

Epilepsy Care in Ontario: An Economic Analysis of Increasing Access to Epilepsy Surgery

JM Bowen, OC Snead, K Chandra, G Blackhouse, R Goeree

July 2012

About Health Quality Ontario

Health Quality Ontario (HQO) is an agency funded by the Ministry of Health and Long-Term Care. An essential part of HQO's mandate is to provide evidence-based recommendations on the coordinated uptake of health services and health technologies in Ontario to the Ministry of Health and Long-Term Care and to the health care system. This mandate helps to ensure that residents of Ontario have access to the best available and most appropriate health services and technologies to improve patient outcomes.

To fulfill its mandate, HQO conducts systematic reviews of evidence and consults with experts in the health care services community. The resulting evidence-based analyses are reviewed by the Ontario Health Technology Advisory Committee, and published in the *Ontario Health Technology Assessment Series*.

About the *Ontario Health Technology Assessment Series*

To conduct its comprehensive analyses, HQO systematically reviews the available scientific literature, making every effort to consider all relevant national and international research; collaborates with partners across relevant government branches; consults with clinical and other external experts and developers of new health technologies; and solicits any necessary supplemental information.

In addition, HQO collects and analyzes information about how a new technology fits within current practice and existing treatment alternatives. Details about the technology's diffusion into current health care practices add an important dimension to the review of the provision and delivery of the health technology in Ontario. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social and legal issues relating to the technology assist decision-makers in making timely and relevant decisions to optimize patient outcomes.

The public consultation process is available to individuals wishing to comment on an analysis prior to publication. For more information, please visit: http://www.hqontario.ca/en/mas/ohtac_public_engage_overview.html.

Disclaimer

This evidence-based analysis was prepared by HQO for the Ontario Health Technology Advisory Committee and developed from analysis, interpretation, and comparison of scientific research and/or technology assessments conducted by other organizations. It also incorporates, when available, Ontario data and information provided by experts and applicants to HQO to inform the analysis. While every effort has been made to reflect all scientific research available, this document may not fully do so. Additionally, other relevant scientific findings may have been reported since completion of the review. This evidence-based analysis is current to the date of the literature review specified in the methods section. This analysis may be superseded by an updated publication on the same topic. Please check the HQO website for a list of all evidence-based analyses: http://www.hqontario.ca/en/mas/mas_ohtas_mn.html.

Epilepsy Care in Ontario: An Economic Analysis of Increasing Access to Epilepsy Surgery

James M. Bowen, BScPhm, MSc,^{1,2} O. Carter Snead, MD, FRCPC,^{3,4}
Kiran Chandra, MSc,^{1,2} Gord Blackhouse, MSc, MBA,^{1,2} Ron Goeree, MA^{1,2}

1. Programs for Assessment of Technology in Health (PATH) Research Institute, St. Joseph's Healthcare, Hamilton, ON, Canada
2. Department of Clinical Epidemiology and Biostatistics, Faculty of Health Sciences, McMaster University, Hamilton, ON, Canada
3. Centre for Brain and Behaviour, Division of Neurology, The Hospital for Sick Children, Toronto, ON, Canada
4. Departments of Pediatrics, Medicine (Neurology), & Pharmacology, Faculty of Medicine, University of Toronto, Toronto, ON, Canada.

Presented to the Ontario Health Technology Advisory Committee on March 21, 2012, and to the Health Quality Ontario Board of Directors on March 29, 2012.

Health Quality Ontario was provided with this report on May 15, 2012.

Suggested Citation

Bowen JM, Snead O Carter, Chandra K, Blackhouse G, Goeree R. Epilepsy care in Ontario: an economic analysis of increasing access to epilepsy surgery. *Ont Health Technol Assess Ser* [Internet]. 2012 July; 12(18):1-41. Available from: <http://www.hqontario.ca/en/documents/eds/2012/econ-epilepsy-surgery.pdf>

Indexing

The *Ontario Health Technology Assessment Series* is currently indexed in MEDLINE/PubMed, Excerpta Medica/EMBASE and the Center for Reviews and Dissemination database.

Permission Requests

All inquiries regarding permission to reproduce any content in the *Ontario Health Technology Assessment Series* should be directed to: EvidenceInfo@hqontario.ca.

How to Obtain Issues in the *Ontario Health Technology Assessment Series*

All reports in the *Ontario Health Technology Assessment Series* are freely available in PDF format at the following URL: http://www.hqontario.ca/en/mas/mas_ohtas_mn.html.

Conflict of Interest Statement

All analyses in the *Ontario Health Technology Assessment Series* are impartial and subject to a systematic evidence-based assessment process. There are no competing interests or conflicts of interest to declare.

Peer Review

All analyses in the *Ontario Health Technology Assessment Series* are subject to external expert peer review. Additionally, the public consultation process is also available to individuals wishing to comment on an analysis prior to finalization. For more information, please visit: http://www.hqontario.ca/en/mas/ohtac_public_engage_overview.html.

Abstract

Background

In August 2011 a proposed epilepsy care model was presented to the Ontario Health Technology Advisory Committee (OHTAC) by an Expert Panel on a Provincial Strategy for Epilepsy Care in Ontario. The Expert Panel recommended leveraging existing infrastructure in the province to provide enhanced capacity for epilepsy care. The point of entry for epilepsy care and the diagnostic evaluation for surgery candidacy and the epilepsy surgery would occur at regional and district epilepsy centres in London, Hamilton, Toronto, and Ottawa and at new centres recommended for northern and eastern Ontario.

This economic analysis report was requested by OHTAC to provide information about the estimated budgetary impact on the Ontario health care system of increasing access to epilepsy surgery and to examine the cost-effectiveness of epilepsy surgery in both children and adults.

Methods

A prevalence-based “top-down” health care system budgetary impact model from the perspective of the Ministry of Health and Long-Term Care was developed to estimate the potential costs associated with expanding health care services to increase access to epilepsy care in general and epilepsy surgery in particular. A 5-year period (i.e., 2012–2016) was used to project annual costs associated with incremental epilepsy care services. Ontario Health Survey estimates of epilepsy prevalence, published epilepsy incidence data, and Canadian Census results for Ontario were used to approximate the number of individuals with epilepsy in the province. Applying these population estimates to data obtained from a recent field evaluation study that examined patterns of care and costs associated with epilepsy surgery in children, a health care system budget impact was calculated and the total costs and incremental costs associated with increasing access to surgery was estimated.

In order to examine the cost-effectiveness of epilepsy surgery in children, a decision analysis compared epilepsy surgery to continued medical management in children with medically intractable epilepsy. Data from the field evaluation were combined with various published data to estimate the costs and outcomes for children with drug-refractory epilepsy over a 20-year period. Outcomes were defined as the number of quality-adjusted life years (QALYs) accumulated over 20 years following epilepsy surgery.

Results

There are about 20,981 individuals with medically intractable epilepsy in Ontario. Of these, 9,619 (1,441 children and 8,178 adults) could potentially be further assessed at regional epilepsy centres for suitability for epilepsy surgery, following initial evaluation at a district epilepsy care centre. The health care system impact analysis related to increasing access to epilepsy surgery in the Ontario through the addition of epilepsy monitoring unit (EMU) beds with video electroencephalography (vEEG) monitoring (total capacity of 15 pediatric EMU beds and 35 adult EMU beds distributed across the province) and the associated clinical resources is estimated to require an incremental \$18.1 million (Cdn) annually over the next 5 years from 2012 to 2016. This would allow for about 675 children and 1050 adults to be evaluated each year for suitability for epilepsy surgery representing a 150% increase in pediatric epilepsy surgery evaluation and a 170% increase in adult epilepsy surgery evaluation.

Epilepsy surgery was found to be cost-effective compared to continued medical management in children with drug-refractory epilepsy with the incremental cost-effectiveness ratio of \$25,020 (Cdn) to \$69,451

(Cdn) per QALY for 2 of the scenarios examined. In the case of choosing epilepsy surgery versus continued medical management in children known to be suitable for surgery, the epilepsy surgery was found to be less costly and provided greater clinical benefit, that is, it was the dominant strategy.

Conclusion

Epilepsy surgery for medically intractable epilepsy in suitable candidates has consistently been found to provide favourable clinical outcomes and has been demonstrated to be cost-effective in both adult and child patient populations. The first step to increasing access to epilepsy surgery is to provide access to evidence-based care for all patients with epilepsy, both adults and children, through the provision of resources to expand EMU bed capacity and associated clinical personnel across the province of Ontario.

Plain Language Summary

Epilepsy, characterized by recurrent, unpredictable, and spontaneous seizures, affects approximately 70,000 people in Ontario. About 30% continue to suffer from seizures despite using 2 or more anti-seizure medications. For these individuals epilepsy surgery is a treatment option to stop the seizures or at least reduce their frequency. Awareness of this treatment option is not widespread and people are not commonly referred to those hospitals in Ontario where this surgery is available. A proposal to increase access to epilepsy care and surgery has been made by an expert committee that provided a report to the Ontario Health Technology Advisory Committee (OHTAC). In order to address the lack of access of patients with medically intractable epilepsy to the possibility of curative surgical treatment, it is necessary to design a system that provides equal availability of evidence-based treatment for all epilepsy patients in Ontario, both adults and children. To this end, the establishment of district epilepsy care centres and the further development of the existing regional epilepsy care centres in the province have been proposed. This report outlines the estimated additional funds that will be required to implement the proposal. It also examines the cost-effectiveness of referral to these centres and epilepsy surgery.

For the 21,000 people in the province with drug-refractory epilepsy, referral to an epilepsy monitoring unit (EMU) located at one of the epilepsy care centres is the first step to determining if epilepsy surgery is an option for them. The expert committee proposal suggests that the number of EMU beds be increased from the current 19 to 50 to allow for the assessment of those individuals with drug-refractory epilepsy. The health care system budget impact model presented in this report estimates that it would cost approximately \$18 million (Cdn) each year over the next 5 years to increase the number of EMU beds and expand associated epilepsy care centres to permit the systematic evidence-based care of all Ontarians with epilepsy and evaluate more people for surgery candidacy. This amount would provide appropriate care for patients with epilepsy and ensure that about 675 children and 1050 adults could be assessed each year for suitability for epilepsy surgery. Surgery could then be made available to just over 300 people per year.

Epilepsy surgery over the long term is a less expensive treatment alternative for adults and children with medically refractory epilepsy compared with continued drug treatment. In addition, drug treatment does not always work for some patients; nor does it necessarily provide improved quality of life.

This report includes a cost-effectiveness analysis comparing referral for assessment for epilepsy surgery with continuing medical management in children with drug-refractory epilepsy. In all the cases examined epilepsy surgery provides good value for money over a 20-year period. Similar studies have found that the benefits from epilepsy surgery outweigh those of continuing medical management in adult patients with medically refractory epilepsy.

Table of Contents

Abstract	5
Background.....	5
Methods.....	5
Results.....	5
Conclusion.....	6
Plain Language Summary	7
Table of Contents	8
List of Tables	10
List of Figures	11
List of Abbreviations	12
Background	13
Objective of Analysis.....	13
Clinical Need and Target Population.....	13
<i>About Epilepsy</i>	13
<i>Evaluation of Epilepsy Surgery Candidates</i>	13
<i>Epilepsy Care Model</i>	13
<i>Health Care System Budgetary Impact and Cost-Effectiveness Analyses</i>	14
Health Care System Budgetary Impact Analysis	16
Purpose.....	16
Research Methods.....	16
<i>Model Description</i>	16
Statistical Analyses.....	16
<i>Ontario Population Estimates</i>	16
<i>Prevalence and Incidence of Epilepsy</i>	16
<i>Health Care Resource Utilization</i>	18
<i>Unit Costs</i>	19
<i>Model Assumptions</i>	19
<i>Summary of Model Parameters</i>	20
Results of Health System Budgetary Impact Analysis.....	21
<i>Estimated Number of Ontarians with Epilepsy</i>	21
<i>Estimated Budgetary Impact Based on Proposed Number of Epilepsy Monitoring Unit Beds</i>	22
<i>Sensitivity Analyses</i>	23
Summary.....	25
Cost-Effectiveness Analysis	26
Methods.....	26
<i>Decision Analytic Model Structure</i>	26
<i>Model Input Variables</i>	29
<i>Sensitivity Analyses</i>	32

Results.....	32
<i>Question 1: Cost-Effectiveness of Referral of Pediatric Patients to a District Epilepsy Centre for Diagnostic Evaluation</i>	32
<i>Question 2: Cost-Effectiveness of Referral of Pediatric Patients to a Regional Epilepsy Centre for Multidisciplinary Evaluation</i>	33
<i>Question 3: Cost-Effectiveness of Referral of Pediatric Patients to a Regional Epilepsy Centre for Surgery</i>	33
<i>One-Way Sensitivity Analyses of Cost-Effectiveness Model</i>	34
Summary	35
Discussion	36
Acknowledgements	37
References	38

List of Tables

Table 1: Estimated Prevalence of Epilepsy in Ontario per 1,000 Population by Age Group	17
Table 2: Estimated Annual Average Ontario Population Growth Rate, 2006–2011	17
Table 3: Estimated Number of Newly Diagnosed or Incident Cases of Epilepsy in Ontario, 2012–2016 .	17
Table 4: Estimated Number of Children (< 18 years) with Epilepsy in Ontario, 2011, and Estimated Newly Diagnosed or Incidence Cases, 2012–2016.....	18
Table 5: Estimated Number of Adults (≥ 18 years) With Epilepsy in Ontario, 2011, and Estimated Newly Diagnosed or Incidence Cases, 2012–2016	18
Table 6: Mean Estimated Average Health Care Resource Utilization Costs Per Patient by Patient Group	19
Table 7: Percentage of Patients Proceeding to Each Level of Diagnostic Evaluation for Surgery Candidacy	20
Table 8: Summary of Base-Case and Sensitivity-Variant Model Parameters for the Health Care System Impact Analysis, Ontario	20
Table 9: Estimated Number of Children (< 18 Years) Who Undergo Each Level of Diagnostic Evaluation for Epilepsy Surgery Candidacy and Who Are Suitable for Epilepsy Surgery, in Ontario, in 2011 and 2012–2016.....	21
Table 10: Estimated Number of Adults (≥ 18 years) Who Are Candidates For Each Level of Diagnostic Evaluation for Epilepsy Surgery Candidacy, in Ontario, in 2011 and 2012–2016.....	22
Table 11: Estimated Health Care Resource Utilization Costs Associated with Implementing Additional EMU Capacity and Associated Epilepsy Care Resources in Ontario	23
Table 12: Impact on Health Care Resource Utilization and Costs by Varying the Number of EMU Beds Introduced for Children in Ontario.	24
Table 13: Impact on Health Care Resource Utilization and Costs by Varying the Number of EMU Beds Introduced for Adults in Ontario.....	24
Table 14: Summary of Evaluation and Surgery Costs for Children with Epilepsy by Starting Point of the Cost-Effectiveness Model.....	30
Table 15: Summary of Long-Term Follow-Up Costs Used in the Cost-Effectiveness Model	31
Table 16: Base-Case Cost-Effectiveness Results of Child Epilepsy Model: Starting the Model at Referral to a District Epilepsy Centre	32
Table 17: Base-Case Cost-Effectiveness Results of Child Epilepsy Model: Starting the Model at Referral to a Regional Epilepsy Centre.....	33
Table 18: Base-case Cost-Effectiveness Results of Child Epilepsy model When Starting the Model at Point of Surgery.	34
Table 19: One-Way Sensitivity Analysis Examined in the Cost-Effectiveness Model	35

List of Figures

Figure 1: Schematic Diagram of Patient Flow Associated with Epilepsy Surgery Candidacy Evaluation at Proposed District and Regional Epilepsy Care Centres in Ontario.....	14
Figure 2: Schematic of Decision Analytic Model for Epilepsy Surgery Candidacy Evaluation	28
Figure 3: Markov Model Structure for Long-Term Health States for Children with Epilepsy.....	29

List of Abbreviations

AED	Antiepileptic drug
EEG	Electroencephalography
EMU	Epilepsy monitoring unit
HSC	Hospital for Sick Children
ICER	Incremental cost-effectiveness ratio
OHTAC	Ontario Health Technology Advisory Committee
QALY	Quality-adjusted life year
vEEG	Video electroencephalography

Background

Objective of Analysis

To estimate the budgetary impact on the health care system of increasing access to epilepsy surgery in Ontario and to determine the cost-effectiveness of epilepsy surgery in both children and adults in a multidisciplinary, tiered approach to organizing care, surgical assessment, surgery, and postoperative care in cases of medically intractable epilepsy.

Clinical Need and Target Population

About Epilepsy

An epileptic seizure is an episodic behavioural event caused by an abnormal, excessive paroxysmal electrical discharge of nerve cells in the brain. Epilepsy is a disorder characterized by spontaneous recurrent seizures. Of the estimated 70,000 people with epilepsy in Ontario, about 30% have medically intractable epilepsy, in which individuals continue to experience seizures despite treatment with 2 or more appropriate antiepileptic drugs. (1;2) Some of these people may be suitable for epilepsy surgery. However, referral to epilepsy surgery is infrequent. In 2010 only 750 Ontarians with drug-refractory epilepsy were referred for epilepsy surgery evaluation, representing about 4% of the potential number of individuals that could be assessed. (3)

Evaluation of Epilepsy Surgery Candidates

Evaluating and determining candidates with medically intractable epilepsy for epilepsy surgery follows a step-wise approach to diagnostic evaluation. The first step is prolonged video electroencephalography (vEEG), available at epilepsy monitoring units (EMU). (4) Ontario has 19 permanent EMU beds (6 pediatric and 13 adult) and 4 non-permanent flex beds that may be used by other hospital services for patient care. Wait times for EMU assessment exist at each of the centres. (5)

Epilepsy Care Model

In August 2011 the Expert Panel on a Provincial Strategy for Epilepsy Care in Ontario proposed an epilepsy care model to the Ontario Health Technology Advisory Committee (OHTAC). (5) The panel recommended leveraging existing infrastructure to provide capacity for diagnostic evaluation and care at regional and district epilepsy centres in London, Hamilton, Toronto, and Ottawa. (5) The Expert Panel emphasized 2 things in the report: first, to properly identify and provide potentially curative surgical treatment for patients with medically refractory epilepsy, an infrastructure needs to be in place to provide evidence-based care to everyone in the province with this disorder; second, since epilepsy occurs across the life span, any strategy for providing access to evidence-based care must be applicable to all ages, hence breaching the silo effect of the traditional pediatric/internal medicine divisions. The panel also proposed 2 phases of evaluation for epilepsy surgery that would take place at district and regional epilepsy centres across the province. District epilepsy care centres would provide initial neurological assessment by epileptologists and electroencephalography (EEG) for patients on their first seizure with recommendations concerning initial treatment provided to the primary care provider. Should this initial treatment fail and the patient becomes medically refractory, the district care centre would further evaluate for surgery candidacy with 3Tesla magnetic resonance imaging (MRI) using standardized epilepsy protocols and vEEG monitoring at the EMU, neuropsychological evaluation (with standardized protocols), and social work evaluation. In addition, patients with newly diagnosed epilepsy would be put in touch with the local epilepsy advocacy groups through either the district or regional epilepsy care

centre to provide advocacy and further psychosocial support. If the patient is deemed a potential surgery candidate as a result of these tests, they would be referred to the regional epilepsy centre for further pre-surgical evaluation and, if indicated, epilepsy surgery. The regional epilepsy centres in the proposed model would perform the same services as the district epilepsy centres as well as provide diagnostic assessment with positron emission tomography (PET) and magnetoencephalography (MEG). These regional epilepsy centres would also evaluate all of the standardized data acquired from the initial assessments, determine surgery candidacy through a multidisciplinary team evaluation (“seizure conference”) and, as stated above, perform the epilepsy surgery and follow-up. Patients seen at both district and regional epilepsy care centres could connect through the centres to epilepsy advocacy groups in their areas of residence.

Figure 1 shows the patient flow associated with evaluating epilepsy surgery candidacy. (5)

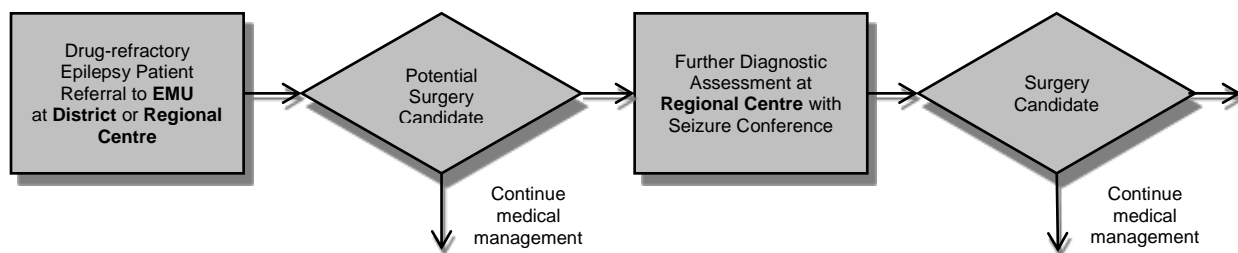


Figure 1: Schematic Diagram of Patient Flow Associated with Epilepsy Surgery Candidacy Evaluation at Proposed District and Regional Epilepsy Care Centres in Ontario

The panel’s proposal also recommended establishing district epilepsy care centres in northern and eastern Ontario that would go toward addressing geographical imbalances and distribute epilepsy care more evenly across the province. (5)

This multidisciplinary, tiered approach to organizing epilepsy care and surgical assessment is aligned with current recommendations for epilepsy care centres and essential services made by the National Association of Epilepsy Centers in the United States. (6)

Health Care System Budgetary Impact and Cost-Effectiveness Analyses

Following the presentation of the Expert Panel’s report to OHTAC, OHTAC and Health Quality Ontario requested an examination of the economic implications of increasing access to epilepsy surgery using the recommendations of the Expert Panel as a guide. (5) In response to this request, input from each of the epilepsy care centres in the province was obtained in February 2012 to identify how access could be enhanced. As a first step to implementing the proposed model, one of the identified issues was the current capacity at EMUs for the initial evaluation. All centres agreed that expanding EMU capacity should be the first stage in increasing access to epilepsy surgery. The centres proposed that an additional 9 pediatric beds and 22 adult beds, distributed across the province, be a starting point to increasing access to epilepsy surgery in the province.

OHTAC requested that this economic analysis provide information on

- the estimated budgetary impact on the health care system of increasing access to epilepsy surgery in Ontario plus evaluating the incremental impact of increased EMU capacity; and

- the cost-effectiveness of epilepsy surgery in both children and adults.

In order to address these 2 issues, a population-based health care system impact analysis was completed and a cost-effectiveness analysis of epilepsy surgery in children was conducted. Cost-effectiveness analyses comparing surgical intervention to continued medical management in adults have been previously published, and repeating these analyses was considered unnecessary. They are described in this report. (7-9)

Health Care System Budgetary Impact Analysis

Purpose

The purpose of this evaluation was to estimate the costs associated with diagnostic evaluation of candidacy of patients with medically refractory epilepsy for the surgical removal of their epileptic focus. Data from a recent field evaluation undertaken for the Ontario Ministry of Health and Long-Term Care were combined with various published data to estimate the costs and outcomes of epilepsy surgery for infants/children/adolescents and adults with drug-refractory epilepsy. (10)

Research Methods

Model Description

A prevalence-based “top-down” health care system budgetary impact model was developed to estimate the potential costs associated with expanding health care services to increase access to epilepsy surgery. A 5-year period (i.e., 2012–2016) was used to project the associated annual costs. The model estimates were based on 2011 population projections from Statistics Canada, published medical literature, and expert opinion. (1;11;12) A Microsoft Excel-based system was designed, with unique spreadsheets describing the Ontario population, prevalence and incidence of epilepsy, costs, and assumptions. These were linked to examine the population-based requirements of an epilepsy monitoring unit (EMU), clinical evaluation and associated surgical capacity in Ontario. The system user is able to alter assumptions in order to choose the various model parameters for the indicated scenario. By manipulating these assumptions, a broad range of sensitivity analyses are available to examine various scenarios. This ability to perform these additional analyses recognizes that the base-case analysis was developed using the published literature and expert opinion and that real-world scenarios may vary from the study results.

Statistical Analyses

Ontario Population Estimates

Ontario population estimates for 2011 were obtained by age and sex. (12) These data were used to project numbers of surgery candidates with drug-refractory epilepsy in the province by age category to enable the delineation of pediatric and adult services.

Prevalence and Incidence of Epilepsy

In 1999 Wiebe et al (11) reported the prevalence of epilepsy in Ontario per 1,000 population by age using data from the Ontario Health Survey. Table 1 shows the prevalence of epilepsy by age group. (1;11)

Table 1: Estimated Prevalence of Epilepsy in Ontario per 1,000 Population by Age Group

Age Group, years	N	Weighted Percentage of Sample, %	Prevalence/1,000
0–11	38	10.66	3.1
12–15	20	3.79	5.7
16–24	29	12.97	4.3
25–44	114	38.85	5.9
45–64	61	17.78	4.9
≥ 65	51	15.95	7.2
Total	313		5.8

Sources: Wiebe et al, 1999 (11) and Tellez-Zenteno et al, 2004. (1;11)

The incidence of newly diagnosed cases of epilepsy is estimated to be 30 to 60 cases per 100,000 population. (11) About 6,500 newly diagnosed cases of epilepsy were used in the first year of the model (2011) and aligned with incidence estimates of 47.4 new epilepsy cases per 100,000 population per year. (13)

An average growth rate for the Ontario population from 2006–2011 was applied to the incidence of epilepsy (6,500 new cases a year) to estimate new cases for the years 2012–2016. (14) The average population growth rate in Ontario was calculated by averaging the increase in population for previous years, 2006–2011 (see Table 2). (14)

Table 2: Estimated Annual Average Ontario Population Growth Rate, 2006–2011

	2006	2007	2008	2009	2010	2011
Population, N	12,665,346	12,792,937	12,932,297	13,064,900	13,210,667	13,372,996
Growth rate, %	1.01	1.09	1.03	1.12	1.23	
Average growth rate, %						1.09

Source: Statistics Canada. (14)

Table 3 describes the estimated incidence of epilepsy in 2012–2016 based on the average Ontario population growth rate.

Table 3: Estimated Number of Newly Diagnosed or Incident Cases of Epilepsy in Ontario, 2012–2016

Year 1* (2012)	Estimated Incidence				Year 5 (2016)	Total Incidence Cases Over 5 years
	Year 2 (2013)	Year 3 (2014)	Year 4 (2015)	Year 5 (2016)		
6,500	6,571	6,643	6,716	6,789	33,219	

* Source: Wiebe et al. (11)

Estimates of the number of individuals with epilepsy in Ontario were determined from Tables 1 and 3. Incidence in each age group was weighted based on the population in Ontario for that age group. Tables 4 and 5 show the prevalence and incidence of epilepsy in children and adults, respectively. In 2011 the

number of children with epilepsy was estimated at about 10,500 (Table 4), and the number of adults with epilepsy at 59,500 (Table 5), making a total of about 70,000.

Table 4: Estimated Number of Children (< 18 years) with Epilepsy in Ontario, 2011, and Estimated Newly Diagnosed or Incidence Cases, 2012–2016

Age Group, years	Population (2011 Population Projection), n	Epilepsy Prevalence 2011	Epilepsy Incidence in 2012	New Epilepsy Incidence Cases (2012–2016)
0–11	1,746,466	5,414	849	4,338
12–15	629,058	3,586	306	1,563
16–17	343,714	1,478	167	854
Total	2,719,238	10,478	1,322	6,755

Table 5: Estimated Number of Adults (≥ 18 years) With Epilepsy in Ontario, 2011, and Estimated Newly Diagnosed or Incidence Cases, 2012–2016

Age Group, years	Population (2011 Population Projection)	Epilepsy Prevalence 2011	Epilepsy Incidence Year 1 (2012)	New Epilepsy Incidence Cases (2012–2016)
18–24	1,310,040	5,633	637	3,254
25–44	3,690,221	21,772	1,794	9,166
45–64	3,761,011	18,429	1,828	9,342
≥ 65	1,892,486	13,626	920	4,701
Total	10,653,758	59,460	5,178	26,464

Health Care Resource Utilization

The costs of surgery along with surgical evaluation were based on a cost analysis done as part of the OHTAC-recommended field evaluation. (10) A retrospective chart review of all infants, children, and adolescents referred to the Hospital for Sick Children (HSC) EMU for elective prolonged video electroencephalography (vEEG) between April 1, 2004, and March 31, 2006 was conducted. These children were followed through the surgery candidacy decision-making process, EMU, diagnostic testing and seizure conference(s) and, if surgery was performed, through the surgery and postoperatively. Data on referral patterns, frequency and wait times of pre-surgical diagnostic tests, physician visits, multidisciplinary seizure conferences, timing of surgery candidacy decisions and subsequent surgical interventions, and associated health care resource utilization were abstracted from the children’s medical records. Health care resources used while evaluating these children’s surgery candidacy, from EMU referral to decision about surgery, were also abstracted. These resources included diagnostic tests, neuropsychological evaluations, seizure conferences, health care visits (e.g., specialists, social work, neurology clinic), surgical procedures, and follow-up visits. The frequency of use of each health care resource was determined per patient. Utilization of health care resources by patients following the previously outlined care paths were outlined (i.e., mean number of seizure conferences for patients undergoing surgical intervention). The frequency of repeat diagnostic evaluations and the mean number of diagnostic tests per patient were also determined. In children undergoing surgical interventions, the

type of intervention, overall length of hospital stay associated with the surgery, as well as the duration of time spent in each hospital care unit (e.g., critical care unit, neuroscience ward) was also evaluated. (10)

Unit Costs

Unit costs for the health care resource utilization items were applied to the resources identified for each patient to estimate the total direct health care costs associated with the evaluation of surgery candidacy for patients referred to the EMU. Where possible, unit costs were obtained from the HSC case costing system and were inflated to 2010 Canadian dollars. The Ontario Schedule of Benefits for Physician's Services was used to estimate the cost of specialists' visits. Estimates for neurology clinic visits, hotel costs, and personnel costs associated with conducting seizure conferences, neuropsychological assessments, social work visits and preparing EMU reports were provided by HSC. Further details regarding the costing analysis are available in the field evaluation report. (10) The mean direct health care costs associated with the diagnostic evaluation for surgery candidacy were calculated per patient (Table 6).

Table 6: Mean Estimated Average Health Care Resource Utilization Costs Per Patient by Patient Group

Health Care Resources Used in Diagnostic Work	Mean Cost Per Patient, \$ (Cdn)		
	vEEG With Or Without EMU Report (n = 189)	Seizure Conference - No Surgery Recommended (n = 96)	Seizure Conference - Surgery Recommended (n = 64)
vEEG	213	9,494	10,396
Other tests	3,331	2,880	8,029
MEG	68	10,951	32,106
EMU reports	2	14	14
Seizure conferences		238	379
Appointments		14	64
Follow-up visits		27	672
Surgical interventions			32,715
Post-surgery tests			1,819
Post-surgery appointments			42
Total Cost	3,614	23,617	86,237

Abbreviations: Cdn, Canadian; EMU, epilepsy monitoring unit; MEG, magnetoencephalography; vEEG, video electroencephalography.

Source: Bowen et al, 2011. (10)

Model Assumptions

Prevalence and Incidence

The budgetary impact model assumed that the proportion of epilepsy cases with drug-refractory disease was 30% for both children and adults. (2)

The field evaluation data showed that 189 pediatric patients were referred to the EMU at HSC and received vEEG without any further evaluation through seizure conference. Further evaluation and diagnostic assessment (i.e., seizure conference) was conducted in 160 children in the cohort, and of these, 64 were identified as surgery candidates (see Table 7). At the time of this analysis, data outlining the

patient flow and numbers progressing through epilepsy surgery evaluation was only available for the pediatric population. As a result, these data were applied to the adult population.

Table 7: Percentage of Patients Proceeding to Each Level of Diagnostic Evaluation for Surgery Candidacy

Diagnostic Work-Up/Surgery	Number of Patients, n/n	Percentage, %	Range (Variation \pm 2.5), %
vEEG only	189/349	54.2	51.7–56.7
Seizure conference	160/349	45.8	43.3–48.3
Surgery candidates	64/160	40.0	37.5–42.5
Not surgery candidates	96/160	60.0	57.5–62.5

Abbreviations: vEEG, video electroencephalography.

Source: Bowen et al, 2011. (10)

Of the 64 candidates, 56 parents/children chose to have epilepsy surgery (88%). However, the budgetary impact model assumed that 100% of cases chose to pursue surgery.

Epilepsy Monitoring Unit Beds

There are 19 EMU beds in Ontario, 6 for children and 13 for adults. Based on 2011 case volume for existing EMU beds in the province and with further advice from the panel, it was assumed that 45 children and 30 adults with epilepsy could use one EMU bed per year (personal communication, expert opinion, February 2012). Based on input from the epilepsy care centres, the number of beds required to implement the proposal from the Expert Panel (5) was assumed to be 15 for children and 35 for adults. The total number of pediatric and adult EMU beds were varied in increments of 5 in order to examine different implementation strategies as a part of the sensitivity analysis. Based on data from one of the epilepsy care centres, the cost of establishing an EMU bed was about \$90,000 (Cdn) each and the annual EMU costs to maintain all EMU beds was \$85,000 (Cdn) per centre.

Summary of Model Parameters

Table 8 describes a summary of the input choices in the budgetary impact model.

Table 8: Summary of Base-Case and Sensitivity-Variant Model Parameters for the Health Care System Impact Analysis, Ontario

Model Parameters	Base Case, %	Available Choices, %
Proportion of children and adults with drug-refractory epilepsy, %	30	10, 15, 20, 25
Proportion of children and adults who choose to pursue EMU/surgical option, %	100	60, 75, 88, 100
Proportion of children and adults who are reviewed at seizure conference, %	45.8	43.3, 48.3
Proportion of children and adults who are surgery candidates based on seizure conference, %	40	37.5, 42.5
Total number of EMU beds for children	15	20, 25, 30, 35, 40
Total number of EMU beds for adults	35	25, 30, 35, 40, 45

Abbreviations: EMU, epilepsy monitoring unit.

The base-case analysis used the best available data to estimate the number of children and adults with drug-refractory epilepsy who are surgery candidates. The proposed number of EMU beds for both children and adults in Ontario was calculated from this estimate. The analysis included all males and females of all ages in Ontario. The model also assumes that all eligible candidates with drug-refractory epilepsy choose to pursue the EMU/surgical option.

All other available options allow the user to estimate costs for different scenarios of prevalence of disease, surgery candidacy, and number of EMU beds in the province.

Results of Health System Budgetary Impact Analysis

Estimated Number of Ontarians with Epilepsy

Taking into account the assumptions stated above, the prevalent and incident cases (years 1–5) with drug-refractory epilepsy who choose to pursue EMU/surgery candidacy were calculated to be 3,143 and 2,027 children, respectively (see Table 9). Of these, 948 would be identified as surgery candidates (both prevalent and incident cases).

Table 9: Estimated Number of Children (< 18 Years) Who Undergo Each Level of Diagnostic Evaluation for Epilepsy Surgery Candidacy and Who Are Suitable for Epilepsy Surgery, in Ontario, in 2011 and 2012–2016

Sample of Children	Proportion Estimate, %	Number of Prevalent Epilepsy Cases in 2011 (n = 10,478)	Total Incident Epilepsy Cases in (Years 1–5: 2012–2016) (n = 6,755)	Total (n = 17,232)
With drug-refractory epilepsy	30	3,143	2,027	5,170
Pursue EMU/surgery candidacy assessment	100	3,143	2,027	5,170
Receive vEEG only	54.2	1,703	1,097	2,800
Reviewed at seizure conference	45.8	1,440	930	2,370
Not surgery candidates based on seizure conference	60.0	864	558	1,422
Surgery candidates based on seizure conference	40.0	576	372	948

Abbreviations: EMU, epilepsy monitoring unit; vEEG, video electroencephalography.

Based on the data available for the pediatric population, the prevalent and incident cases (years 1–5) of adults with drug-refractory epilepsy who would choose to pursue EMU/surgery candidacy assessment were estimated to be 17,838 and 7,939, respectively (see Table 10). Of these, a total of 4,727 cases would be identified as surgery candidates (both prevalent and incident cases).

Table 10: Estimated Number of Adults (≥ 18 years) Who Are Candidates For Each Level of Diagnostic Evaluation for Epilepsy Surgery Candidacy, in Ontario, in 2011 and 2012–2016

Sample of Adults	Proportion Estimate, %	Number of Prevalent Epilepsy Cases in 2011 (n = 59,460)	Total Incident Epilepsy Cases in (Years 1–5: 2012–2016) (n = 26,464)	Total (n = 85,924)
With drug-refractory epilepsy	30	17,838	7,939	25,777
Pursue EMU/ surgery candidacy assessment	100	17,838	7,939	25,777
Receive vEEG only	54.2	9,660	4,300	13,960
Receive further diagnostic work-up at seizure conference	45.8	8,178	3,639	11,817
Not surgery candidates based on seizure conference	60.0	4,907	2,183	7,090
Surgery candidates based on seizure conference	40.0	3,271	1,456	4,727

Abbreviations: EMU, epilepsy monitoring unit; vEEG, video electroencephalography.

Estimated Budgetary Impact Based on Proposed Number of Epilepsy Monitoring Unit Beds

As mentioned earlier, based on input from the epilepsy care centres, the number of permanent EMU beds proposed for Ontario is 15 for children and 35 for adults. This would yield an incremental number of candidates accessing EMU beds annually as 405 children and 660 adults, translating to an annual incremental cost of \$18 million (Cdn) to the health care system (see Table 11). The added assessment through the EMUs across the province would identify an additional 227 surgery candidates. The incremental cost estimate encompasses costs associated with the initial referral and diagnostic assessment at the EMU, all of the way through to the surgical intervention and follow-up, and accounts for the attrition of individuals through the entire surgery candidacy evaluation process.

Table 11: Estimated Health Care Resource Utilization Costs Associated with Implementing Additional EMU Capacity and Associated Epilepsy Care Resources in Ontario

	Candidates		
	Children	Adult	Total
Number of candidates per EMU bed/year	45	30	n/a
Number of permanent EMU beds			
Current	6	13	19
Proposed	15	35	50
Incremental	9	22	31
Number of candidates accessing permanent EMU beds/year			
Current	270	390	660
Proposed	675	1,050	1,725
Incremental	405	660	1,065
Number of surgical procedures/year			
Current	30	60	90
Proposed	124	193	317
Incremental	94	133	227
Cost/year, \$ Cdn (millions)			
Current	4.6	6.6	11.2
Proposed	11.5	17.8	29.3
Incremental	6.9	11.2	18.1

Abbreviations: Cdn, Canadian; EMU, epilepsy monitoring unit.

Sensitivity Analyses

Sensitivity analyses were conducted on the proposed number of permanent EMU beds in the province. The number of these beds was varied by increments of 5 for children (Table 12) and adults (Table 13).

Table 12: Impact on Health Care Resource Utilization and Costs by Varying the Number of EMU Beds Introduced for Children in Ontario.

	Number of Child Candidates					
Number of permanent EMU beds						
Current	6	6	6	6	6	6
Proposed	15	20	25	30	35	40
Incremental	9	14	19	24	29	34
Number of candidates accessing permanent EMU beds/year						
Current	270	270	270	270	270	270
Proposed	675	900	1,125	1,350	1,575	1,800
Incremental	405	630	855	1,080	1,305	1,530
Cost/year, \$ Cdn (millions)						
Current	4.5	4.5	4.5	4.5	4.5	4.5
Proposed	11.3	15.1	18.8	22.6	26.4	30.2
Incremental	6.8	10.6	14.3	18.1	21.9	25.7

Abbreviations: Cdn, Canadian; EMU, epilepsy monitoring unit.

The number of beds varying from 15 to 40 translated to a potential annual cost ranging from \$6.8 million (Cdn) to \$25.6 million (Cdn) for pediatric cases.

Table 13: Impact on Health Care Resource Utilization and Costs by Varying the Number of EMU Beds Introduced for Adults in Ontario.

	Number of Adult Candidates					
Number of permanent EMU beds						
Current	13	13	13	13	13	13
Proposed	20	25	30	35	40	45
Incremental	7	12	17	22	27	32
Number of candidates accessing permanent EMU beds/year						
Current	390	390	390	390	390	390
Proposed	600	750	900	1,050	1,200	1,350
Incremental	210	360	510	660	810	960
Cost/year, \$ Cdn (millions)						
Current	6.6	6.6	6.6	6.6	6.6	6.6
Proposed	10.2	12.7	15.3	17.8	20.4	22.9
Incremental	3.6	6.1	8.7	11.2	13.7	16.3

Abbreviations: Cdn, Canadian; EMU, epilepsy monitoring unit.

The number of beds varying from 20 to 45 translated to a potential annual cost ranging from \$3.6 million (Cdn) to \$16.3 million (Cdn) for adult cases.

Summary

There are about 21,000 people with medically intractable epilepsy in Ontario. Of these, about 9,600 (1,441 children and 8,178 adults) could be assessed at regional epilepsy centres to determine suitability for epilepsy surgery, provided the health care system infrastructure is available. Surgical intervention could be clinically indicated in 3,850 people to either stop the seizures (in about two-thirds to three-quarters of individuals undergoing surgery) or reduce seizure activity. (10;15)

Increasing access to epilepsy surgery in Ontario through the addition of 15 pediatric and 35 adult EMU beds with vEEG monitoring and the associated clinical resources is estimated to require an incremental \$18.1 million (Cdn) annually over the next 5 years.

The expansion of epilepsy care services is estimated to provide capacity to evaluate 675 children and 1,050 adults for epilepsy surgery each year. This would represent a 150% increase in pediatric epilepsy surgery evaluation and a 170% increase in adult epilepsy surgery evaluation. The total number of surgery candidates identified would be 317 people with medically intractable epilepsy per year. The overall estimated annual health care resource utilization cost related to the epilepsy care with proposed infrastructural enhancements (as outlined in the model) is \$29.3 million (Cdn), \$11.5 million towards pediatric epilepsy care and \$17.8 million (Cdn) for adult epilepsy care. These health care resources and the associated funding would provide increased support towards epilepsy care and access to epilepsy surgery at the established and proposed new epilepsy care centres across the province.

Cost-Effectiveness Analysis

Methods

A decision analysis was undertaken to evaluate the cost-effectiveness of epilepsy surgery and evaluation of surgery candidacy for children with drug-refractory epilepsy. Data from a recent field evaluation undertaken for the Ontario Ministry of Health and Long-Term Care was combined with various published data to estimate the costs and outcomes for children with drug-refractory epilepsy over a 20-year period. (10) Outcomes were defined as the number of quality-adjusted life years (QALYs) accumulated over the 20 year period. This outcome was chosen because it incorporates both mortality and quality of life. The cost-effectiveness outcome used in the analysis was the incremental cost per QALY. The analysis was taken from the perspective of the Ministry of Health and Long-Term Care.

As outlined in the health care system budget impact analysis, not all individuals referred to the epilepsy monitoring unit (EMU) are candidates for surgery. Nevertheless, evaluating surgery candidacy incurs health care resource use and associated costs. Choosing whether to include the evaluation phase in the analysis has obvious implications on the results of the cost-effectiveness analysis. Therefore, the cost-effectiveness analysis was evaluated from different starting points: 1) starting with the video electroencephalography (vEEG) monitoring phase at the EMU; 2) starting at the seizure conference phase following the initial diagnostic assessment; and 3) starting at the point of surgery. It was assumed that vEEG monitoring would require referral to a district epilepsy centre and that evaluation of surgery candidacy would require a referral to a regional epilepsy centre.

Based on these starting points, this analysis addresses 3 separate questions:

1. In children with drug-refractory epilepsy, what is the cost-effectiveness of referral to a district epilepsy centre for diagnostic evaluation and medical treatment compared with continued medical management (no referral to a district epilepsy centre)?
2. In children with confirmed epilepsy and who are potential candidates for surgery, what is the cost-effectiveness of referral to a regional epilepsy centre for determination of surgery candidacy versus continued medical management (no referral to a regional epilepsy centre)?
3. In children who are epilepsy surgery candidates, what is the cost-effectiveness of surgery versus medical management?

Decision Analytic Model Structure

The decision analytic model is made up of 2 parts: the first part follows patients through the surgery candidacy evaluation phase up to 1 year of follow-up, and the second is a long-term Markov model that tracks the “health states” of the patients every year. The health states in the long-term model are primarily based on patient seizure status.

Figure 2 shows the first part of the decision analytic model. The different starting points that address the 3 different cost-effectiveness questions are circled. The model starts with a cohort of children with drug-refractory epilepsy. Corresponding to question 1, the decision is whether to refer the patients to a district epilepsy centre for initial diagnostic assessment. Children who are not referred to a district epilepsy centre are assumed to continue on medical therapy and continue to experience seizures despite receiving pharmacotherapy. Children who are referred to a district epilepsy centre have an EMU evaluation with vEEG as well as other previously discussed clinical assessments. After this evaluation some patients are confirmed as having epilepsy that may be suitable for surgical intervention while the remainder will continue on medical management. Those that are considered possible surgery candidates are referred to a

regional district epilepsy centre where further clinical and diagnostics details are obtained and seizure conference(s) determine surgery candidacy.

When addressing cost-effectiveness question 1, it is assumed that all children who are considered possible surgery candidates after EMU are referred to regional epilepsy centres. When addressing question 2, it is assumed that the starting decision point is whether to refer these children to a regional epilepsy centre.

The decision analytic model used those proportions observed in the field evaluation that relate to the progression of individuals that reach each stage of surgery candidacy assessment. (10) A proportion of patients for whom a seizure conference is conducted are deemed to be surgery candidates while the remainder are assumed to continue with medical management. Some of the children who are surgery candidates choose not to proceed with surgical options. Surgical mortality is considered in the model as this is an infrequent but nevertheless possible risk associated with surgery. For cost-effectiveness question 3, the decision point for surgery candidates is considered to be whether to have surgery or continue with medical management.

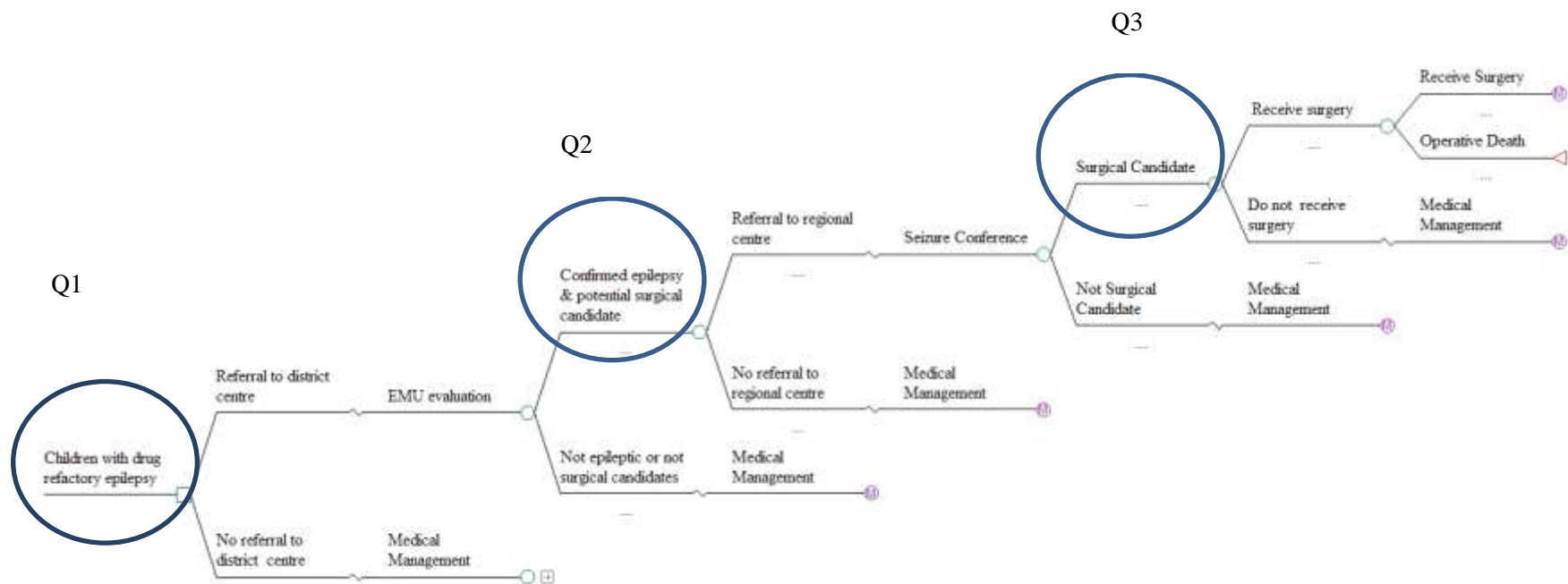


Figure 2: Schematic of Decision Analytic Model for Epilepsy Surgery Candidacy Evaluation

Figure 3 represents the long-term structure of the model. After surgery or continued medical management, children can be in one of several health states every year primarily based on seizure status after treatment. These health states can be either “seizure-free,” “seizure reduction,” or “no improvement” or else “death from all causes.” Patients can transition or move from one health state to another every year. Assumptions on the proportion of patients in each health state are described in this report. Every year patients accumulate costs and QALYs that differ depending on which health state they are in. For example, patients who are seizure-free are assigned lower costs and greater QALYs than patients who have no improvement in seizure frequency.

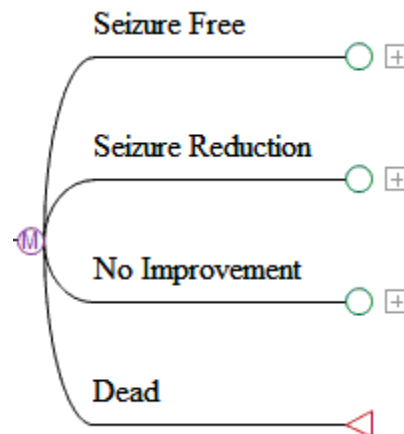


Figure 3: Markov Model Structure for Long-Term Health States for Children with Epilepsy

Model Input Variables

A number of clinical and cost input variables were used to populate the model and estimate the costs and QALYs of patients over a 20-year time horizon. These input variables include the seizure status of patients after treatment, mortality, utility values, the cost of evaluating surgery candidacy, the cost of the surgery, and follow-up health care resource costs. Details for each of these model variables and their sources are provided below.

Seizure Status

Based on the 1-year outcomes from the field evaluation, (10) the proportion of children who are seizure-free, have seizure reduction, and have no improvement was assumed to be 0.73, 0.21, and 0.04, respectively. For children not receiving surgery but continuing medical management, it was assumed that everyone remains drug-refractory (i.e., no improvement) throughout the 20-year period of the model. For the sensitivity analysis, the model is run assuming that some children who go through evaluation of surgery candidacy improve their seizure status.

Surgery Candidacy Evaluation and Surgery Costs

The costs of surgery along with surgical evaluation were based on a cost analysis done as part of the OHTAC-recommended field evaluation. (10) The cost of surgery is assumed to be \$35,776 (Cdn) (see Table 14). This cost includes those related to the procedure, inpatient stay after surgery, and post-surgery test costs. Evaluation costs depend on whether children go on to receive surgery as well as the starting point of the analysis. If the starting point of the model is the district epilepsy centre (question 1), average diagnostic evaluation costs are assumed to be \$8,174 (Cdn) for patients who do not go on to receive surgery and \$19,147 (Cdn) for patients who do. If the starting point of the model is the regional centre (question 2), the evaluation costs are assumed to be \$5,664 (Cdn) for patients who do not go on to receive

surgery and \$12,977 (Cdn) for patients who do. No pre-surgical evaluation costs are applied when the model starts at the point of surgery (question 3). Based on observations from the field evaluation, (10) the proportion of patients who go on to surgery when the starting point is the district epilepsy centre (EMU evaluation), regional centre (seizure conference), and surgery was assumed to be 0.16, 0.36, and 1.0, respectively.

Table 14: Summary of Evaluation and Surgery Costs for Children with Epilepsy by Starting Point of the Cost-Effectiveness Model

Variable	Average Cost Per Patient, \$ Cdn
Starting population: district epilepsy centre	
Evaluation costs – patients do not have surgery	8,174
Evaluation costs – patients have surgery	19,147
Surgery costs	35,776
Starting population: regional epilepsy centre	
Evaluation costs – patients do not having surgery	5,664
Evaluation costs – patients have surgery	12,977
Surgery costs	35,776
Starting population: surgery candidates	
Evaluation costs – patients do not have surgery	n/a
Evaluation costs – patients have surgery	n/a
Surgery costs	35,776

Abbreviations: Cdn, Canadian; n/a, not available.

Source: Bowen et al, 2011. (10)

Follow-Up Costs

Table 15 summarizes follow-up costs for those children undergoing surgery and for those remaining on medical management. The annual follow-up costs for the first 2 years of the model were derived from a recent Canadian-based patient-level cost-effectiveness study of pediatric epilepsy surgery that included estimates of 1-year follow-up costs. (16) The study found antiepileptic drug (AED) costs to be higher in patients receiving surgery than in those on medical management. The costs were adjusted from the report by Widjaja et al (16) by assuming that AED costs would be the same for surgery and medical management patients for the first 2 years of the model. As shown in Table 15, the model assumes that children receiving surgery would incur \$6,219 (Cdn) annual follow-up costs while medically managed children would incur \$4,629 (Cdn) annual follow-up costs during the first 2 years. Costs for AED and epilepsy-related hospitalizations were differentiated for children according to seizure status (seizure-free, seizure reduction, no improvement) in the following years. Based on a number of sources, (7;17;18) annual hospitalization costs for patients with no improvement in seizure frequency were estimated to be \$2,964 (Cdn). These costs were based on the average cost of epilepsy-related hospitalization for children (\$5,614 [Cdn]), the proportion of children with epilepsy who would be hospitalized during a year (24%), (17) and the average number of annual admissions for patients with one or more epilepsy-related hospitalizations (2.2). (7) It was assumed that seizure-free pediatric patients would not incur any hospitalization costs. For patients with seizure reduction, costs were interpolated from the costs for both seizure-free children and for those with no improvement and on data from the field evaluation. Children with seizure reduction had a mean 73% reduction in seizure frequency at 1-year post-surgery. (10)

The annual AED costs for children with no improvement in seizure frequency were assumed to be \$1,715 (Cdn). (16) For patients who were seizure-free, the annual AED costs were assumed to be \$446 (Cdn). This cost was based on the AED cost of patients with no seizure improvement and the average reduction in number of AEDs consumed by patients after epileptic surgery (74%). (19) The annual AED cost for children with seizure reduction was interpolated in the same manner as the costs for epilepsy-related hospitalizations.

Table 15: Summary of Long-Term Follow-Up Costs Used in the Cost-Effectiveness Model

Variable	Average cost per patient, \$ Cdn	Source
Annual follow-up costs: first 2 years		
Surgery	6,219	Widjaja et al (16)
Medical management	4,629	Widjaja et al (16)
Annual follow-up costs: subsequent years		
Hospitalization costs		
Seizure-free	0	
Reduction in seizures	771	Assumption
No response (drug-refractory)	2,964	OCCI (18), Jette et al (17), Langfitt & Wiebe (7)
Antiepileptic drug costs		
Seizure-free	446	Widjaja et al (16), Tanriverdi et al (19)
Reduction in seizures	786	
No response (drug-refractory)	1,715	Widjaja et al (16)

Utility Values

Different utility values were assigned to patients each year depending on seizure status. For children with no improvement in seizure frequency, a utility value of 0.82 was applied in the model. For children who were seizure-free after surgery, a utility value of 0.92 was applied each year. These utility values were based on a utility study of 125 drug-refractory patients with epilepsy who were about to start a new adjunctive AED. (20) Utility was measured using the EQ5D instrument. After 6 months of treatment, patients who were seizure-free had a mean utility score of 0.92 while patients who had not achieved a 50% reduction in seizure frequency had a mean utility value of 0.82. This study was used as the source of utility values in a cost-effectiveness analysis of epilepsy medications (21;22) and in a recent health technology assessment. (21;22) The utility value applied to patients with seizure reduction (0.89) was estimated by interpolating the utility values for children who were seizure-free and those who had had no improvement in seizure frequency. Utility values based on an alternate source are used in the following sensitivity analyses.

Mortality

The model assumed an operative mortality rate of 1.8% based upon the operative mortality rate observed in the Ministry of Health and Long-Term Care field evaluation. (10) Age-specific all-cause mortality was based on Canadian life table data. (23;24)

Sensitivity Analyses

The decision analytic model results were tested using a number of one-way sensitivity analyses. Specifically, the model was run using alternate time horizons (10 years, 40 years), discount rates (0%, 3%), and utility values and assuming a treatment effect for children who are referred to either a regional or district epilepsy centre but who do not go on to have surgery. This last assumption is based on the possibility that referral to an epilepsy centre may result in improved medical management. For the sensitivity analyses, Messori et al (25) was a source of utility values. As part of their cost-effectiveness analysis, the authors conducted a utility study on patients with epilepsy using the time-trade-off method. The authors found the mean utility value for seizure-free patients to be 0.96 and that for those with no change in seizure frequency to be 0.66. (25) The sensitivity analysis of the assumption that a clinical benefit was derived from referral to an epilepsy centre used data from a recent study (16) comparing surgical treatment with medical management in children with refractory epilepsy. In that study (16) medical management subjects were randomly chosen from among children evaluated for surgery but not deemed to be surgery candidates. This sensitivity analysis assumed that among those children referred to but not undergoing surgery, 6% were seizure-free while 28% had seizure reduction.

Results

Question 1: Cost-Effectiveness of Referral of Pediatric Patients to a District Epilepsy Centre for Diagnostic Evaluation

Table 16 shows the base-case results when the model starts from when a general practitioner or neurologist refers a child with drug-refractory epilepsy to a district epilepsy centre. The model estimates that children referred for surgery have total expected costs of \$70,583 (Cdn) over the 20-year period, while children with epilepsy who are not referred to a district epilepsy centre have total expected costs of \$60,985 (Cdn). Expected costs are therefore \$9,598 (Cdn) higher for the referral strategy compared with the no-referral strategy. Children who are referred for surgery incur on average \$9,695 (Cdn) of evaluation costs and \$5,545 (Cdn) of surgery costs. Children who are not referred to a district epilepsy centre incur neither evaluation nor surgery costs. However, children who are referred to a district epilepsy centre have \$5,642 (Cdn) less in follow-up costs compared with children who are not referred, reflecting reduced AED and hospitalization costs for the 15.5% of patients who go on to receive surgery in the referral group. Children referred to a district epilepsy centre are estimated to accumulate 10.895 QALYs over the 20-year period, while children who are not referred are estimated to accumulate 10.757 QALYs, a difference of 0.138 QALYs. Based upon the incremental costs and QALYs for the referral strategy, the incremental cost per QALY of referral is estimated to be \$69,451 (Cdn). Therefore, if a decision-maker's willingness to pay for a QALY is \$69,451 (Cdn) or more, then referral to a district epilepsy centre would be cost-effective; otherwise no referral would be cost-effective.

Table 16: Base-Case Cost-Effectiveness Results of Child Epilepsy Model: Starting the Model at Referral to a District Epilepsy Centre

Strategy	Average Expected Cost per Patient, \$ Cdn				QALYs	ICER
	Evaluation	Surgery	Follow-up	Total		
Referral	9,695	5,545	55,343	70,583	10.895	
No referral	0	0	60,985	60,985	10.757	
Incremental difference	9,695	5,545	-5,642	9,598	0.138	69,451

Abbreviations: Cdn, Canadian; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Question 2: Cost-Effectiveness of Referral of Pediatric Patients to a Regional Epilepsy Centre for Multidisciplinary Evaluation

Table 17 shows the base-case results when the model starts from the point of referral to a regional epilepsy centre. The model estimates that children referred for surgery have total expected costs of \$68,514 (Cdn) over 20 years while children not referred to a regional epilepsy centre have total expected costs of \$60,985 (Cdn). Expected costs are therefore \$7,529 higher for the referral strategy compared with the no-referral strategy. Children who are referred incur \$8,132 (Cdn) expected evaluation costs and \$12,074 (Cdn) expected surgery costs, while children who are not referred incur neither evaluation nor surgery costs. Children who are referred to a regional epilepsy centre have \$12,677 (Cdn) less in follow-up costs compared with children who are not referred, reflecting reduced AED and hospitalization costs for the 35% of patients who go on to receive surgery in the referral group. Children referred to a regional epilepsy centre are estimated to accumulate 11.058 QALYs over the 20-year period, while those not referred to a regional health centre are estimated to accumulate 10.757 QALYs, a difference of 0.301 incremental QALYs. The incremental cost per QALY of referral is predicted to be \$25,020 (Cdn). Therefore, if a decision-maker's willingness to pay for a QALY is \$25,020 (Cdn) or greater, referral to a regional epilepsy centre would be considered cost-effective; otherwise no referral would be considered cost-effective.

Table 17: Base-Case Cost-Effectiveness Results of Child Epilepsy Model: Starting the Model at Referral to a Regional Epilepsy Centre

Strategy	Average Expected Cost per Patient, \$ Cdn				QALYs	ICER
	Evaluation	Surgery	Follow-up	Total		
Referral	8,132	12,074	48,308	68,514	11.058	
No referral	0	0	60,985	60,985	10.757	
Incremental difference	8,132	12,074	-12,677	7,529	0.301	25,020

Abbreviations: Cdn, Canadian; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Question 3: Cost-Effectiveness of Referral of Pediatric Patients to a Regional Epilepsy Centre for Surgery

Table 18 presents base-case results for the model starting at the point of deciding whether children undergo epilepsy surgery. Surgery alone costs \$35,776 (Cdn). However, surgery results in \$37,564 less in follow-up costs compared with no surgery, resulting in total expected costs for surgery over the 20-year time horizon to be \$1,788 less than for the no-surgery strategy. Surgery leads to 0.892 more QALYs compared with the no-surgery strategy. Since surgery has both lower costs and greater expected QALYs compared with no surgery, it can be considered to dominate the no-surgery strategy in terms of cost-effectiveness and is therefore the preferred strategy, regardless of a decision-maker's willingness to pay for a QALY.

Table 18: Base-case Cost-Effectiveness Results of Child Epilepsy model When Starting the Model at Point of Surgery.

Strategy	Average Expected Cost per Patient, \$ (Cdn)				QALYs	ICER
	Evaluation	Surgery	Follow-up	Total		
Surgery	0	35,776	23,421	59,197	11.648	
No Surgery	0	0	60,985	60,985	10.757	
Incremental difference	0	35,776	-37,564	-1,788	0.892	Surgery dominates

Abbreviations: Cdn, Canadian; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

One-Way Sensitivity Analyses of Cost-Effectiveness Model

The model was run with a number of one-way sensitivity analyses on various model assumptions. Table 19 shows the incremental cost per QALY resulting from these sensitivity analyses for each of the 3 model starting points. As shown, the time horizon chosen for the analysis has a large impact on cost-effectiveness results. If a 10-year time horizon is used for the model, the cost per QALY for district referral is \$141,733 (Cdn), for regional referral is \$71,259 (Cdn), and for surgery is \$28,392 (Cdn). Using a 40-year model time horizon results in lower cost per QALY for district referral and regional referral compared with the base-case assumption of 20 years.

Using either 0% or 3% discounting results in more favourable cost-effectiveness than the base-case assumption of 5% discounting. If no discounting is applied (i.e., 0%), regional referral dominates over no regional referral. If Messori et al (25) is used as the source for utility values in the model, the utility applied to patients who are seizure-free becomes 0.96, while the utility value applied to patients with no seizure improvement becomes 0.66. (25) This compares to the base-case utility values of 0.92 (for seizure-free patients) and 0.82 (for patients who did not achieved a 50% reduction in seizure frequency). If the Messori et al (25) utility values are used, the cost per QALY for the district referral compared with no-district referral becomes \$19,685 (Cdn) while the cost per QALY of regional referral compared with no regional referral becomes \$13,795 (Cdn). If some seizure improvement is assumed for children who are referred to either a district or regional epilepsy centre but do not receive surgery (due to improved medical management), then district referral dominates over no-district referral and regional referral dominates over no regional referral.

Table 19: One-Way Sensitivity Analysis Examined in the Cost-Effectiveness Model

	Incremental Cost per QALY for Alternate Starting Points, \$ (Cdn)		
	District Referral	Regional Referral	Surgery
Base case	69,451	25,019	Surgery dominates
Sensitivity variant			
Time Horizon			
10	141,733	71,259	28,392
40	37,749	4,884	Surgery dominates
Discount rate, %			
0	27,620	Surgery dominates	Surgery dominates
3	51,843	13,795	Surgery dominates
Alternate utility source (25)	19,685	7,072	Surgery dominates
Efficacy for children referred to epilepsy centre who do not receive surgery	Surgery dominates	Surgery dominates	Surgery dominates

Abbreviations: Cdn, Canadian; QALY, quality-adjusted life year.

Summary

The cost-effectiveness of epilepsy surgery versus continued medical management was evaluated using 3 scenarios. Each of the analyses found that epilepsy surgery was cost-effective compared with continued medical management in children with drug-refractory epilepsy; the incremental cost-effectiveness ratios (ICERs) were \$25,020 (Cdn) and \$69,451 (Cdn) for 2 scenarios (starting the model at referral to a regional epilepsy centre and at referral to a district epilepsy centre, respectively). In the case of choosing epilepsy surgery versus continued medical management in children known to be suitable candidates for surgery, the epilepsy surgery was found to be less costly and provided greater clinical benefit (i.e., is a dominant strategy).

Discussion

About 400 Ontarian children and adults with medically intractable epilepsy could potentially benefit from surgical intervention every year. Epilepsy surgery in both children and adults has been found to be a cost-effective treatment compared with continued medical management. (7-9;16) Langfitt et al (7) determined the cost-effectiveness of anterotemporal lobectomy in adult patients with medically intractable epilepsy to be \$15,581 per quality-adjusted life year (QALY). (7) Similarly, King et al (9) calculated the incremental cost-effectiveness ratio (ICER) to be \$27,200/QALY. Both of these models examined the costs and consequences over a lifetime. (7;9) Wiebe et al (8) examined the expected costs per seizure-free patient over a 35-year time horizon. The total cumulative costs associated with continued medical management became greater than that of surgical intervention after 8.5 years. (8) The ICER of pediatric epilepsy surgery compared with medical management was determined to be \$369 per patient for each percentage point reduction in seizures.

The cost-effectiveness analysis of pediatric epilepsy surgery completed as a part of this evaluation also found surgical intervention to be favourable compared with continued medical management, with an ICER of \$69,451 (Cdn)/QALY when the entire diagnostic evaluation process was included in the analysis and accounting for the associated costs of those individuals deemed not to be suitable candidates for surgery. When examining the cost-effectiveness of determining surgery candidacy through a multidisciplinary review, the ICER of surgery to medical management was estimated to be \$25,020 (Cdn), similar to the models described above. Epilepsy surgery was a dominant strategy (costing less with incremental clinical benefit) when considering individuals who were surgery candidates. It should be noted that the cost-effectiveness calculations completed for this report are from a Ministry of Health and Long-Term Care perspective, and the analysis does not include productivity losses (or gains). The yearly productivity losses associated with epilepsy have been previously estimated using data from the Ontario Health Survey and found to be \$2,962.30 (Cdn) (in 1991 dollars) per individual with epilepsy or equivalent to \$139.23 million for the epilepsy population in the province.(11)

Epilepsy surgery for medically intractable epilepsy in suitable candidates has consistently been found to provide favourable clinical outcomes as demonstrated through randomized controlled trials with a calculated number-needed-to-treat of only 2. (15;26) In a recent review Wiebe and Jetté (26) examined the reasons why surgical intervention is not more commonly used or even considered by general practitioners or neurologists. They summarized the criteria for referral to a comprehensive epilepsy program for epilepsy surgery evaluation. (26) In addition, the American Academy of Neurology recently recommended that patients with medically intractable epilepsy be considered for epilepsy surgery evaluation at least every 3 years as a part of their quality-of-care indicators for epilepsy. (27)

This economic analysis examined increasing access to epilepsy surgery evaluation and surgery in Ontario. The expansion of epilepsy monitoring unit (EMU) bed capacity and epilepsy care services is the first step to achieving this goal. Through input from the clinical and administrative personnel at the epilepsy care centres in London, Hamilton, Toronto, and Ottawa, an initial total EMU bed complement of 50 beds was suggested. The health care system budgetary impact analysis estimated an additional \$18 million (Cdn) annually across all centres to support the incremental number of EMU beds. The estimate, however, is based on detailed health care resource utilization data obtained from a retrospective chart review for all children referred to the EMU at the Hospital for Sick Children (HSC) over a 2-year period. It followed the proposed district and regional epilepsy care model by the OHTAC Expert Panel and may require a more detailed centre-specific analysis of health care resources and funding as centre-specific information was not employed to calculate this estimate. (5)

Acknowledgements

The authors would like to thank Dr. Les Levin and Dr. Ben Chan of the Medical Advisory Secretariat, Health Quality Ontario, and the Ontario Health Technology Advisory Committee (OHTAC). We would like to thank Laura Mattila and Elizabeth Ferguson for their advice and support and their coordination of the data collection from the Epilepsy Care Centres. We would also like to thank the members of the Epilepsy Care Centres in Hamilton, London, Toronto, and Ottawa as well as the Epilepsy Expert Panel for their input.

References

- (1) Tellez-Zenteno JF, Pondal-Sordo M, Matijevic S, Wiebe S. National and regional prevalence of self-reported epilepsy in Canada. *Epilepsia*. 2004 Dec;45(12):1623-9.
- (2) Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Engl J Med*. 2000 Feb 3;342(5):314-9.
- (3) Ontario Health Technology Advisory Committee (OHTAC). Appendix 1. Epilepsy surgery in Ontario: increasing access and standardizing care (March 2011). In: OHTAC recommendation: care for drug-refractory epilepsy in Ontario. Toronto: Ontario Health Technology Advisory Committee (OHTAC); 2012. [cited 15-May-2012]. Available from: http://www.hqontario.ca/en/mas/ohtac_rec_openComment.html
- (4) Cross JH, Jayakar P, Nordli D, Delalande O, Duchowny M, Wieser HG et al. Proposed criteria for referral and evaluation of children for epilepsy surgery: recommendations of the Subcommittee for Pediatric Epilepsy Surgery. *Epilepsia*. 2006 Jun;47(6):952-9.
- (5) Ontario Health Technology Advisory Committee (OHTAC). Appendix 2. Report of the OHTAC Expert Panel on a Provincial Strategy for Epilepsy Care in Ontario (August 2011). In: OHTAC recommendation: care for drug-refractory epilepsy in Ontario. Toronto: Ontario Health Technology Advisory Committee (OHTAC); 2012. [cited 15-May-2012]. Available from: http://www.hqontario.ca/en/mas/ohtac_rec_openComment.html
- (6) Labiner DM, Bagic AI, Herman ST, Fountain NB, Walczak TS, Gumnit RJ. Essential services, personnel, and facilities in specialized epilepsy centers--revised 2010 guidelines. *Epilepsia*. 2010 Nov;51(11):2322-33.
- (7) Langfitt J, Wiebe S. Cost-effectiveness of epilepsy therapy: How should treatment effects be measured? *Epilepsia*. 2002;43(Suppl 4):17-24.
- (8) Wiebe S, Gafni A, Blume WT, Girvin JP. The economics of surgery for temporal lobe epilepsy. *J Epilepsy*. 1996;9(2):144-5.
- (9) King JT, Jr., Sperling MR, Justice AC, O'Connor MJ. A cost-effectiveness analysis of anterior temporal lobectomy for intractable temporal lobe epilepsy. *J Neurosurg*. 1997;87(1):20-8.
- (10) Bowen JM, Snead OC, Hopkins RB, Elliott I, Burke N, Atkin J et al. Diagnostic evaluation of infants, children and adolescents with epilepsy for surgery candidacy and the role of magnetoencephalography (MEG). Hamilton (ON): Programs for Assessment of Technology in Health, St. Joseph's Healthcare Hamilton/McMaster University; 2011 [cited 9-May-2012]. Available from: http://www.path-hta.ca/Libraries/Reports/MEG_OHTAC_report.sflb.ashx.
- (11) Wiebe S, Bellhouse DR, Fallahay C, Eliasziw M. Burden of epilepsy: the Ontario Health Survey. *Can J Neurol Sci*. 1999 Nov;26(4):263-70.
- (12) Statistics Canada. Estimates of population, by age group and sex for July 1, Canada, provinces and territories annual (persons unless otherwise noted) - Table 051-0001. Ottawa: Government of Canada; 2011 [cited 15-Feb-2012]. Available from:

<http://www5.statcan.gc.ca/cansim/a26?lang=eng&retrLang=eng&id=0510001&tabMode=dataTable&srchLan=-1&p1=-1&p2=9>.

- (13) Kotsopoulos IA, van MT, Kessels FG, de Krom MC, Knottnerus JA. Systematic review and meta-analysis of incidence studies of epilepsy and unprovoked seizures. *Epilepsia*. 2002 Nov;43(11):1402-9.
- (14) Statistics Canada. Estimates of population (2006 Census and administrative data), by age group and sex, Canada, provinces, territories, health regions (2011 boundaries) and peer groups annual (number) - Table 109-5325. Ottawa: Government of Canada; 2011 [cited 15-Feb-2012]. Available from: <http://www5.statcan.gc.ca/cansim/a26?lang=eng&retrLang=eng&id=1095325&tabMode=dataTable&srchLan=-1&p1=-1&p2=9>.
- (15) Wiebe S, Blume WT, Girvin JP, Eliasziw M. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *N Engl J Med*. 2001;345(5):311-8.
- (16) Widjaja E, Li B, Schinkel CD, Ritchie LP, Weaver J, Snead OC et al. Cost-effectiveness of pediatric epilepsy surgery compared to medical treatment in children with intractable epilepsy. *Epilepsy Res*. 2011;94(1-2):61-8.
- (17) Jette N, Quan H, Faris P, Dean S, Li B, Fong A et al. Health resource use in epilepsy: significant disparities by age, gender, and aboriginal status. *Epilepsia*. 2008 Apr;49(4):586-93.
- (18) Ontario Case Costing Initiative. OCCI Case Analysis Tool. Toronto: Ontario Case Costing Initiative; 2012 [cited 15-Feb-2012]. Available from: <http://www.occp.com/mainPage.htm>.
- (19) Tanriverdi T, Poulin N, Olivier A. Life 12 years after temporal lobe epilepsy surgery: a long-term, prospective clinical study. *Seizure*. 2008 Jun;17(4):339-49.
- (20) Selai C, Kaiser S, Trimble M, Price M. Evaluation of the relationship between epilepsy severity and utility. *5[6]* . 2002 512-513 p.
- (21) Hawkins N, Epstein D, Drummond M, Wilby J, Kainth A, Chadwick D et al. Assessing the cost-effectiveness of new pharmaceuticals in epilepsy in adults: the results of a probabilistic decision model. *Med Decis Making*. 2005 Sep;25(5):493-510.
- (22) Wilby J, Kainth A, Hawkins N, Epstein D, McIntosh H, McDaid C et al. Clinical effectiveness, tolerability and cost-effectiveness of newer drugs for epilepsy in adults: a systematic review and economic evaluation. *Health Technol Assess*. 2005 Apr;9(15):1-157, iii-iv.
- (23) Statistics Canada. Life Tables, Canada, Provinces and Territories, 2000-2002. Table 2b Complete life table, Canada, 2000 to 2002: females. Ottawa: Statistics Canada; 2006 [cited 14-May-2012]. Available from: <http://www.statcan.gc.ca/pub/84-537-x/t/pdf/4198611-eng.pdf>.
- (24) Statistics Canada. Life Tables, Canada, Provinces and Territories, 2000-2002. Table 2b Complete life table, Canada, 2000 to 2002: males. Ottawa: Statistics Canada; 2006 [cited 14-May-2012]. Available from: <http://www.statcan.gc.ca/pub/84-537-x/t/pdf/4198612-eng.pdf>.

- (25) Messori A, Trippoli S, Becagli P, Cincotta M, Labbate MG, Zaccara G. Adjunctive lamotrigine therapy in patients with refractory seizures: a lifetime cost-utility analysis. *Eur J Clin Pharmacol*. 1998 Feb;53(6):421-7.
- (26) Wiebe S, Jette N. Epilepsy surgery utilization: who, when, where, and why? *Curr Opin Neurol*. 2012 Apr;25(2):187-93.
- (27) Fountain NB, Van Ness PC, Swain-Eng R, Tonn S, Bever CT, Jr. Quality improvement in neurology: AAN epilepsy quality measures: report of the Quality Measurement and Reporting Subcommittee of the American Academy of Neurology. *Neurology*. 2011 Jan 4;76(1):94-9.

Health Quality Ontario
130 Bloor Street West, 10th Floor
Toronto, Ontario
M5S 1N5
Tel: 416-323-6868
Toll Free: 1-866-623-6868
Fax: 416-323-9261
Email: MASinfo@hqontario.ca
www.hqontario.ca

ISSN 1915-7398 (online)
ISBN 978-1-4435-9975-7 (PDF)

© Queen's Printer for Ontario, 2012