE COSTS OF CARDIOVASCULAR AND METABOLIC ADVERSE EVENTS AND WEIGHT GAIN.

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**Abstract:**

**OBJECTIVES:** Second-generation antipsychotics have similar effectiveness for the treatment of schizophrenia symptoms, so drug choice is often based on differences in rates of adverse events. Relapse is also a key driver of treatment costs. The key aim of this study was to compare the costs due to adverse events, and how they varied across European countries.

**METHODS:** Systematic searches were conducted to identify evidence on effectiveness and costs. A Markov model was developed to assess the costs of ten antipsychotics: aripiprazole, brexpiprazole, cariprazine, lumateperone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone and ziprasidone. Costs were obtained for seven countries: Italy, Hungary, France, Slovenia, Spain, Sweden and the UK. The costs considered were adverse events (including diabetes, myocardial infarction, stroke and weight gain), drug costs, relapse, treatment discontinuation and schizophrenia management. Acute and stable adult populations were modelled, with a life-time horizon for both.

**RESULTS:** For the acute population, the lowest lifetime costs were observed for lurasidone for all seven countries. The second lowest costs were for ziprasidone. The main drivers of cost differences were diabetes and cardiovascular diseases, which were lowest for lurasidone, followed by ziprasidone then lumateperone. Costs for managing weight gain were lowest for ziprasidone and lurasidone. The stable population provided similar results. The contribution of diabetes and cardiovascular diseases to total costs varied from less than 40% in Slovenia and Sweden to over 70% in Hungary and Italy.

**CONCLUSION:** Lurasidone was associated with the lowest total lifetime costs in the acute population in seven European countries compared to nine antipsychotics. This was primarily due to the avoidance of diabetes and cardiovascular events. The rankings of the remaining antipsychotics varied by country, emphasising the importance of considering country-specific costs. Future research should investigate the individual costs of relapse management, including differences in the costs and proportions of hospitalizations.