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

Kearns B¹, Cooper K¹, Cantrell A¹

¹School of Health and Related Research, The University of Sheffield

Introduction

Treating cardiovascular and metabolic diseases can be very costly. 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. As schizophrenia is a life-long disorder it is important to consider the lifetime costs associated with the choice of antipsychotic. The aim of this study was to estimate these costs, 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 country-specific costs used are provided in Table 1 in US\$ for comparability. For analyses, country-specific currencies were used. Acute and stable adult populations were modelled, with a life-time horizon for both. Risk models (QRisk3, Qdiabetes) were used to predict the incidence of cardiovascular and metabolic events. Both short-term and long-term evidence was considered for the outcomes of Table 1, with evidence taken primarily from published network meta-analyses [1-4]. A model schematic is provided in Figure 1.

Table 1: Country-specific annual per patient costs (US \$2018).

	France	Hungary	Italy	Slovenia	Spain	Sweden	UK
Weight gain	624	47	229	229	229	463	208
Diabetes	6,677	5,046	3,478	1,242	2,062	3,417	6,553
Fatal CVD event	8,142	4,137	5,178	4,137	10,575	8,175	5,158
CVD event Year 1	23,572	3,006	7,310	11,685	13,557	6,325	4,093
CVD event Years 2+	3,272	1,170	6,405	496	11,060	2,207	1,702
Metabolic syndrome	970	970	970	970	970	970	970
Hyperprolactinaemia	172	83	197	83	360	860	404
QT prolongation	441	129	493	129	477	1,461	832
Stable disease	1,508	612	341	1,089	4,949	10,826	2,497
Relapse	13,707	3,960	1,746	13,352	9,866	16,687	10,605
Treatment switching	330	97	370	97	358	1,096	624

CVD: Cardiovascular disease. Includes country-specific proportions of stroke and myocardial infarction.

Figure 1: Model schematic.

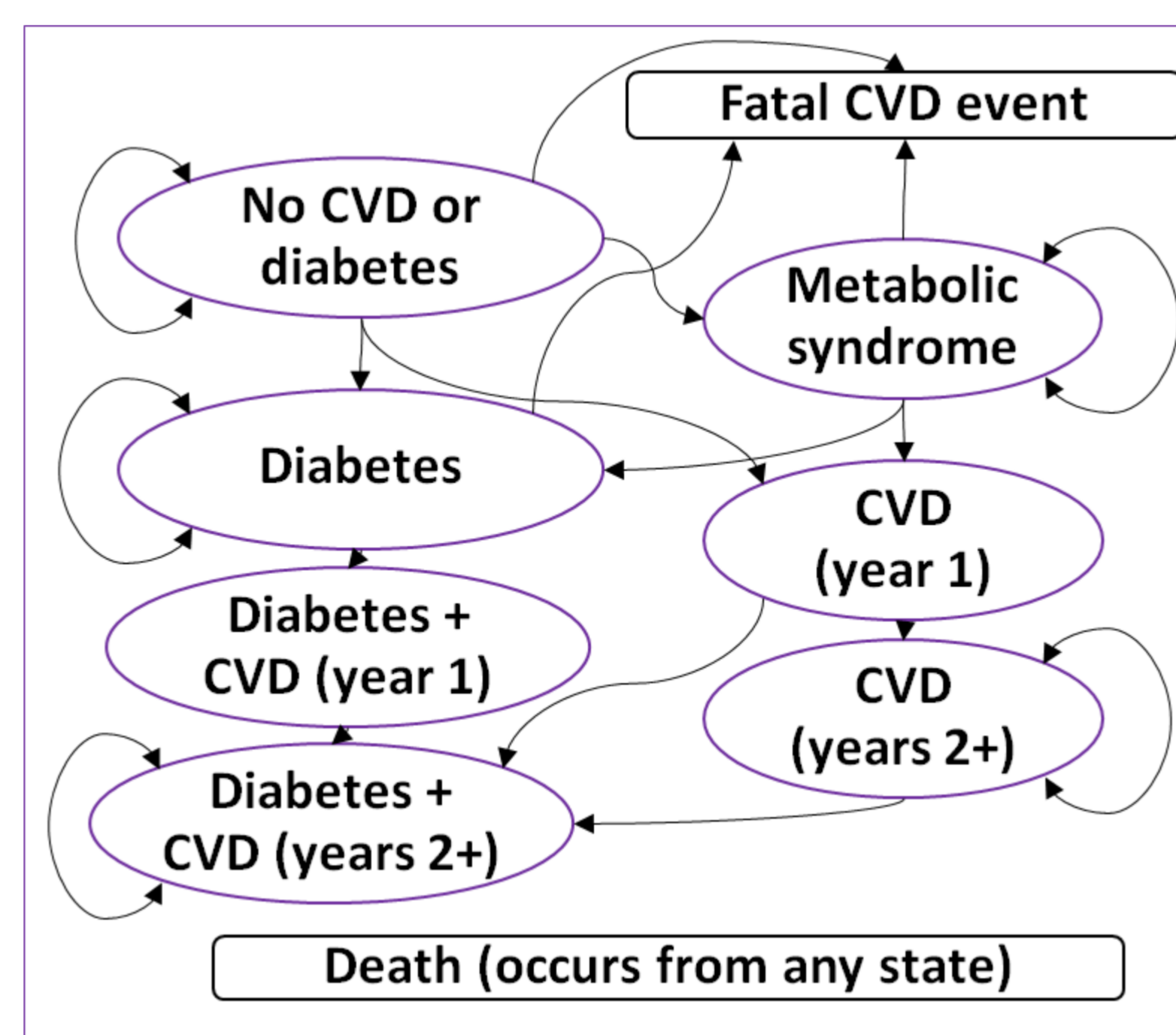


Figure 2: Heat map of total costs: green = lowest, red = highest.

	France	Hungary	Italy	Slovenia	Spain	Sweden	UK
Lurasidone	Green	Green	Green	Green	Green	Green	Green
Ziprasidone	Green	Green	Green	Green	Green	Green	Green
Risperidone	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green
Aripiprazole	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green
Brexpiprazole	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green
Paliperidone	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green
Quetiapine	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green
Cariprazine	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green
Lumateperone	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green
Olanzapine	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green	Light Green

Results

An overview of total costs by drug and country is provided in Figure 2 for the acute population as a heat map. Green and red colours indicate lower and higher total costs, respectively. Results were similar for the stable population.

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 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.

Olanzapine and lumateperone had the highest total cost for all seven countries. For lumateperone, the main cost driver was the drug cost which contributed to between 21% and 46% of total costs. For the other antipsychotics, drug costs varied from 1% of the total cost (olanzapine in France and Spain) to 10% (lurasidone in Hungary).

Discussion

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, although costs of weight gain were also lowest for these two drugs. The rankings of the remaining antipsychotics varied by country, emphasising the importance of considering country-specific costs. Future research could investigate the costs of relapse management, including differences in the costs and proportions of hospitalizations.

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