ODPRN ONTARIO DRUG POLICY RESEARCH NETWORK

Atypical Antipsychotic Use for the Behavioural and Psychological Symptoms of Dementia in the Elderly

Final Report: Pharmacoeconomic Unit

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Executive Briefing

- In this report, the current evidence for the cost-effectiveness of atypical antipsychotics versus typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly, and the economic impact of alternative changes to the funding status of atypical antipsychotics, were assessed.

- Two relevant economic evaluations were identified for inclusion in this review. Assessment of these two studies revealed a lack of information from a Canadian perspective and limited evidence comparing active treatments. Therefore, no inferences could be made about the cost effectiveness of atypical antipsychotics versus typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly.

- Given the paucity of published economic evidence, a Markov model was developed to facilitate assessment of the cost effectiveness of atypical antipsychotics. However, the lack of pertinent clinical evidence precluded the conduct of the necessary analysis. Thus, no conclusions over the cost effectiveness of atypical antipsychotics can be made.

- In 2013, Ontario Public Drug Plan (OPDP) expenditure for atypical antipsychotics was just over $35 million among patients ages 65 and over ($15.9 million for patients 65-74 years, $10.7 million for patients 75-84, and $8.3 for patients >85 years). Expenditure on all antipsychotics was $38.1 million of which $16.4 million was for residents of long term care facilities. Strategies to reduce prescribing of all antipsychotics for all patients within long term care facilities could reduce expenditure by up to $8.1 million, although under less favourable assumptions the reduction ranged from $2.5 to $5.0 million.

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List of Abbreviations

AD	Alzheimer's disease
ADCS-ADL	Alzheimer's Disease Cooperative Study Activities of Daily Living Scale
ADRQOL	Alzheimer's Disease Related Quality of Life Scale
CAD$	Canadian dollars
CDR	Clinical Dementia Rating
CIHI	Canadian Institute for Health Information
CMA	cost-minimization analysis
CUA	cost-utility analysis
ICES	Institute for Clinical Evaluative Sciences
ICUR	incremental cost-utility ratio
KAS	Kelley-Anne Sabarre
KT	Kylie Tingley
MMSE	mini-mental state examination
MOHLTC	Ministry of Health and Long-Term Care (Ontario)
N/A	not applicable
ODPRN	Ontario Drug Research Policy Network
OPDP	Ontario Public Drug Plan
PSA	probabilistic sensitivity analysis
QALY	quality-adjusted life year
RCT	randomized controlled trial
USD$	American dollars

Acknowledgments

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Executive Summary

Research Questions

RQ1. What is the current evidence for the cost-effectiveness of atypical antipsychotics versus typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly?

RQ2. Based on a de novo economic model, what is the cost-effectiveness of atypical antipsychotics versus typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly?

RQ3. What is the economic impact of alternative policies for reimbursing atypical antipsychotics versus typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly?

Review of Economic Literature for Antipsychotics

Two studies met the criteria for inclusion for this review[1,2]. The study by Kirbach et al[1] was a cost utility analysis of olanzapine compared with no treatment in patients aged 65 years and over with agitation and psychosis related to Alzheimer's disease. From a health care system perspective, the incremental cost-utility ratio for olanzapine compared with no treatment was $49,762 per QALY in CAD$ 2014 [1 USD$= 1.1571 CAD$]. From a societal perspective, the incremental cost-utility ratio for olanzapine compared with no treatment was $17,636 per QALY in CAD$ 2014.

The study by Rosenheck et al[2] was a cost-utility analysis of initiation of therapy with an atypical antipsychotic (olanzapine, quetiapine, or risperidone) compared with watchful waiting (delay in initiation of therapy) in ambulatory outpatients living at home or in assisted living with Alzheimer's disease. The average age of this patient population was 77.9 years and patients had a Mini-Mental State Examination score between 5 and 26. From a health care system perspective, total health costs were lower for watchful waiting compared with olanzapine, quetiapine, or risperidone; and, there was no significant difference in QALYs. Although not a focus of this study, a comparison across the antipsychotics can be made with risperidone appearing less costly and resulting in more QALYs than olanzapine and quetiapine.

Applicability of these studies to the present research question is limited given that they are not from the Canadian perspective, nor do they include any analyses directly comparing active treatments.

Refer to Appendix A - A Systematic Review of Economic Evidence for a detailed report of the review of economic literature for atypical antipsychotics.

De novo Economic Evaluation

Given the results of the review of the economic literature, a Markov model was designed to assess the cost effectiveness of atypical antipsychotics in the management of behavioural and

psychological symptoms of dementia in the elderly. The model simulated both the progression of Alzheimer's disease and the movement to long term care with transition probabilities affected by the presence of behavioural and psychological symptoms. The model utilized the most recent data on the costs and utilities associated with progression with Alzheimer's disease, the location of care and the presence or absence of behavioural or psychological symptoms.

Data on the effectiveness of atypical antipsychotics on the relief of behavioural and psychological symptoms were unavailable. Thus, no analysis could be conducted. The Markov model is available for analysis should such data become available.

Given the results of the review and the inability to conduct any de novo economic modelling, no statements relating to the cost effectiveness of atypical antipsychotics in the management of behavioural and psychological symptoms of dementia in the elderly can be made.

Refer to Appendix B – De novo Economic Evaluation for a more detailed report.

Reimbursement Based Economic Evaluation

Total OPDP expenditure for atypical antipsychotics in 2013 for patients 65 years and older was just over $35 million. This represents 92% of OPDP expenditure on antipsychotics among those aged 65 and over. Broken down by age, 2013 expenditure for atypical antipsychotics was $15.9 million for patients 65-74 years, $10.7 million for patients 75-84, and $8.3 for patients >85 years. Expenditure in 2013 for atypical antipsychotics among patients living in long-term care facilities was lower ($15.4 million) than for those living in the community ($19.6 million).

Given that antipsychotics are used off-label for the treatment of Alzheimer's disease and dementia, conclusions of the analysis can be considered preliminary due to difficulties in obtaining accurate data. However, estimates of the impact of various initiatives to reduce the use of antipsychotics in long-term care facilities were explored using data from 2013. Based three such initiatives, two from Canada (Alberta and Manitoba) and one from the United States, we estimate that expenditure for all antipsychotics could be reduced by up to $8.1 million.

Further analysis was conducted to assess the impact of reducing antipsychotic prescribing by assuming there would be modest reductions (15-30%) in antipsychotic use in only those with dementia. Based on forecasting expenditure for 2016, we estimate that expenditure for all antipsychotics could be reduced by up to $5.0 million.

Refer to Appendix C – Reimbursement Based Economic Evaluation for a more detailed report.

Appendices

Appendix A - A Systematic Review of Economic Evidence

Research Question

RQ1. What is the current evidence for the cost-effectiveness of atypical antipsychotics versus typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly?

Review of Published Literature

Search Strategy and Search Findings

Search Strategy

A search of the literature from 1946 to present (2014 September 30) in Ovid Medline (indexed, in-process and other non-indexed) and Embase Classic & Embase 1947 to 2014 September 29 was conducted in order to capture all relevant literature. Key words relating to antipsychotics for the management of behavioural and psychological symptoms of dementia were combined with a standardized search strategy for identifying economic analyses adopted by National Health Service Economic Evaluation Database (NHSEED). The complete search strategy can be found in Appendix A1: Search Strategy.

The Tufts CEA registry and NHSEED were also searched for relevant articles. Grey literature was identified through the Canadian Agency for Drugs and Technologies in Health and National Institute for Health and Care Excellence websites. Reference lists from relevant reports were hand searched to identify any additional potentially relevant articles. Finally, we searched evidence submission packages from manufacturers for any relevant reports.

Search Findings

A total of 702 reports were identified: 700 reports from the original search, 0 additional citations from manufacturers, and 2 from grey literature. Results of the search can be found in Appendix A2: Results of Literature Search.

Two reviewers (KAS and KT) independently reviewed the literature to identify potentially relevant articles for the review. Any disagreements were resolved through consensus. Based on titles and abstracts, 74/702 studies were selected as potentially relevant for the review. 628 citations were excluded for the following reasons: not an economic analysis, not dementia, or not relevant intervention. An additional 14 citations were excluded because the reports were non-English, not available or not full text.

Full reports for the 74 potential studies were reviewed by two reviewers (KAS and KT). Of these, 2 publications which addressed the objective of this review were selected for inclusion. Those studies that were not included in the review along with the reasons for exclusion are detailed in Appendix A3: List of

Excluded Studies

Included Studies

The comprehensive list of included studies can be found in Appendix A4: List of Included Studies.

Summary and Critical Appraisal of Included Studies: Antipsychotics for Dementia

Included Studies

The two included studies adopted different analytical frameworks. The more recent study was cost-utility analysis using a Markov model with a 13 year timeframe. The other study was a cost-utility analysis using a trial-based approach and a 9 month timeframe. Both studies were conducted from a health care system perspective; however, one study also included analyses from a societal perspective. Each study adopted at least one form of sensitivity analysis, either one- and multi- way sensitivity analysis or probabilistic sensitivity analysis.

Different patient populations were described for each study. One analysis focused on patients aged 65 and older with with agitation and psychosis related to Alzheimer's disease. The other study considered ambulatory outpatients living at home or in assisted living with Alzheimer's disease, an average age of 77.9 years, and a Mini-Mental State Examination score between 5 and 26.

In terms of treatment comparisons, one study compared a single atypical antipsychotic to no treatment whilst the other compared initiation of therapy with one of three atypical antipsychotics versus watchful waiting with delayed initiation of therapy.

A table summarizing included studies is provided in Appendix A5: Characteristics of Reviewed Studies.

The quality of each study was assessed in terms of: source of effectiveness data; whether cost effectiveness was measured in terms of final outcomes; and adoption of sensitivity analysis.

The applicability of each study was assessed in terms of: sponsorship, perspective, distinct populations and reporting of results compared to active treatments.

Concerns and Considerations Relating to the Literature

<u>Paucity of evidence</u>

Given only two studies met the inclusion criteria for this review, we conclude that there is a paucity of evidence regarding the cost effectiveness of atypical antipsychotics compared with typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly.

<u>Comparators</u>

In terms of treatment comparisons, one study compared a single atypical antipsychotic with no treatment, whilst the other study compared initiation of therapy with one of three atypical antipsychotics with watchful waiting with delayed initiation of therapy. Although not a focus of the

latter study, it was possible to infer the cost effectiveness between the atypical antipsychotics.

Canadian context

There were no relevant reports from a Canadian perspective. The available studies were from a US perspective.

Distinct Population

In the context of reimbursement, it may be important to consider patient groups based on location of residence: institutionalized patients compared with community dwellers. In one study, institutionalized patients were modelled in a separate health state from community dwellers. However, in the other study, both institutionalized patients and community dwellers were combined.

Included Studies

Kirbach et al. (2008)

Kirbach et al[1] considered the cost effectiveness of olanzapine (5.5 mg daily) compared with no treatment in patients aged 65 years and over with agitation and psychosis related to Alzheimer's disease from a US health care system and societal perspective. The authors report that no funding was received to complete this study.

The study was conducted using a Markov model with a lifetime timeframe (13 years) and a 6 month cycle length. Institutionalized patients were modelled in a separate health state compared to community dwellers. Efficacy measures included percentage of minimal improvement in Global Impression of Change scale. Effectiveness data were derived from a randomized controlled trial. Utility values were derived from the Health Utilities Index using published literature; utilities for patients with profound or terminal Alzheimer's disease were used as a proxy for utilities for institutionalized patients. Utilities used for adjustment of treatment effects were extrapolated from schizophrenia literature. Costs included within the model were cost of inpatient hospitalizations, cost of outpatient care, cost of medication, cost of adult home care, and unpaid caregiving time (for societal perspective).

From a health care system perspective, the incremental cost-utility ratio for olanzapine versus no treatment was USD$37,331 per QALY ($49,762 per QALY in CAD$ 2014 [1 USD$= 1.1571 CAD$]).[3,4] From a societal perspective, the incremental cost-utility ratio for olanzapine versus no treatment was USD$13,230 per QALY ($17,636 per QALY in CAD$ 2014 [1 USD$= 1.1571 CAD$]).[3,4] In one-way deterministic analysis, results were not sensitive to changes in transition probabilities, costs, and treatment effect. In multi-way deterministic analysis, results were most sensitive to changes in transition probabilities + treatment effect + costs.

Limitations of this study include: the use of proxy utilities for nursing home patients and utilities derived from schizophrenia research for treatment effectiveness; the possibility of double counting of utility benefits; a lack of transparency in reporting of data and results; and not including a probabilistic

sensitivity analysis.

Applicability of this study is limited given that it is not from the Canadian perspective and it is not a comparison of active treatments.

Rosenheck et al. (2007)

Rosenheck et al[2] conducted a cost-utility analysis of initiation of therapies with atypical antipsychotics (olanzapine, quetiapine, or risperidone) compared with watchful waiting in patients with Alzheimer's disease from a health care system perspective. This analysis was funded by the National Institute of Mental Health in the US.

The study was conducted using a trial-based analysis with a 9 month timeframe. The population included ambulatory outpatients living at home or in assisted living with Alzheimer's disease, with an average age of 77.9 and a Mini-Mental State Examination (MMSE) score between 5 and 26. Two separate analyses were performed: Intention to Treat Analysis and Phase 1-Only Analysis. The former analysis more accurately reflects the study question. Net monetary benefit was assessed through estimation of total costs and QALYs. Data were derived from a randomized controlled trial. Utility values were derived from the Health Utilities Index Mark 3. Costs included within the model were cost of medication (experimental and concomitant) and cost of health care service.

In the Intent to Treat Analysis, total health costs were lower for watchful waiting compared with initiation of olanzapine, quetiapine, or risperidone. There was no significant difference in QALYs across all treatment strategies. At a willingness to pay of USD$50,000 per QALY ($97,895 in 2014 CAD$ [1 2007 USD$=1.5704 2014 CAD$]),[3,5] the probability of watchful waiting being cost effective compared with initiation with olanzapine and quetiapine was 88% and 89% respectively; while the probability of initiation with risperidone being cost effective compared with watchful waiting was 51%. Total costs were lower and QALYs higher for initiation with risperidone compared with olanzapine and quetiapine although no analysis addressing the uncertainty of this finding is presented.

Limitations of this study include: derivation of effectiveness data from a single randomized controlled trial; limited data relating to the comparison between atypical antipsychotics; and that both institutionalized patients and community dwellers were combined in the analysis rather than analysing separately the distinct patients groups.

Applicability of this study is limited given that it is not from the Canadian perspective and it is not a comparison of active treatments.

Summary

Overall, only two studies[1,2] were identified for inclusion in our review, both of which were comparing atypical antipsychotics with no treatment. One was funded by the National Institute of Mental Health, while the other stated no funding was received.

The study by Kirbach and colleagues[1] was a cost utility analysis of olanzapine and no treatment in patients aged 65 and over with agitation and psychosis related to Alzheimer's disease from a health care system and societal perspective. From a health care system perspective, the incremental cost-utility ratio for olanzapine versus no treatment was $49,762 per QALY in CAD$ 2014 [1 US$= 1.1571 CAD$]. From a societal perspective, the incremental cost-utility ratio for olanzapine versus no treatment was $17,636 per QALY in CAD$ 2014.

The study by Rosenheck and associates[2] was a cost-utility analysis of initiation of therapy with atypical antipsychotics (olanzapine, quetiapine, and risperidone) compared to watchful waiting in ambulatory outpatients living at home or in assisted living with Alzheimer's disease, with an average age of 77.9 and a MMSE score between 5 and 26. From a health care system perspective, total health costs were lower for watchful waiting compared with olanzapine, quetiapine, or risperidone, and there was no significant difference in QALYs across all treatment strategies. Thus results suggest that watchful waiting is cost effective compared with immediate initiation of therapy.

Applicability of these studies is limited given that they are not from the Canadian perspective and both analyses compare active treatments to placebo or no treatment rather than to a second active treatment.

Conclusions

In brief, this review highlights the paucity of current economic evidence for the cost-effectiveness of atypical antipsychotics compared with typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly. Given the lack of Canadian evidence and the limited evidence comparing active treatments, no inferences can be drawn regarding the cost effectiveness of atypical antipsychotics compared with typical antipsychotics or antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly can be made.

Therefore, to assist with the ODPRN review, an independent de novo economic model would be required to address the cost effectiveness of antipsychotics versus typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly from the Canadian context. This model could then be used to assess the relative cost effectiveness of alternative reimbursement scenarios relating to atypical antipsychotics.

Appendix A1: Search Strategy

The following is the search strategy used in Medline (Ovid) and Embase.

Embase Classic+Embase (1946 to present (2014 September 29), Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations (1947 to 2014 September 30)

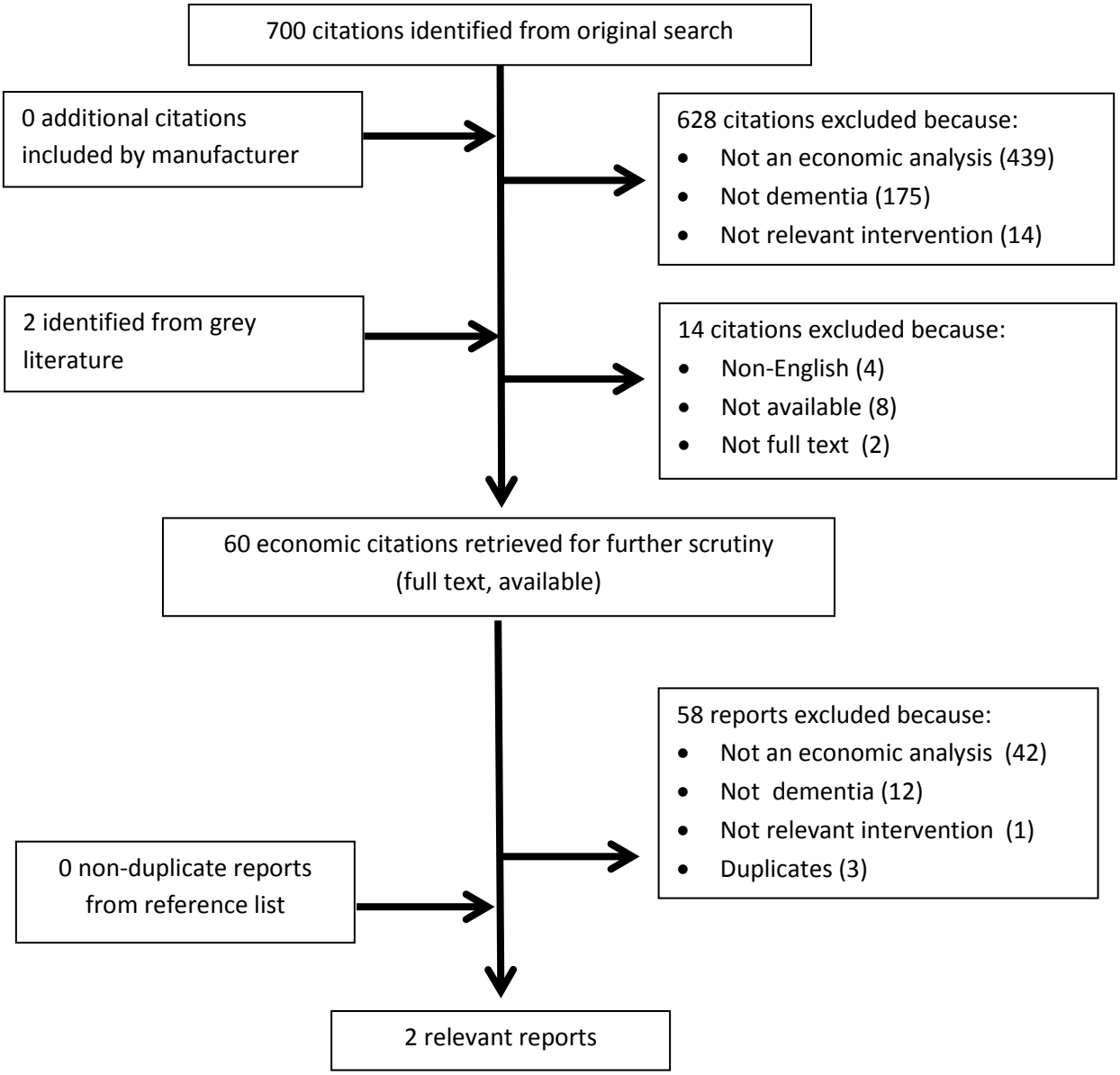
1. exp Antipsychotic Agents/
2. exp Tranquilizing Agents/
3. (neuroleptic adj2 (agent* or drug*)).tw.
4. or/1-3
5. SGA antipsychotic$.tw.
6. ((second or 2nd) adj generation adj antipsychotic*).tw.
7. ((third or 3rd) adj generation adj antipsychotic*).tw.
8. Asenapine/
9. 65576-45-6.rn.
10. (Asenapine or EINECS 265-829-4).mp.
11. clozapine/
12. 5786-21-0.rn.
13. (Clozapin or Clozapina or Clozapine or Clozapinum or Clorazil or Clozaril or FazaClo or Leponex or LX 100-129 or Zaponex).mp.
14. risperidone/
15. 106266-06-2.rn.
16. (Apexidone or Psychodal or Risperdal or Risperidona or Risperidone or Risperidonum or Risperin or Risperilept or Rispolin or Spiron).mp.
17. olanzapine.mp.
18. 132539-06-1.rn.
19. (Zyprexa or Olantsapiini or Olanzapin or Olanzapina or Olanzapinum or Olansek or Zalasta or Zypadhera or Symbyax).mp.
20. quetiapine.mp.
21. (111974-69-7 or 111974-72-2).rn.
22. (Co-Quetiapine or HSDB 7557 or Seroquel).mp.
23. ziprasidone.mp.
24. 146939-27-7.rn.
25. (Zeldox or zeldrox or geodon).mp.
26. aripiprazole.mp.

27. 129722-12-9.rn.
28. (Abilitat or Abilify or Aripiprazole or Discmelt or OPC 31 or OPC 14597).mp.
29. paliperidone.mp.
30. 144598-75-4.rn.
31. (9-Hydroxyrisperidone or Invega or R 76477 or RO76477).mp.
32. Iloperidone/
33. 133454-47-4.rn.
34. (Fanapt or Iloperidone or HP 873 or Zomaril).mp.
35. or/5-34
36. 4 and 35
37. (dementia adj (praecox or precox)).tw.
38. exp dementia/
39. (alzheimer adj disease).tw.
40. exp alzheimer disease/
41. (lewy adj body adj disease).tw.
42. exp lewy body disease/
43. (frontotemporal adj dementia).tw.
44. exp frontotemporal dementia/
45. (delusional adj2 disorder*).tw.
46. exp delusional disorder/
47. or/37-46
48. 36 and 47
49. health economics/
50. exp economic evaluation/
51. exp "health care cost"/
52. exp pharmacoeconomics/
53. 49 or 50 or 51 or 52
54. (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab.
55. (expenditure$ not energy).ti,ab.
56. (value adj2 money).ti,ab.
57. budget$.ti,ab.
58. 54 or 55 or 56 or 57
59. 53 or 58
60. Economics/

61. exp "Costs and Cost Analysis"/
62. "Value of Life"/
63. exp Economics, Hospital/
64. Economics, Medical/
65. Economics, Nursing/
66. Economics, Pharmaceutical/
67. 60 or 61 or 62 or 63 or 64 or 65 or 66
68. (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab.
69. (expenditure$ not energy).ti,ab.
70. (value adj1 money).ti,ab.
71. budget$.ti,ab.
72. 68 or 69 or 70 or 71
73. 67 or 72
74. 59 or 73
75. 48 and 74
76. remove duplicates from 75

Appendix A2: Results of Literature Search

The following illustrates the selected studies for the review.



Appendix A3: List of Excluded Studies

The following table lists the studies excluded from the review in addition to the rationale for their exclusion.

Reference #	Study Reference	Reason for exclusion
6	Small GW. Treating dementia and agitation. JAMA - Journal of the American Medical Association. 2014;311(7):677-8.	Not economic evaluation
7	Desai AK, Schwartz L, Grossberg GT. Behavioral disturbance in dementia. Current Psychiatry Reports. 2012;14(4):298-309.	Not economic evaluation
8	Burns A, Iliffe S. Dementia. BMJ (Online). 2009;338(7691):405-9.	Not economic evaluation
9	Potocnik FCV. Dementia. South African Journal of Psychiatry. 2013;19(3):141-52.	Not economic evaluation
10	Jeste DV, Maglione JE. Atypical antipsychotics for older adults: Are they safe and effective as we once thought? Journal of Comparative Effectiveness Research. 2013;2(4):355-8.	Not economic evaluation
11	Jennings L, Grossberg GT. Antipsychotics continue to have a place in the management of difficult behavior problems in patients with dementia. Journal of the American Medical Directors Association. 2013;14(6):447-9.	Not economic evaluation
12	Azermai M, Kane J, Liperoti R, Tsolaki M, Landi F, Passmore AP, et al. Management of behavioural and psychological symptoms of dementia: Belgium, Greece, Italy, United Kingdom. European Geriatric Medicine. 2013;4(1):50-8.	Not economic evaluation
13	Morley JE. Antipsychotics and Dementia: A Time for Restraint? Journal of the American Medical Directors Association. 2012;13(9):761-3.	Not economic evaluation
14	Blomgren D. Neuropsychiatry. Journal of Pharmacy Practice and Research. 2012;42(2):160-1.	Not economic evaluation
15	Volicer L. Antipsychotics Do Not Have To Be Used "Off Label" in Dementia. Journal of the American Medical Directors Association. 2012;13(6):495-6.	Not economic evaluation
16	Ibrahim F, Knight SR, Cramer RL. Addressing the controversial use of antipsychotic drugs for behavioral and psychological symptoms of dementia. Journal of Pharmacy Technology. 2012;28(1):3-9.	Not economic evaluation
17	Van NR. New year, new science. Nature. 2012;481(7379):12.	Not economic evaluation
18	Spivack BS. New AGS guide offers useful information on the management of psychotic disorders and neuropsychiatric symptoms of dementia in older adults. Clinical Geriatrics. 2011;19(9):14-6.	Not economic evaluation
19	Hollingworth SA, Lie DC, Siskind DJ, Byrne GJ, Hall WD, Whiteford HA. Psychiatric drug prescribing in elderly Australians: Time for action. Australian and New Zealand Journal of Psychiatry. 2011;45(9):705-8.	Not economic evaluation
20	Gebhart F. Antipsychotics overused in LTC setting, OIG says. Drug Topics. 2011;155(7):28.	Not economic evaluation

Reference #	Study Reference	Reason for exclusion
21	Jones RW. Drug treatment for people with dementia. Clinical Medicine, Journal of the Royal College of Physicians of London. 2011;11(1):67-71.	Not economic evaluation
22	Ghio L, Natta W, Fravega R, Gotelli S, Pannocchia F, Puppo S, et al. Cognitive impairment and psychopharmacological treatment: A drug utilization study in the emergency department. International Journal of Geriatric Psychiatry. 2011;26(4):438-9.	Not economic evaluation
23	Kuehn BM. Questionable antipsychotic prescribing remains common, despite serious risks. JAMA - Journal of the American Medical Association. 2010;303(16):1582-4.	Not economic evaluation
24	Theodorou AA, Johnson KM, Moore M, Ruf S, Wade T, Szychowski JA. Drug utilization patterns in patients with Alzheimer's disease. American Journal of Pharmacy Benefits. 2010;2(1):77-82.	Not economic evaluation
25	Mitchell AJ. Do antipsychotics cost lives or save lives? Risks versus benefits from large epidemiological studies. Journal of Clinical Psychopharmacology. 2009;29(6):517-9.	Not economic evaluation
26	Kuehn BM. FDA panel issues mixed decision on quetiapine in depression and anxiety. JAMA - Journal of the American Medical Association. 2009;301(20):2081-2.	Not economic evaluation
27	Farley SJ. Bush's 'parting gifts'. Nature Clinical Practice Urology. 2009;6(3):117.	Not economic evaluation
28	Steve TA, Kirk A, Crossley M, Morgan D, D'Arcy C, Biem J, et al. Medication use in patients presenting to a rural and remote memory clinic. Canadian Journal of Neurological Sciences. 2008;35(5):669-71.	Not economic evaluation
29	Croucher M. Psychotropic medications for elders in residential care. New Zealand Medical Journal. 2008;121(1274):7-9.	Not economic evaluation
30	Homma A. Roles of specialists in psychogeriatrics. Psychogeriatrics. 2008;8(2):57-61.	Not economic evaluation
31	Morley JE. Managing Persons with Dementia in the Nursing Home: High Touch Trumps High Tech. Journal of the American Medical Directors Association. 2008;9(3):139-46.	Not economic evaluation
32	Jeste DV, Meeks T. To prescribe or not to prescribe? Atypical antipsychotic drugs in patients with dementia. Southern Medical Journal. 2007;100(10):961-3.	Not economic evaluation
33	Yaffe K. Treatment of neuropsychiatric symptoms in patients with dementia. New England Journal of Medicine. 2007;357(14):1441-3.	Not economic evaluation
34	Tariot PN. Neuropsychiatric features of dementia: What is the big picture? American Journal of Geriatric Psychiatry. 2006;14(7):557-60.	Not economic evaluation
35	O'Neill MF. Difficult times for Alzheimer's treatments. Drug Discovery Today. 2005;10(20):1333-5.	Not economic evaluation
36	Murman DL, Colenda CC. The economic impact of neuropsychiatric symptoms in Alzheimer's disease: Can drugs ease the burden? PharmacoEconomics. 2005;23(3):227-42.	Not economic evaluation

Reference #	Study Reference	Reason for exclusion
37	Antipsychotics: First-line treatments for behavioural and psychological symptoms of dementia. Drugs and Therapy Perspectives. 2002;18(3):15-8.	Not economic evaluation
38	Dale MC, Jagus C, Barnes R, Akinpelu I, McWilliam C. Melleril: Gone forever! British Journal of General Practice. 2002;52(475):155.	Not economic evaluation
39	Targum SD. New Rx for psychoses in Alzheimer's, Parkinson's. Contemporary longterm care. 2001;24(1):39-40.	Not economic evaluation
40	Hemels ME, Lanctot KL, Iskedjian M, Einarson TR. Clinical and economic factors in the treatment of behavioural and psychological symptoms of dementia. Drugs and Aging. 2001;18(7):527-50.	Not economic evaluation
41	Fergusson E, Howard R. Donepezil for the treatment of psychosis in dementia with Lewy bodies. International Journal of Geriatric Psychiatry. 2000;15(3):280-1.	Not economic evaluation
42	Aronson SM. Cost-effectiveness and quality of life in psychosis: The pharmacoeconomics of risperidone. Clinical Therapeutics. 1997;19(1):139-47.	Not economic evaluation
43	Hikal AH, Hikal EM. Dementia in the elderly. Drug Topics. 1998;142(20):81-90.	Not economic evaluation
44	Allardyce J, McKeith IG. Dementia with Lewy bodies. Reviews in Clinical Gerontology. 1997;7(2):163-70.	Not economic evaluation
45	Nadkarni A, Kalsekar I, You M, Forbes R, Hebden T. Medical costs and utilization in patients with depression treated with adjunctive atypical antipsychotic therapy. ClinicoEconomics and Outcomes Research. 2013;5(1):49-57.	Not economic evaluation
46	Canadian Agency for Drugs and Technologies in Health. Quetiapine for Agitation and Aggression in Dementia. Canadian Agency for Drugs and Technologies in Health. 2007 Available from: http://www.cadth.ca/media/pdf/htis/Quetiapine%20for%20Agitation%20and%20Aggression%20in%20Dementia.pdf	Not economic evaluation
47	Canadian Coordinating Office for Health Technology Assessment. Aripiprazole No. 28. Canadian Coordinating Office for Health Technology Assessment. 2002 Available from: http://www.cadth.ca/media/pdf/108_No28_aripiprazole_edrug_e.pdf	Not economic evaluation
48	Taneja C, Papakostas GI, Jing Y, Baker RA, Forbes RA, Oster G. Cost-effectiveness of adjunctive therapy with atypical antipsychotics for acute treatment of major depressive disorder. Annals of Pharmacotherapy. 2012;46(5):642-9.	Not dementia
49	Edwards NC, Muser E, Doshi D, Fastenau J. The threshold rate of oral atypical anti-psychotic adherence at which paliperidone palmitate is cost saving. Journal of Medical Economics. 2012;15(4):623-34.	Not dementia
50	Tyrer P, Oliver-Africano P, Romeo R, Knapp M, Dickens S, Bouras N, et al. Neuroleptics in the treatment of aggressive challenging behaviour for people with intellectual disabilities: A randomised controlled trial (NACHBID). Health Technology Assessment. 2009;13(21):1-54.	Not dementia

Reference #	Study Reference	Reason for exclusion
[51]	Romeo R, Knapp M, Tyrer P, Crawford M, Oliver-Africano P. The treatment of challenging behaviour in intellectual disabilities: Cost-effectiveness analysis. Journal of Intellectual Disability Research. 2009;53(7):633-43.	Not dementia
[52]	Davies LM, Barnes TRE, Jones PB, Lewis S, Gaughran F, Hayhurst K, et al. A randomized controlled trial of the cost-utility of second-generation antipsychotics in people with psychosis and eligible for clozapine. Value in Health. 2008;11(4):549-62.	Not dementia
[53]	Heeg BM, Antunes J, Figueira ML, Jara JM, Marques TJ, Palha AP, et al. Cost-effectiveness and budget impact of long-acting risperidone in Portugal: a modeling exercise. Curr Med Res Opin. 2008 Feb;24(2):349-58.	Not dementia
[54]	Stant AD, TenVergert EM, Wunderink L, Nienhuis FJ, Wiersma D. Economic consequences of alternative medication strategies in first episode non-affective psychosis. Eur Psychiatry. 2007 Sep;22(6):347-53.	Not dementia
[55]	Niaz OS, Haddad PM. Thirty-five months experience of risperidone long-acting injection in a UK psychiatric service including a mirror-image analysis of in-patient care. Acta Psychiatr Scand. 2007 Jul;116(1):36-46.	Not dementia
[56]	Kashner TM, Rush AJ, Crismon ML, Toprac M, Carmody TJ, Miller AL, et al. An empirical analysis of cost outcomes of the Texas Medication Algorithm Project. Psychiatric Services. 2006;57(5):648-59.	Not dementia
[57]	Mortimer A, Williams P, Meddis D. Impact of side-effects of atypical antipsychotics on non-compliance, relapse and cost. Journal of International Medical Research. 2003;31(3):188-96.	Not dementia
[58]	Verma S, Orengo CA, Kunik ME, Hale D, Molinari VA. Tolerability and effectiveness of atypical antipsychotics in male geriatric inpatients. International Journal of Geriatric Psychiatry. 2001;16(2):223-7.	Not dementia
[59]	Nightengale BS, Garrett L, Waugh S, Lawrence BJ, Andrus J. Economic outcomes associated with the use of risperidone in a naturalistic group practice setting. Am J Manag Care. 1998 Mar;4(3):360-6.	Not dementia
[60]	Edwards SJ. Lithium or an atypical antipsychotic drug in the management of treatment-resistant depression: A systematic review and economic evaluation. Health Technology Assessment. 2013;17(54):1-34.	Not relevant intervention

Appendix A4: List of Included Studies

The following table lists the studies included within the review.

Reference #	Study Reference
[1]	Kirbach S, Simpson K, Nietert PJ, Mintzer J. A Markov model of the cost effectiveness of olanzapine treatment for agitation and psychosis in Alzheimer's disease. Clinical Drug Investigation. 2008;28(5):291-303.
[2]	Rosenheck RA, Leslie DL, Sindelar JL, Miller EA, Tariot PN, Dagerman KS, et al. Cost-benefit analysis of second-generation antipsychotics and placebo in a randomized trial of the treatment of psychosis and aggression in alzheimer disease. Archives of General Psychiatry. 2007;64(11):1259-68.

Appendix A5: Characteristics of Reviewed Studies

The following tables list characteristics of reviewed studies.

Study	Kirbach et al. (2008)[1]
Sponsorship	None
Country	US
Perspective	Health care system perspective Societal perspective
Study type	CUA
Comparators	Olanzapine (5.5 mg daily – assumed weighted mean dose) No treatment
Populations	Patients with agitation and psychosis related to Alzheimer's disease Aged 65 and over
Time horizon	13 years (lifetime)
Type of model	Markov model
Cycle length	6 months
Efficacy inputs	Percentage with minimal improvement in Global Impression of Change scale
Adverse events	Not included; discontinuation based on lack of treatment effect or adverse events
Utilities	Health Utilities Index, published literature
Discounting	Cost and outcomes @ 3%
Outcomes	Incremental cost utility ratio
Results	From a health care system perspective, ICUR for olanzapine versus no treatment was $37,331 per QALY From a societal perspective, ICUR for olanzapine versus no treatment was $13,230 per QALY
Types of sensitivity analysis	Deterministic analysis (one-way) Transition probabilities Costs Treatment effect Deterministic analysis (multi-way) Transition probabilities + Treatment effect Treatment effect + Costs Transition probabilities + Treatment effect + Costs

Study	Kirbach et al. (2008)[1]
Sensitivity analysis results	Deterministic analysis (one-way) Results not sensitive to changes in transition probabilities, costs, and treatment effect Deterministic analysis (multi-way) Results most sensitive to changes in transition probabilities + treatment effect + costs.
Points to consider	Costs (2006) USD$ Possible double counting of utility benefits from treatment Lack of transparency in reporting data and results Markov model based analysis; institutionalized patients in separate health state compared to community dwellers Utility values derived from literature; utilities for patients with profound or terminal Alzheimer's disease were a proxy for utilities for institutionalized patients and utilities for treatment effectiveness derived from schizophrenia literature PSA not conducted Atypical antipsychotic compared to no treatment

Study	Rosenheck et al. 2007[2]
Sponsorship	National Institute of Mental Health
Country	US
Perspective	Health care system perspective
Study type	CUA
Comparators	Initiation of therapy with Olanzapine Initiation of therapy with Quetiapine Initiation of therapy with Risperidone Watchful waiting
Populations	Ambulatory outpatients living at home or in assisted living with Alzheimer's disease and a Mini-Mental State Examination score between 5 and 26. Average age 77.9 years
Time horizon	9 months
Type of model	N/A
Cycle length	Trial based analysis
Efficacy inputs	Total health costs QALY ADRQOL ADCS-ADL AD Dependence Scale

Study	Rosenheck et al. 2007[2]
Adverse events	Trial based study so effects of adverse events on costs and utilities likely included
Utilities	Health Utilities Index Mark 3, published literature
Discounting	N/A
Outcomes	Net monetary benefit incorporating total health costs and QALYs
Results	Total health costs were lower for watchful waiting compared to initiation with olanzapine, quetiapine or risperidone. No significant difference in QALYs Total health costs were lower and QALys higher for risperidone compared to olanzapine and quetiapine
Types of sensitivity analysis	Probabilistic analysis (using net benefit regression)
Sensitivity analysis results	At a willingness to pay of $50,000 per QALY, the probability of watchful waiting being cost effective compared to olanzapine and quetiapine was 88% and 89% respectively; while the probability of risperidone being cost effective compared to watchful waiting was 51%.
Points to consider	Costs (2002) USD$ Effectiveness data derived from RCT Trial based analysis Utility values derived from Health Utilities Index Mark 3 Atypical antipsychotics compared to watchful waiting Possible to derive limited results comparing atypical antipsychotics

Appendix B – De novo Economic Evaluation

Research Question

RQ2. Based on a de novo economic model, what is the cost-effectiveness of atypical antipsychotics versus typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly?

Study Objectives

Based on the research question, the objectives of the study were to address the following specific questions:

- What is the cost effectiveness of atypical antipsychotics compared to conventional antipsychotics, antidepressants and placebo and each other?

Introduction

Among Alzheimer's disease patients the prevalence of mood and behavioural symptoms, also referred to as neuropsychiatric symptoms and behavioural and psychological symptoms of dementia (BPSD),occur at some point in the disease process and lead to an increased risk for transition to institutional care.[1,61] As dementia is a progressive process, halting the disease process is unlikely, but it is possible to reduce the rate of cognitive decline with the use of cognitive enhancers.[62]

BPSD can be managed with a number of options. Non-pharmacologic interventions targeted to both the patient and caregiver have been used as well as pharmacological approaches using conventional antipsychotic agents, antidepressants and more recently atypical antipsychotics.[63,64]

The intention of this analysis was to compare the available pharmaceutical drugs used in the management of the behavioral and psychological symptoms of dementia compared against placebo or no treatment.

Methods

Model Structure

The model was designed to estimate the medium term costs and quality adjusted life years (QALYs) associated with the use of conventional antipsychotics, antidepressants, and atypical antipsychotics compared with no intervention in the management of Alzheimer's disease among elderly patients using a Markov model. These estimates would then be used to estimate the relative cost effectiveness of alternative strategies for reimbursement for the coverage of atypical antipsychotics.

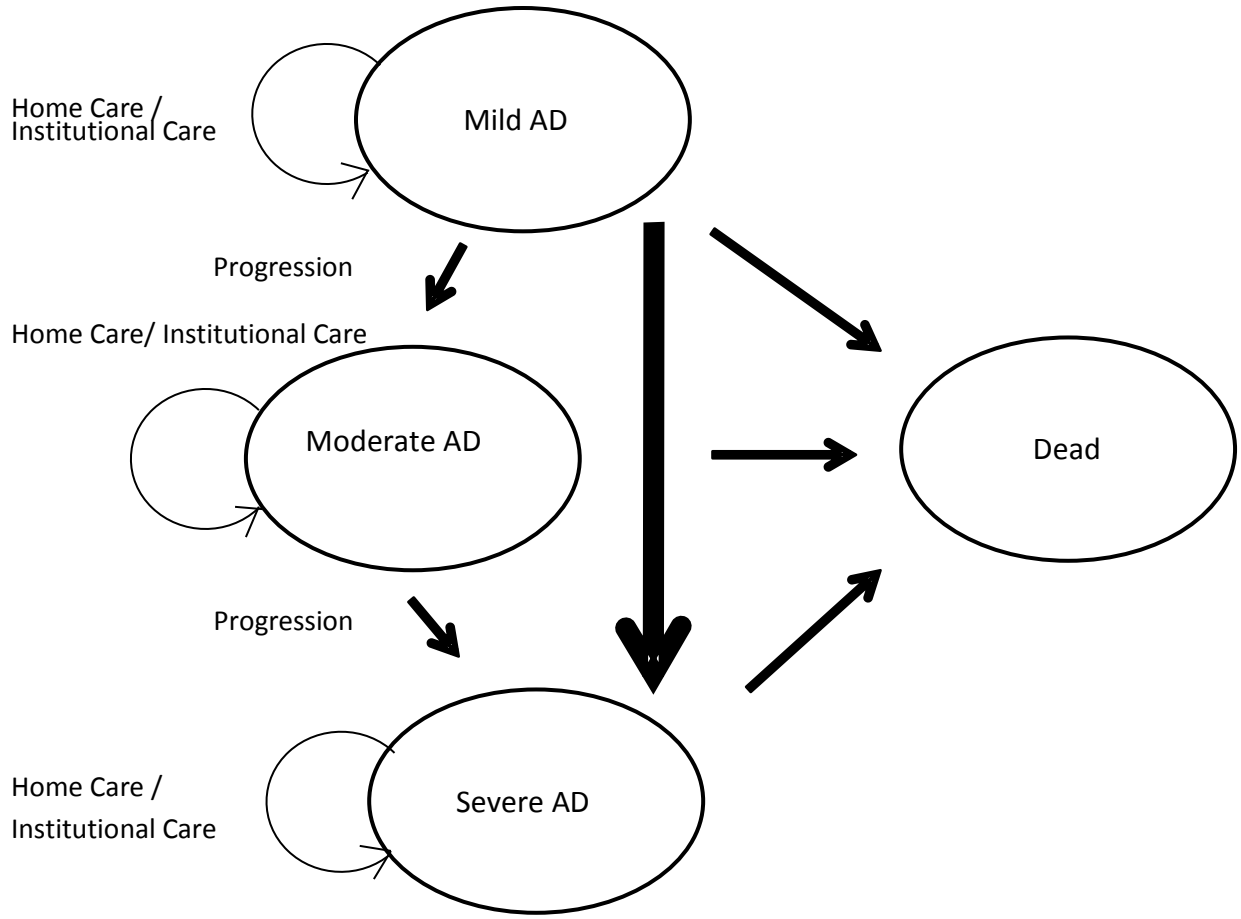
To model disease progression, previous models assessed disease severity by a number of scales, including the cognitive function based mini-mental state examination scores (MMSE) and clinical dementia rating (CDR) scale that incorporates a measure of patient function in its assessment of dementia severity. [1,65] We were able to use studies based on the MMSE and CDR because there has been demonstrated correlation between both instruments.[66,67] Similar to the model used by Jones et al, we identified disease severity based on MMSE scores with seven health states (including death) defined using the following severity levels: mild (MMSE score > 21); moderate disease (MMSE score 11–20); and

severe (MMSE score <11).[65] Care setting is identified as one of the following two options: institution/nursing home or community/home care. To facilitate the specific research question of interest, the model incorporated the presence of behavioural and psychological symptoms as an important factor that increases the likelihood of transition to institutional care. See Figure 1 for a schematic of the proposed Markov model.

The proposed cycle length is six months, similar to what has been used previously in the literature and corresponding to the usual frequency of geriatric/memory clinic appointments.[62,65] A time horizon of 10 years is being proposed based on the natural history of the disease which ranges from 1 to 10 years from onset until death.[68] The choice of a 10 year time horizon is predicated on our estimates from the model proposed by Nagy et al of at least 8.6 years for patients to deteriorate from an MMSE of 26 to six as well as this being a realistic time frame required for disease progression and ultimately death of patients.[69]

During each cycle, patients can be in any of the model combination states and progress to the next severity disease state. Given that Alzheimer's disease is progressive, the direction of transition is only towards increased severity and only from community care to institutional care. Reverse transition back into the community is not a possibility for our model.

Figure 1 Schematic of Proposed Markov Model



Data Inputs

Given the structure of the model data on the following would be required:

- Disease progression
- Utilities
- Resource use and costs
- Treatment effectiveness

Progression of disease

Transition probabilities were required which allowed modelling = the progression of Alzheimer's disease, the presence and absence of behavioural and psychological symptoms, the move to institutional care and mortality. Utilities

Utility values were obtained for Alzheimer's disease states taking into consideration the care settings and noting that there is an associated decrement associated with institutional care and with the presence of behavioural and psychological symptoms.

Resource Use and Costs

The costs associated with Alzheimer's disease will include medication costs, cost due to provision of care in the community and the costs associated with institutional care varied by disease severity which dictates the level of care required. All costs would be to 2014 dollars using the Bank of Canada Inflation calculator.[3]

Treatment Effectiveness

It was hoped that the comparative effects of treatments on the ability to resolve behavioural symptoms could be obtained from the network meta-analysis in the companion systematic review. However, data were not available and no analyses could be conducted.

Cost Effectiveness

Had data on treatment effectiveness been available, a cost utility analysis would have been conducted where costs and effects, as measured by life years and QALYs gained with treatment of mood and behavioural symptoms in Alzheimer's disease, would have been obtained from the model. Costs and QALYs would have been discounted at a standard rate of 5% per annum.[75] The cost effectiveness of each of the treatments would have been estimated as the cost per QALY gained relative to the comparator treatment.

Deterministic Sensitivity Analyses

A range of deterministic sensitivity analysis would have been conducted to determine impact of the following parameter inputs on the results: time horizon (2 & 5years), discounting (0% and 3%), and assuming treatment had no impact on the transition to institutional care. Additional sensitivity analyses varying the costs of community care increasing the current estimates by 50% would have been conducted.

Probabilistic Sensitivity Analyses

A probabilistic sensitivity analysis (PSA) would have been conducted in order to estimate the impact of parameter uncertainty on the cost effectiveness. The PSA would have involved a Monte Carlo simulation with 5000 estimates of outcomes obtained by sampling from the probability distributions for each parameter. The parameters that would have been included within the PSA and their corresponding distributions are as follows: a normal distribution was used for costs. A log normal distribution would have been used for treatment effectiveness and utility values.

The results of the PSA would have been presented by cost effectiveness acceptability curves depicting the probability, with respect to each research question, that each comparator is the most cost effective given different threshold values for a QALY.

Findings

Given the lack of available clinical data on the impact of antipsychotics on the control of behavioural symptoms no economic analysis was possible.

Conclusions

A Markov model designed to assess the cost effectiveness of atypical antipsychotics in the management of behavioural and psychological symptoms of dementia in the elderly. However, clinical data on the control of such symptoms were unavailable. The Markov model is available for analysis should such data become available. Given the results of the review and the inability to conduct any de novo economic modelling, no statements relating to the cost effectiveness of atypical antipsychotics in the management of behavioural and psychological symptoms of dementia in the elderly can be made.

Appendix C – Reimbursement Based Economic Evaluation

Research Question

RQ3. What is the economic impact of alternative policies for reimbursing atypical antipsychotics versus typical antipsychotics and antidepressants in the management of behavioural and psychological symptoms of dementia in the elderly?

Methods

Given that antipsychotics are used off-label for the treatment of Alzheimer's disease and dementia, analysis can be considered preliminary due to difficulties in obtaining accurate data. However, current and past usage data for antipsychotics were used in combination with results from recent initiatives to reduce the use of antipsychotics in long-term care facilities to estimate the potential cost-savings of these initiatives.

Results

Current Expenditure

Total OPDP expenditure for atypical antipsychotics in 2013 was just over $35 million. This represents 92% of OPDP expenditure on antipsychotics among those aged 65 and over (Table 4).

Table 1 Total OPDP expenditure for antipsychotics from 2011-2013

DRUG NAME	FISCAL YEAR		
	2013	2012	2011
Total	$ 38,076,764.42	$ 34,944,358.78	$ 30,726,613.13
Atypicals	$ 35,011,335.38	$ 32,192,972.68	$ 28,115,225.18
Aripiprazole	$ 3,940,503.21	$ 1,994,360.54	$ 167,375.08
Clozapine	$ -	$ -	$ -
Olanzapine	$ 7,727,823.52	$ 7,762,387.07	$ 7,935,157.49
Paliperidone	$ 1,902,426.52	$ 1,027,510.62	$ 453,991.77
Quetiapine	$ 12,628,500.71	$ 12,895,545.88	$ 11,386,609.71
Risperidone	$ 8,541,539.97	$ 8,251,141.91	$ 7,930,804.48
Ziprasidone	$ 270,541.45	$ 262,026.66	$ 241,286.65
Typicals	$ 3,065,429.04	$ 2,751,386.10	$ 2,611,387.95
Chlorpromazine	$ 133,713.93	$ 140,434.15	$ 136,744.27
Flupentixol	$ 267,336.16	$ 253,007.97	$ 222,618.38
Fluphenazine	$ 224,747.40	$ 205,332.19	$ 210,965.06
Haloperidol	$ 965,248.98	$ 732,942.19	$ 738,837.23
Loxapine	$ 228,401.81	$ 210,599.74	$ 211,853.20
Methotrimeprazine	$ 357,078.09	$ 289,284.29	$ 252,819.57
Periciazine	$ 4,309.82	$ 10,163.47	$ 8,634.49
Perphenazine	$ 128,872.71	$ 127,731.05	$ 129,296.93
Pimozide	$ 29,176.48	$ 32,847.00	$ 31,708.17
Pipotiazine	$ 39,141.95	$ 38,030.95	$ 67,512.57
Prochlorperazine	$ 443,919.92	$ 478,662.25	$ 365,809.59
Thioridazine	$ -	$ -	$ -
Thiothixene	$ 7,398.92	$ 6,325.92	$ 7,433.08
Trifluoperazine	$ 194,914.73	$ 194,512.77	$ 204,970.15
Zuclopenthixol	$ 41,168.14	$ 31,512.16	$ 22,185.26

Broken down by age, 2013 expenditure for atypical antipsychotics was $15.9 million for patients 65-74 years, $10.7 million for patients 75-84, and $8.3 for patients >85 years (Table 5).

Table 2 Total OPDP expenditure for antipsychotics by age group

ANTIPSYCHOTIC	YEAR		
	2013	2012	2011
Age 65-74			
Atypicals	$ 15,902,888.24	$ 14,071,765.57	$ 11,196,362.77
Typicals	$ 1,566,219.31	$ 1,409,754.15	$ 1,310,453.41
Total	$ 17,469,107.55	$ 15,481,519.72	$ 12,506,816.18
Age 75-84			
Atypicals	$ 10,751,325.01	$ 10,226,355.45	$ 9,467,902.34
Typicals	$ 939,773.09	$ 847,016.65	$ 827,425.25
Total	$ 11,691,098.10	$ 11,073,372.10	$ 10,295,327.59
Age >85			
Atypicals	$ 8,316,266.28	$ 7,868,063.55	$ 7,450,960.07
Typicals	$ 546,106.17	$ 467,886.77	$ 442,032.21
Total	$ 8,862,372.45	$ 8,335,950.32	$ 7,892,992.28

Expenditure in 2013 for atypical antipsychotics among patients living in long-term care facilities was $15.4 million with expenditure for those living in the community being $19.6 million (Table 6).

Table 3 Total OPDP expenditure for antipsychotics by dwelling

ANTIPSYCHOTIC	YEAR		
	2013	2012	2011
Community dwelling			
Atypicals	$ 19,648,905.36	$ 17,237,206.91	$ 13,691,155.53
Typicals	$ 2,055,461.72	$ 1,848,456.03	$ 1,694,177.51
Total	$ 21,704,367.08	$ 19,085,662.94	$ 15,385,333.04
Long-term care			
Atypicals	$ 15,362,430.02	$ 14,955,765.77	$ 14,424,069.65
Typicals	$ 1,005,657.50	$ 902,930.07	$ 901,142.87
Total	$ 16,368,087.52	$ 15,858,695.84	$ 15,325,212.52

Potential reductions

As a means of reducing the inappropriate prescription of antipsychotic medication in the elderly, particularly among those living in long-term care facilities, several interventions, including educational-based and interdisciplinary interventions, have been used. A report from Alberta Health Services Seniors Health Strategic Clinical Network recently indicated a 49.2% reduction in the number of residents using antipsychotics without an appropriate diagnosis as the result of a program incorporating a toolkit for appropriate use of antipsychotics.[76] A second report from the Winnipeg Health Region in Manitoba recently indicated that under their new training program aimed to reduce the use of antipsychotics in the elderly, 25% of residents were taken off of their antipsychotic medication.[77] Finally, a third program, initiated in the United States, has reported a reduction of 15% in inappropriate antipsychotics use

among those in long-stay nursing homes.[78] Based on findings from these three programs and using data from 2013, we estimated the cost-savings if Ontario were to adopt a program focused on reducing the use of antipsychotics among elderly patients with dementia living in long-term care facilities. Our results suggest potential cost-savings between $2.5 million and $8.1 million for antipsychotics (Table 4), depending on the level of success achieved by such an initiative.

Table 4 Estimated cost-savings based on initiatives[76-78] meant to reduce the inappropriate use of antipsychotics among elderly patients with dementia living in long-term care facilities

ANTIPSYCHOTIC MEDICATION	ORIGINAL DATA	SCENARIOS FOR REDUCING ANTIPSYCHOTIC USE		
	2013	Scenario 1[a]	Scenario 2[b]	Scenario 3[c]
Atypicals (cost/savings)	$ 15,362,430.02	$ 7,804,114.45 (-$ 7,558,315.57)	$ 11,521,822.52 (-$3,840,607.51)	$ 13,058,065.52 (-$2,304,364.50)
Typicals (cost/savings)	$ 1,005,657.50	$ 510,874.01 (-$ 494,783.49)	$ 754,243.13 (-$ 251,414.38)	$ 854,808.88 (-$ 150,848.63)
Total (cost/savings)	$ 16,368,087.52	$ 8,314,988.46 (-$ 8,053,099.06)	$ 12,276,065.64 (-$ 4,092,021.88)	$ 13,912,874.39 (-$ 2,455,213.13)

[a] based on a report from Alberta Health Services – reduction of 49.2%; [b] based on a report from Winnipeg Health Region – reduction of 25%; [c] based on report from the United States Centres for Medicare and Medicaid Services – reduction of 15%

A further analysis was conducted to assess the impact of interventions to reduce antipsychotic prescribing with alternate assumptions to the above – reductions of 15, 25 and 30%. For this analysis, reductions were assumed to occur only in the population with dementia (note: prevalence based on the accompanying pharmacoepidemiology report) Our results suggest potential cost-savings between $2.5 million and $5.0 million for antipsychotics for 2016 (Table 5), depending on the level of success achieved by such an initiative.

Table 5 Revised estimates of cost-savings based on initiatives meant to reduce the inappropriate use of antipsychotics among elderly patients with dementia living in long-term care facilities

ANTIPSYCHOTIC MEDICATION	FORECAST DATA	SCENARIOS FOR REDUCING ANTIPSYCHOTIC USE		
	2016	15% reduction	25% reduction	30% reduction
Atypicals (cost/savings)	$17,984,704.95	$15,570,258.31 ($2,414,446.64)	$13,960,627.22 ($4,024,077.73)	$13,155,811.67 ($4,828,893.28)
Use in patients with dementia (89.5%)	$16,096,310.93	$13,681,864.29	$12,072,233.20	$11,267,417.65
Use in patients with no dementia (10.5%)	$1,888,394.02	$1,888,394.02	$1,888,394.02	$1,888,394.02
Typicals (cost/savings)	$904,052.15	$802,346.28 ($101,705.87)	$658,262.97 ($245,789.18)	$700,640.42 ($203,411.73)
Use in patients with dementia (75%)	$678,039.11	$576,333.25	$432,249.94	$474,627.38
Use in patients with no dementia (25%)	$226,013.04	$226,013.04	$226,013.04	$226,013.04
Total (cost/savings)	$18,888,757.10	$16,372,604.60 ($2,516,152.51)	$14,618,890.19 ($4,269,866.91)	$13,856,452.09 ($5,032,305.01)

Conclusions

A review of OPDP claims indicate that current expenditure for atypical antipsychotics represents the majority of all OPDP spending on antipsychotic medication. Efforts to reduce the inappropriate use of antipsychotics, particularly among elderly patients with dementia, could help to reduce overall expenditure in Ontario.

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