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# Research Submission

## Reimbursement-Based Economics – What Is It and How Can We Use It to Inform Drug Policy Reform?

Doug Coyle, MA, MSc, PhD; Karen M. Lee, MA; Muhammad Mamdani, MPH, MA, PharmD; Kelley-Anne Sabarre, MSc; Kylie Tingley, BSc, PhD (cand.)

**Background.—In Ontario, approximately $3.8 billion is spent annually on publicly funded drug programs. The annual growth in Ontario Public Drug Program (OPDP) expenditure has been limited to 1.2% over the course of 3 years. Concurrently, the Ontario Drug Policy Research Network (ODPRN) was appointed to conduct drug class review research relating to formulary modernization within the OPDP. Drug class reviews by ODPRN incorporate a novel methodological technique called reimbursement-based economics, which focuses on reimbursement strategies and may be particularly relevant for policy-makers.**

**Objectives.—To describe the reimbursement-based economics approach.**

**Methods.—Reimbursement-based economics aims to identify the optimal reimbursement strategy for drug classes by incorporating a review of economic literature, comprehensive budget impact analyses, and consideration of cost-effectiveness. This 3-step approach is novel in its focus on the economic impact of alternate reimbursement strategies rather than individual therapies.**

**Results.—The methods involved within the reimbursement-based approach are detailed. To facilitate the description, summary methods and findings from a recent application to formulary modernization with respect to the drug class tryptamine-based selective serotonin receptor agonists (triptans) used to treat migraine headaches are presented.**

**Conclusions.—The application of reimbursement-based economics in drug policy reforms allows policy-makers to consider the cost-effectiveness and budget impact of different reimbursement strategies allowing consideration of the trade-off between potential cost savings vs increased access to cost-effective treatments.**

**Key words: cost-effectiveness, drug reimbursement, triptan**

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**From the School of Epidemiology, Public Health and Preventive Medicine, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada (D. Coyle, K.M. Lee, and K. Tingley); Canadian Agency for Drugs and Technologies in Health, Ottawa, ON, Canada (K.M. Lee, K.-A. Sabarre, and K. Tingley); Li Ka Shing Knowledge Institute of St. Michael's Hospital, Toronto, ON, Canada (M. Mamdani); Institute of Health Policy, Management and Evaluation and Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada (M. Mamdani); Institute for Clinical Evaluative Sciences, Toronto, ON, Canada (M. Mamdani).**

**Address all correspondence to D. Coyle, School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, 451 Smyth Road, Ottawa, ON K1H 8M5, Canada, email: dcoyle@uottawa.ca**

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In Ontario, approximately $3.8 billion is spent annually through the Ontario Public Drug Program (OPDP), which is funded through general taxation revenues.[1] Approximately 20% of Ontarians are eligible to receive drugs through the OPDP – access is restricted to those over age 65 years, those receiving welfare, and those receiving home care or living in long-term care facilities.

Typically, drugs that are publicly funded are either listed in the Ontario Drug Benefit (ODB)

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Formulary or are part of the Exceptional Access Program (EAP). Within the ODB Formulary, drugs can be available as either general benefit (GB) or limited use (LU). Under GB, drugs are available to all covered by the OPDP with a prescription completed by a physician. Under LU, drugs are available to all covered by the OPDP with a prescription and who meet specified criteria as assessed by a physician. For EAP, drugs are available only when patients meet specified criteria as assessed by a physician and further evaluated by the OPDP staff.

More than 3200 drug products are currently listed under the ODB Formulary[2] and a further 850 drug products are available under EAP.[3]

In 2012, as part of the strategy to eliminate provincial debt by 2017-2018, the OPDP expenditure was limited to a spending growth of 1.2% over the course of 3 years.[4] Consequently, the OPDP emphasized its commitment to continue to publicly fund drugs for Ontarians and to identify areas for savings and efficiencies in the health system.[4] Concurrently, the Ontario Drug Policy Research Network (ODPRN) was awarded provincial government funding to conduct research relating to formulary modernization (a re-evaluation of currently publicly funded drugs through the review of "current evidence to support clinical benefit, safety, and value for money").[5] This could help OPDP's objectives by identifying areas for savings and efficiencies but also identify areas in need of improved access to effective drug therapies. The ODPRN process is a novel, integrated program that includes systematic reviews of the literature, real-world, population-based analyses of drug utilization trends and qualitative analyses of the opinions and perspectives of patients, prescribers, and dispensers of the drugs. In addition, the drug class reviews incorporates a novel methodological technique called reimbursement-based economics, which is the focus of this article. The ODPRN approach to evidence-informed formulary modernization is unique worldwide.

The objective of this article is to describe the constituent components of the reimbursement-based economics approach. The initial application of the ODPRN process to the treatment of migraines by triptans is used to demonstrate how reimbursement-based economics is being applied to OPDP formulary modernization initiatives. Given the explicit purpose of this article is to highlight the approach adopted, the methods and findings of this analysis are summarized in this study with greater details provided in the completed study report.[6]

## CASE STUDY: TRIPTANS FOR THE MANAGEMENT OF MIGRAINES[6]

To demonstrate how reimbursement-based economics can help facilitate formulary modernization – the ODPRN drug class review for tryptamine-based selective serotonin receptor agonists (triptans) used to treat migraine headaches is presented as a case study.

Currently, there are 7 triptans available for the management of migraines in Canada, of which 5 are publicly funded in Ontario and available via restricted benefit (through EAP). Unlike other Canadian provinces, the OPDP does not enforce a monthly quantity limit. For example, in Manitoba, 4 triptans are publicly funded and available with a quantity limit of 12 per month, and in Quebec, 6 triptans are publicly funded and available via GB.[7] At the time of the review, ergots were the only other class of drugs funded under OPDP for the treatment of migraine and were judged by the clinical experts as the appropriate comparator for analysis.

Of the 7 marketed triptans in Canada, 6 are available in generic formulation.[7] For products available as GB in Ontario, generic substitution for branded products is required, and generic equivalents must cost no more than 25% of the equivalent brand cost. However in Ontario, as triptans are only available under EAP, neither of these requirements is in place. Moving triptans to GB appears to be an intuitive strategy. However, there are concerns that such a switch may lead to potential overuse of triptans, which may be clinically harmful, and the possible expansion of its indication to patients with cluster headaches and other non-classic migraine headaches (off-label use). Thus, the triptans drug class review takes place in this context. After engagement with relevant stakeholders, the following research questions were identified:

1. What is the current evidence for the cost-effectiveness of triptans (alone or in combination with other drugs) for acute treatment of migraines compared with: other triptans, acetaminophen, antiemetics, acetylsalicylic acid, and ergots?
2. What is the economic impact of alternative reimbursement strategies for triptans (eg, restricted vs more open access)?

## WHAT IS REIMBURSEMENT-BASED ECONOMICS?

Reimbursement-based economics is a novel, pragmatic approach to pharmacoeconomics. Rather than considering the traditional approach of comparing 2 or more treatment options, reimbursement-based economics focuses on comparing alternate reimbursement strategies. Thus, the focus is on identifying the optimal reimbursement strategy.

Reimbursement-based economics involves: a review of existing economic literature; a comprehensive budget impact analysis assessing the impact different reimbursement strategies; and consideration of the cost-effectiveness of such strategies, which will include, where warranted, the development of traditional de novo pharmacoeconomic models focusing on reimbursement strategies rather than treatment options. The initial stage of the process is to determine the appropriate research questions with respect to assessing cost-effectiveness and budget impact – as illustrated above for the triptans analysis. An essential component of this stage is engagement with decision makers to determine feasible alternative reimbursement strategies that are operationalizible.

**Review of Economic Literature.—***Methods.*—The goal of the systematic review of economic evidence is to identify existing relevant, well-conducted economic evaluations to inform the strategies considered within the comprehensive budget impact analysis, as well as assessing the need for de novo economic modeling. A detailed review of the existing literature is conducted using a standardized health economics search strategy.[8] The review is qualitative by nature as meta-analysis of cost-effectiveness studies is neither feasible nor appropriate given the multitude study designs and study contexts. Focus is on identifying the relevance of the current literature with respect to the current Canadian context. Studies are assessed in terms of their methodological rigor. It is important to note that standard health economics checklists have relatively limited discriminatory power with respect to assessing study quality within a specific clinical area – most studies will meet the base requirements of such checklists but there may still be fundamental flaws with the modeling approaches adopted. Thus, it is necessary to identify the key areas of potential concern particular to the disease of interest and focus on the relevance of the methodology adopted within studies to address these concerns. Studies from other jurisdictions may have limited applicability to the Canadian setting although consistency in study findings can allow generalizability to findings to other jurisdictions such as Canada.

The systematic review may further inform a decision to conduct a de novo economic modeling exercise. Thus, the focus of the systematic review of economic evidence is on the quality and the applicability of the economic evidence in relation to the reimbursement question.

*Application to Triptans.*—A systematic review of published literature which compared the cost-effectiveness of triptans to other triptans, acetaminophen, antiemetics, acetylsalicylic acid, and ergot alkaloid-based medications (ergots) for the acute treatment of migraines was conducted. The following databases were searched using a standard health economics search strategy augmented with terms related to migraine and migraine therapy: Medline, Embase, National Health Service Economic Evaluation Database, and Tufts CEA registry (Table 1). As well, relevant health technology assessment agency websites were searched for grey literature. In addition, the reference lists of relevant studies were hand searched for additional relevant literature.

The comprehensive search strategy identified 920 citations. Of these, 72 citations were identified for full-text review. Citations were excluded for the following reasons: not an economic analysis, not migraine related, not relevant intervention, non-English, not available, or not full text. Of the 72 economic citations retrieved for detailed review, 21

**Table 1.—Search Strategy for Review of Economic Evaluations of Triptans (Medline (Ovid) In Process and Other Non-Index Citations 1946 to present (2013 November 11); Embase Classic & Embase 1947 to 2013 November 08)**

1. exp Migraine Disorders/
2. (migrain* or migran*).tw.
3. (anti-migrain* or antimigrain* or anti-migran* or antimigran*).tw.
4. sick headache*.tw.
5. 1 or 2 or 3 or 4
6. exp Tryptamines/
7. (tryptamin* or tryptomin* or triptan* or indolylethylamine* or NSC 73938 or NSC73938).tw.
8. ("BRN 0125513" or CCRIS 8959 or EINECS 200-510-5 or Indol-3-ethylamine or UNII-422ZU9N5TV).tw.
9. Tryptamines.rn.
10. (almotriptan* or Almogran or Almotrex or Amignul or Axert or PNU 180638E or PNU-180638E or UNII-PJP312605E).tw.
11. almotriptan.rn.
12. (eletriptan* or Relpax or Relert or Relepax or "UK 116044" or "UK 116,044" or "UK-116044" or "UK-116,044" or UNII-22QOO9B8KI).tw.
13. eletriptan.rn.
14. (frovatriptan* or Allegro or Frova or Frovelan or Migard or Miguard or SB 209509 or VML-251 or VML251).tw.
15. frovatriptan.rn.
16. (naratriptan* or Amerge or Colatan or Naragran or Naramig or UNII-QX3KXL1ZA2).tw.
17. naratriptan.rn.
18. (rizatriptan* or Risatriptan* or "L 705,126" or "L 705126" or "L-705,126" or "L-705126" or Maxalt or "MK 0462" or MK 462 or MK-0462 or MK-462 or rizalief or rizalt or rizaliv or UNII-51086HBW8G).tw.
19. rizatriptan.rn.
20. (sumatriptan* or Arcoiran or Alsuma or BRN 6930870 or Diletan or Dolmigral or GR 43175 or GR 43175X or GR-43175 or HSDB 7742 or Imigran* or Imiject or Imitrex or micranil or Migril or Novelian or Sumigrene or Suminat or Sumatran or Sumatriptanum or Sumax or UNII-8R78F6L9VO or Zecuity).tw.
21. sumatriptan.rn.
22. (Zolmitriptan* or AscoTop or Flezol or Rapimelt or UNII-2FS66TH3YW or Zolmitriptan or Zomig or Zomig-ZMT or Zomigon or Zomigoro).tw.
23. Zolmitriptan.rn.
24. (Treximet or Trexima).tw.
25. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
26. 5 and 25
27. Economics/
28. exp "Costs and Cost Analysis"/
29. "Value of Life"/
30. exp Economics, Hospital/
31. Economics, Medical/
32. Economics, Nursing/
33. Economics, Pharmaceutical/
34. 27 or 28 or 29 or 30 or 31 or 32 or 33
35. (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab.
36. (expenditure$ not energy).ti,ab.
37. (value adj1 money).ti,ab.
38. budget$.ti,ab.
39. 35 or 36 or 37 or 38
40. 34 or 39
41. 26 and 40
42. exp migraine/
43. (migrain* or migran*).tw.
44. (anti-migrain* or antimigrain* or anti-migran* or antimigran*).tw.
45. sick headache*.tw.
46. 42 or 43 or 44 or 45
47. tryptamine derivative/
48. triptan derivative/
49. (tryptamin* or tryptomin* or triptan* or indolylethylamine* or NSC 73938 or NSC73938).tw,tn.
50. ("BRN 0125513" or CCRIS 8959 or EINECS 200-510-5 or Indol-3-ethylamine or UNII-422ZU9N5TV).tw,tn.
51. 61-54-1.rn.
52. almotriptan/
53. (almotriptan* or Almogran or Almotrex or Amignul or Axert or PNU 180638E or PNU-180638E or UNII-PJP312605E).tw,tn.

**Table 1.—*Continued***

54. 154323-57-6.rn.
55. eletriptan/
56. (eletriptan* or Relpax or Relert or Relepax or "UK 116044" or "UK 116,044" or "UK-116044" or "UK-116,044" or UNII-22QOO9B8KI).tw,tn.
57. 143322-58-1.rn.
58. frovatriptan/
59. (frovatriptan* or Allegro or Frova or Frovelan or Migard or Miguard or SB 209509 or VML-251 or VML251).tw,tn.
60. 158747-02-5.rn.
61. naratriptan/
62. (naratriptan* or Amerge or Colatan or Naragran or Naramig or UNII-QX3KXL1ZA2).tw,tn.
63. 121679-13-8.rn.
64. rizatriptan/
65. (rizatriptan* or Risatriptan* or "L 705,126" or "L 705126" or "L-705,126" or "L-705126" or Maxalt or "MK 0462" or MK 462 or MK-0462 or MK-462 or rizalief or rizalt or rizaliv or UNII-51086HBW8G).tw,tn.
66. 144034-80-0.rn.
67. sumatriptan/
68. (sumatriptan* or Arcoiran or Alsuma or BRN 6930870 or Diletan or Dolmigral or GR 43175 or GR 43175X or GR-43175 or HSDB 7742 or Imigran* or Imiject or Imitrex or micranil or Migril or Novelian or Sumigrene or Suminat or Sumatran or Sumatriptanum or Sumax or UNII-8R78F6L9VO or Zecuity).tw,tn.
69. 103628-46-2.rn.
70. zolmitriptan/
71. (Zolmitriptan* or AscoTop or Flezol or Rapimelt or UNII-2FS66TH3YW or Zolmitriptan or Zomig or Zomig-ZMT or Zomigon or Zomigoro).tw,tn.
72. 139264-17-8.rn.
73. naproxen plus sumatriptan succinate/
74. (Treximet or Trexima).tw,tn.
75. 811794-26-0.rn.
76. 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75
77. 46 and 76
78. health economics/
79. exp economic evaluation/
80. exp "health care cost"/
81. exp pharmacoeconomics/
82. 78 or 79 or 80 or 81
83. (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab.
84. (expenditure$ not energy).ti,ab.
85. (value adj2 money).ti,ab.
86. budget$.ti,ab.
87. 83 or 84 or 85 or 86
88. 82 or 87
89. 77 and 88
90. 41 or 89
91. remove duplicates from 90

publications addressed the objective of the review and were selected for inclusion (Fig. 1).[9-29]

Common limitations relating to methodology and applicability of the economic evaluations were identified: limited generalizability to the Canadian context, inappropriate outcomes (focus on costs per successful treatment rather than incremental costs per outcomes), analyses based on poor-quality effectiveness and utility data, and lack of independence in terms of study funding.

In terms of generalizability, only 3 of the 21 studies were Canadian.[9,15,25] All of these studies were published between 1995 and 2002 and therefore were based on dated information and included drug costs prior to the availability of generic formulations. Nine out of the 21 studies considered outcomes that would be considered inappropriate for making funding recommendations within the context of economic evaluation.[11,13,16-19,21,23,26]

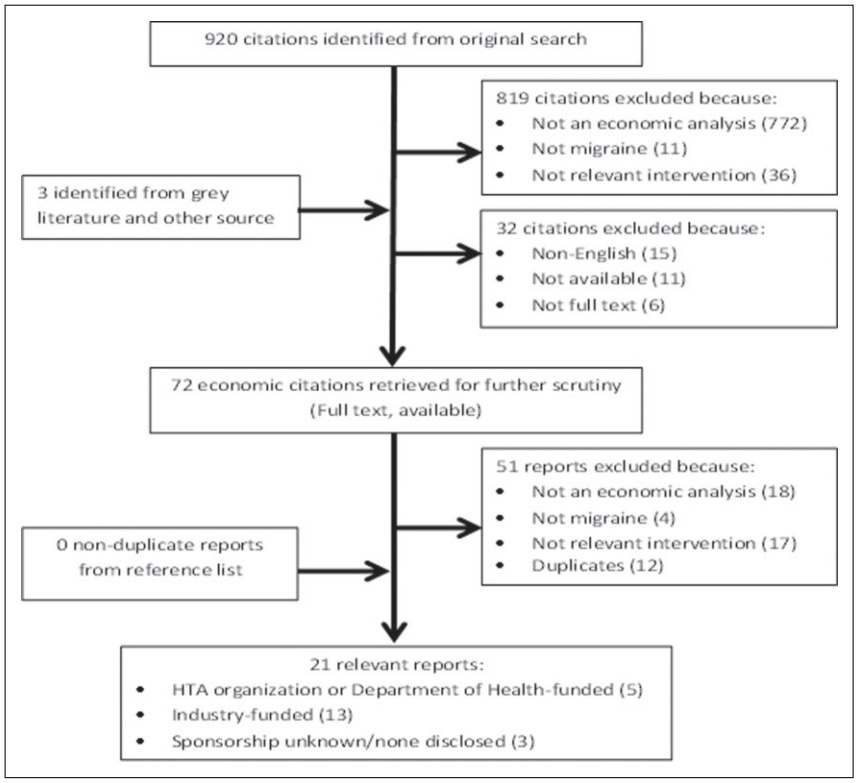


**Fig. 1.—Results of literature search.**

Eleven out of 21 studies[17-19,21-25,27-29] used effectiveness data,[30] which had previously been considered of low quality by the Canadian Agency for Drugs and Technology in Health.[31] None of the studies used utility values that met Canadian guidelines for economic evaluation.[32] Only 8 of the 21 studies were independent from industry funding.[9,10,12,15,16,20,22,23]

Two studies were assessed to be of suitable quality for informing reimbursement strategies.[10,12] A report from the UK National Clinical Guideline Centre suggested that for naïve patients, triptans were more cost-effective than acetaminophen, ergots, and non-steroidal anti-inflammatory drugs NSAIDs, and that for experienced patients, the addition of NSAIDs or acetaminophen to triptans dominated triptans alone.[10] The results from a Finnish Medicines Agency-sponsored report imply that sumatriptan 100 mg dominated all other triptans with the exception of eletriptan 40 mg.[12] Thus, the evidence from these 2 studies suggests that triptans are cost-effective compared with ergots in the management of migraines.

**Budget Impact Analysis.—***Methods.*—The focus of the budget impact analysis is to identify the impact on drug formulary expenditure of alternate reimbursement strategies. This is done in 3 steps: forecast future drug expenditure, identify candidate reimbursement strategies, and assess budget impact of each candidate reimbursement strategy.

The forecast of future expenditure involves the use of historical drug utilization data to predict future expenditure. Given the likely changing clinical environment, typically future expenditure is forecasted for no more than a 3-year period.

Analysis will typically use data from the OPDP for each drug within the relevant class as well as, where pertinent, drug expenditure for other alternate drugs outside of the class of interest. Alternate model specifications for predicting future expenditures are examined: typically a linear model assuming a constant increase by the same amount each year; an exponential model assuming an exponential relationship between expenditure and time; a power-based

model assuming a flexible non-linear relationship between time and expenditure; and a constant growth model assuming a constant percentage increase in expenditure for each quarter. Additional covariates may be included within the model. These may include, among others, the number of drugs within a specific class to allow for any expansion of the expenditure, changes to access within the drug formulary (eg, a change in listing status), and the availability of newer classes of drugs for the specific condition. In addition, both absolute and Winter's seasonal effects are examined for significance.

The choice of the most appropriate model is based on statistical criteria – specifically the most suitable model is selected based on both the Bayesian information criterion (BIC) and Akaike information criterion (AIC). All analyses are conducted within Microsoft Excel to facilitate the use of the models by relevant decision makers within the OPDP.

At the onset of the reimbursement-based economic analysis, it is necessary to identify potential reimbursement strategies for the specific class under review. Strategies are identified through involvement of specific stakeholders: OPDP representatives and clinical experts. Strategies could involve providing either greater or more limited access through change in listing status (eg, a movement from EAP or LU would represent improved access, while movement to EAP from GB would represent limited access). Changes with respect to improved access may be combined with strategies to reduce budgetary impact through negotiated price reductions. Strategies may also involve preferential listing of specific products – such listings may be based on greater effectiveness for 1 product vs others within the same class, or may be optimal due to differential costs of products within the same class.

The final step within the budget impact analysis is to estimate the impact on expenditure of the different candidate reimbursement strategies. This involves forecast of the change in volume of use for each drug within the specific class. Ideally, such estimates will be obtained by utilizing data from other jurisdictions that have adopted similar reimbursement strategies to the candidate strategies. When this is not possible, the impact on volume can be assessed through elicitation of clinical expert opinion regarding the likely impact on prescribing habits of changes in listing status.

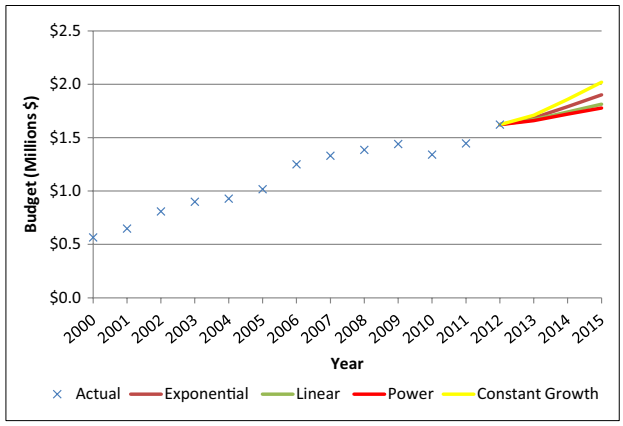


**Fig. 2.—Forecast of triptan expenditure.**
**Source: Ontario Public Drug Programs claims data 2000-2012.**

*Application to Triptans.*—Within the context of triptans, analysis used quarterly OPDP data on the usage of triptans (almotriptan, naratriptan, rizatriptan, sumatriptan, and zolmitriptan) from 2000 to 2012. Costs for each quarter were standardized based on unit costs for each product from 2012 with expenditure predicted for the next 3 years, 2013-2015. All 4 forecasting models (linear, exponential power, and constant growth) suggest an increase in triptan expenditure over the next 3 years (Fig. 2). The BIC (range 3633 to 3645) and AIC (range 3629 to 3638) were similar across all models. Thus, the most simple model (linear model) was adopted for assessing the impact of alternate reimbursement strategies. Without any change to the current reimbursement of triptans, it is expected that triptan expenditure would be approximately $1.75 million in 2014 (status quo) (Table 2).

Given the different reimbursement policies adopted across Canada, availability of generic triptans and possibility of medication overuse for headache, the following alternative approaches to reimbursement were considered: changing listing status (from EAP to GB or LU), enforcing generic pricing restrains and/or generic substitution within EAP, and incorporating monthly quantity limits (6, 12, and 18). A total of 20 reimbursement strategies were identified during the scoping assessment along

**Table 2.—List of Potential Reimbursement Strategies and Their Predicted Budget Impact**

| Strategy | Reimbursement Strategy | 2014 Expected Cost† | Impact‡ |
|---|---|---|---|
| Status Quo | No change to current reimbursement of triptans | $1,752,377 | – |
| EAP1 | EAP with generic pricing | $1,467,247 | ↓ of 16% |
| EAP2 | EAP with generic pricing and substitution, if available | $550,268 | ↓ of 69% |
| EAP3 | EAP for generic products only | $537,515 | ↓ of 69% |
| EAP4 | EAP 1 with quantity limit of 6 per month | $744,842 | ↓ of 57% |
| EAP5 | EAP 2 with quantity limit of 6 per month | $277,003 | ↓ of 84% |
| EAP6 | EAP 3 with quantity limit of 6 per month | $271,781 | ↓ of 84% |
| EAP7 | EAP 1 with quantity limit of 12 per month | $1,073,446 | ↓ of 39% |
| EAP8 | EAP 2 with quantity limit of 12 per month | $398,617 | ↓ of 77% |
| EAP9 | EAP 3 with quantity limit of 12 per month | $390,668 | ↓ of 78% |
| EAP10 | EAP 1 with quantity limit of 18 per month | $1,308,618 | ↓ of 25% |
| EAP11 | EAP 2 with quantity limit of 18 per month | $490,977 | ↓ of 72% |
| EAP12 | EAP 3 with quantity limit of 18 per month | $479,870 | ↓ of 73% |
| LU1 | LU listing with generic pricing and substitution, if available | $5,211,634 | ↑ of 197% |
| LU2 | LU listing for generic products only | $5,088,066 | ↑ of 190% |
| LU3 | LU1 with quantity limit of 6 per month | $4,052,143 | ↑ of 131% |
| LU4 | LU2 with quantity limit of 6 per month | $3,960,532 | ↑ of 126% |
| LU5 | LU1 with quantity limit of 12 per month | $4,904,750 | ↑ of 180% |
| LU6 | LU2 with quantity limit of 12 per month | $4,790,905 | ↑ of 173% |
| LU7 | LU1 with quantity limit of 18 per month | $5,071,950 | ↑ of 189% |
| LU8 | LU2 with quantity limit of 18 per month | $4,953,481 | ↑ of 183% |
| GB1 | GB listing with generic pricing and substitution, if available | $7,050,685 | ↑ of 302% |
| GB2 | GB listing for generic products only | $6,883,513 | ↑ of 293% |
| GB3 | GB1 with quantity limit of 6 per month | $4,189,249 | ↑ of 139% |
| GB4 | GB2 with quantity limit of 6 per month | $4,100,941 | ↑ of 134% |
| GB5 | GB1 with quantity limit of 12 per month | $5,619,145 | ↑ of 221% |
| GB6 | GB2 with quantity limit of 12 per month | $5,497,328 | ↑ of 214% |
| GB7 | GB1 with quantity limit of 18 per month | $6,251,231 | ↑ of 257% |
| GB8 | GB2 with quantity limit of 18 per month | $6,113,241 | ↑ of 249% |

†Based on the linear model; results reported in 2014 Canadian dollars.
‡% change vs status quo.
GB strategies based on current prescribing practice in Alberta, where triptans are available similar to GB for eligible patients aged 18-64 years.
LU strategies based on current prescribing practice in Manitoba, where triptans are available similar to LU for eligible patients aged 18-64 years.
EAP = Exceptional Access Program; GB = general benefit; LU = limited use.

with further consultation with the OPDP (Table 1). For EAP scenarios without quantity limits, the unit cost of triptans were changed to allow for generic pricing and applied to the forecasted volume of triptan use. For EAP scenarios with quantity limits, the appropriate unit costs were applied to a reduced volume based on the proportion of prescribed units which would fall under the various limits. To estimate the volume of use under less restrictive listing (GB/LU) in Ontario, the volume of triptan use in any given year for Ontario was multiplied by the ratio of the use of triptans by beneficiary for other regions (in this case Alberta/Manitoba) where less restrictive listing is available. The costs of EAP were included in the analysis based on the average cost of processing 1 application. For GB/LU with quantity limits, the same adjustment as for EAP was then applied. For all GB/LU strategies, the generic costs for triptans were applied to the forecasted volume of triptan use.

A policy that requires generics to be priced at 25% of average branded cost may reduce expenditure by 16% (EAP1) (Table 1). Combining reduced generic costs with the requirement of replacement of brand name agents with their generic formulation, when available (EAP2), may reduce expenditure by 69% (Table 1). A similar policy, but with the addition

of a quantity limit of 12 per patient per month (EAP8), may lead to a greater reduction in costs (77%) (Table 1).

Coverage of triptans through GB without quantity limit is expected to lead to an increase in triptan expenditure by 302% (GB/LU1), while coverage of triptans through LU with quantity limit of 12 per month (GB/LU5), is forecasted to lead to an increase of 221% (Table 1).

**Consideration of Cost-Effectiveness.—***Methods.*—The third stage is to consider the cost-effectiveness of alternate reimbursement strategies. Where there is sufficient evidence from existing literature, this can be conducted based on the literature review in step 1. In some cases, de novo economic evaluations are warranted. In such instances, an economic model adhering to current standards in the conduct of economic evaluation will be developed.[32] The focus of the de novo economic evaluation would be to demonstrate the relative value for money of alternate reimbursement strategies rather than individual therapies – the typical approach of economic evaluation. The first step of this approach will be to estimate the associated costs and outcomes for each potential treatment. Following this, the likely use of each intervention under each reimbursement strategy will be estimated based on similar approaches adopted within the budget impact analysis. Finally, the costs and outcomes of each reimbursement strategy are estimated by weighting the costs and outcomes for each therapy by their expected utilization. From this, the costs and outcomes of each strategy are estimated and their relative cost-effectiveness can be estimated using standard methodology. Thus, the goal of this stage is to support the findings from the budget impact analysis, identifying reimbursement strategies that may be cost-effective and ruling out strategies which are not.

*Application to Triptans.*—Based on the nature of the research question, the results of the companion clinical systematic review,[33] and the consistent cost of triptans (with the availability of many in generic formulations), stakeholders concluded that there was no requirement for a traditional economic evaluation to assess the value for money for each of the candidate treatments or reimbursement strategies. Specifically, stakeholders argued that there was adequate evidence to suggest that triptans are effective when given to migraine patients, and cost-effective, especially given the availability of generic formulations.

## DISCUSSION

Reimbursement-based economics is a novel approach to pharmacoeconomics. Traditional economic evaluation focuses on the economic attractiveness of specific therapies. Studies are conducted when new technologies become available and funding is requested – hence, the high proportion of existing studies which are directly sponsored by industry. Within reimbursement-based economics, the focus is explicitly on the decision problem facing decision makers with respect to the desire for formulary modernization and the related need to review the listing status of drugs within specific classes or specific diseases. The reimbursement-based economic approach developed within the ODPRN involves a systematic review of economic literature, comprehensive budget impact analysis, and when warranted, a de novo economic evaluation. The objective is to identify the optimal reimbursement strategy for available drug products.

Given the challenging fiscal situation and the budgeted growth in OPDP expenditure for the next few years, reimbursement-based economics has the potential to be a valuable approach in helping develop cost-effective and efficient use of the scarce resources available for public drug funding. This potential is highlighted through reference to a recent application of reimbursement-based economics in the context of triptans in the treatment of migraine.

Within the ODPRN analysis of triptans, the evidence suggests that the use of triptans is cost-effective if restricted to migraineurs, especially given the availability of generic equivalents. Reimbursement of triptans through a less restrictive listing (GB or LU) would lead to a substantially wider use of triptans at an increased expenditure. The findings from the reimbursement-based economic analysis were then considered in combination with findings related to accessibility, effectiveness, and safety derived from the other components of the class review.[33,34] From this, 2 reimbursement options for

triptans were considered as potential funding alternatives for OPDP and presented to the Ministry for consideration.

There are limitations to the reimbursement-based approach detailed. The limited time to conduct the research (20 weeks from identification of research questions to final report) precludes the conduct of any primary research. Furthermore, the likely impact of alternate reimbursement strategies cannot be directly estimated empirically. Pilot studies to assess changes in reimbursement status are neither feasible nor desirable given the timely nature of the decisions to be made. At best, inferences from other jurisdictions can be drawn although in certain circumstances analysis will be reliant on expert opinion relating to likely changes in prescribing status.

A limitation of the example provided is the limited evidence on the cost-effectiveness of triptans in the current Canadian context. Ideally in situations where the evidence base may be considered limited, further studies may be commissioned. However, it should be noted that the analysis relates to an actual process of formulary modernization where the production for research is highly time sensitive. In this context, decision makers have identified a decision problem and a willingness to address this through changes in formulary listing. Decision makers considered the evidence available with respect to the cost-effectiveness, effectiveness, and budget impact of the alternate reimbursement strategies, and felt that although limited, there was sufficient evidence to make conclusions regarding the cost-effectiveness of triptans. Thus, in the first application of the ODPRN process, there was no requirement for de novo economic modeling. Economics by its nature is a decision science and research must be pertinent to real-world decision making. Although the evidence base may not be strong, identifying what evidence is available is still a vital component of ensuring that the decisions that will be made are as ideal as possible. Thus, the reimbursement-based approach detailed is inherently related to the decision-making process.

In this article, we have detailed the reimbursement-based approach. It is a novel application of pharmacoeconomics aiming to help facilitate decisions relating to formulary modernization. The conduct of this research in conjunction with other qualitative and quantitative analyses is unique within the health services literature and should ensure that changes to formulary listing status in Ontario should be evidence based.

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## STATEMENT OF AUTHORSHIP

**Category 1**

**(a) Conception and Design**
Doug Coyle; Karen M. Lee; Kelley-Anne Sabarre; Muhammad Mamdani

**(b) Acquisition of Data**
Doug Coyle; Karen M. Lee; Muhammad Mamdani

**(c) Analysis and Interpretation of Data**
Doug Coyle; Karen M. Lee; Kelley-Anne Sabarre; Muhammad Mamdani; Kylie Tingley

**Category 2**

**(a) Drafting the Manuscript**
Doug Coyle; Karen M. Lee; Kelley-Anne Sabarre; Muhammad Mamdani; Kylie Tingley

**(b) Revising It for Intellectual Content**
Doug Coyle; Karen M. Lee; Kelley-Anne Sabarre; Muhammad Mamdani; Kylie Tingley

**Category 3**

**(a) Final Approval of the Completed Manuscript**

Doug Coyle; Karen M. Lee; Kelley-Anne Sabarre; Muhammad Mamdani; Kylie Tingley

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