A Comparison of Pharmaceutical Budget Impact Analysis (BIA) Recommendations Amongst the Canadian Patented Medicine Prices Review Board (PMPRB), Public and Private Payers

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Abstract
The Canadian budget impact analysis (BIA) guidelines were published by the Patented Medicine Prices Review Board (PMPRB) in 2007. Some Canadian federal, provincial and territorial (F/P/T) drug plans have updated their BIA guidelines since then. The aim of the present review was to provide a comprehensive list of the key BIA recommendations from the various Canadian F/P/T drug plans and private payers and to highlight the differences between those guidelines and the recommendations that were in the Canadian PMPRB 2007 BIA guidelines. We searched the websites of fifteen F/P/T public drug benefit programs including the Canadian Agency for Drugs and Technologies in Health (CADTH) and Non-Insured Health Benefits Program (NIHB) and five private payers’ websites. An Excel-based data abstraction form was designed to highlight differences between recommendations relating to the BIA key elements made by different guidelines. Eight BIA guidelines (PMPRB 2007, Alberta, British Columbia, Manitoba, Ontario, Quebec, CADTH, and Medavie Blue Cross) were identified and reviewed, and a comprehensive list of recommendations was abstracted. Recommendations were similar to the 2007 guidelines in terms of time horizon duration, comparators, target population assessment and use of direct drug costs in BIAs. Differences were mostly related to actual acquisition cost, such as whether or not to include markups and dispensing fees, the patients’ perspective, cost of supplies, cost of health care utilization, and scenario analysis. The recommendations that were not included in the PMPRB 2007 guidelines but were included in at least one of the Canadian F/P/T or private guidelines were related to the inclusion of the patients’ perspective (i.e., co-payment), the costing, the handling of uncertainty and the reporting format. The present study is a comparative review of recommendations between the Canadian PMPRB 2007 guidelines and the F/P/T or private payers’ BIA guidelines, and provides a most up-to-date list of recommendations for revising the Canadian BIA guidelines, with applicability for both public and private plan new drug submissions in Canada.

1 Introduction

Canada is among the highest spenders on health care in the Organisation for Economic Co-operation and Development (OECD) [1, 2]. In Canada, public insurance covers only 43% of prescription drug cost, while the remainder is paid by private payers (35%) or patients (out of pocket). In the public sector, provincial/territorial programs and federal direct drug subsidy programs are the main payers. In the private sector, payers include private health insurance and either households or individuals paying out of pocket [1, 2].

1.1 Drug Pricing and Reimbursement in Canada

In Canada, to obtain public reimbursement, cost-effectiveness reports are prepared by manufacturers in accordance
Key Points for Decision Makers

Only six out of 15 federal, provincial and territorial (F/P/T) drug plans [i.e., those of Alberta, Ontario, British Columbia, Manitoba, Quebec and the Canadian Agency for Drugs and Technologies in Health (CADTH)] have published their budget impact analysis (BIA) requirements for drug submissions on their websites. For private payers, very limited information is available online.

There was more consistency between the F/P/T BIA requirements and the Patented Medicine Prices Review Board (PMPRB) 2007 BIA guidelines, compared with private payers. Private payers’ requirements were not included in the PMPRB 2007 BIA guidelines.

There is a discordance between F/P/T BIA recommendations and the PMPRB 2007 BIA guidelines, including the cost of health care utilization (e.g., Manitoba), scenario analysis (e.g., Quebec), the patients’ perspective (e.g., Alberta), and reporting total, gross and net impact on the budget (e.g., Quebec) in BIAs, which were not discussed in the PMPRB 2007 BIA guidelines.

Fig. 1 Drug approval and reimbursement process in Canada. CADTH Canadian Agency for Drugs and Technologies in Health, CDR Common Drug Review, INESSS Institut national d’excellence en santé et en services sociaux, pCODR pan-Canadian Oncology Drug Review, pCPA pan-Canadian Pharmaceutical Alliance, PMPRB Patented Medicine Prices Review Board, R&D research and development

with the Canadian Agency for Drugs and Technologies in Health (CADTH) economic evaluation guidelines [3] (submitted to the Common Drug Review (CDR), the pan-Canadian Oncology Drug Review (pCODR) [4]) and/or those of the Institut national d’excellence en santé et en services sociaux (INESSS) in Quebec [5]. Drug submissions that receive a positive listing recommendation are submitted to the pan-Canadian Pharmaceutical Alliance (pCPA) for price negotiations (for the provincial price negotiation including Quebec) [6]. All provinces participating in the pCPA process require the submission of a budget impact analysis (BIA) that applies to their jurisdiction. The federally operated drug programs [i.e., the Non-Insured Health Benefits Program (NIHBP)] and private payers also require BIA reports for new drug submissions.

For patented drugs, since 1988, the Patented Medicine Prices Review Board (PMPRB) regulates and defines the ceiling price, i.e., the non-excessive price. Figure 1 illustrates the PMPRB as part of Canada’s pharmaceutical regulatory and reimbursement system. In 2005, the PMPRB initiated the development of the Canadian BIA guidelines on behalf of the National Prescription Drug Utilization Information System, and these were published in 2007 [7, 8]. The guidelines were initially developed to provide a standard for BIA accompanying new drug submissions to public drug plans. This was supplemented with an interactive Excel-based template to address provincial differences in drug regulations (e.g., drug prices, markups, professional fees, co-payments, discounts and cost analyses). However, over the last few years, some federal, provincial and territorial (F/T/P) drug plans have updated their specific BIA requirements [9–12]. The present study will provide a most
A standard abstraction form was developed for extracting data from BIA guidelines by Foroutan et al. [13] and was applied for abstracting data from the Canadian public and private plans’ BIA guidelines in the current study. The first literature review [13] focused on national and transnational BIA guidelines including those of Australia [14], Canada1 [7], the United Kingdom (UK) [15], Belgium [16], Ireland [17], France [18], Poland [19], Brazil [20] and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) [21], whereas in the present study, we performed a comparative review of the Canadian public, private and PMPRB 2007 BIA guidelines.

2 Methods

The websites of the CADTH (i.e., CDR and pCODR), pCPA, Canadian federal, provincial and territorial (F/P/T) drug plans (public drug plans which participate in pCPA negotiations) and five private payers (chosen from a list of private payers for drug submissions in a consulting company database) were manually searched (May 2018) for BIA guidelines, BIA guidance documents or (Excel-based) templates for new drug submissions. The first author also contacted private drug plans to get their BIA templates for new drug submissions. A total of 14 F/P/T public drug benefit programs (including Quebec), pCODR (CADTH) and five private payers’ websites were searched (Tables 1 and 2). Where guidelines were available in both English and French, we used the English version for our review. When a BIA guideline was updated, we only included the latest version of the BIA guideline in order to avoid duplication in data abstraction. In the present study, we used our standard

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1 PMPRB 2007 BIA guidelines.
Excel-based data abstraction form—which was developed in our previous peer-reviewed systematic literature review of national and transnational BIA guidelines [13]—for data abstraction. Then we highlighted similarities and differences between recommendations related to the BIA key elements provided by the Canadian PMPRB and F/P/T BIA guidelines or templates.

### 3 Results

The BIA guidelines for Canadian publicly funded drug programs were from Alberta [11], Ontario [9], Manitoba [10], Quebec [12], British Columbia [2] and the CADTH (pCODR) [22] (see Table 1 and Appendix 1). Only one BIA checklist for new drug submissions was found for private payers (Table 2). Some private payers (e.g., Green Shield and TELUS Health Benefits and Payment Solutions) in Canada use the Academy of Managed Care Pharmacy (AMCP) document (United States) [23] as their template for BIA (which is adopted in the ISPOR BIA guidelines).

Table 2  List of Canadian private health insurance companies included in this review

| #  | Private payers                                      | Review BIA for new drug submissions | Template or guidelines                  |
|----|------------------------------------------------------|-------------------------------------|-----------------------------------------|
| 1  | Green Shield                                        | Yes                                 | AMCP document (USA) [23]                |
| 2  | Great-West Life                                     | No information                      | No information                          |
| 3  | Express Scripts Canada                              | No information                      | No information                          |
| 4  | Medavie Blue Cross                                  | Yes                                 | BIA checklist for new drug submissions  |
| 5  | TELUS Health Benefits and Payment Solutions (Pharmacy Benefit Manager) | Yes                                 | AMCP document (USA) [23]                |

*AMCP Academy of Managed Care Pharmacy, BIA budget impact analysis*

Based on information found on the website or through contacting people who are responsible for reviewing BIAs

#### 3.1 Analytical Model Structure

##### 3.1.1 Perspective

The perspective of the health care budget holders in Canada (public and private drug plans) should be adopted in conducting a BIA [7, 9–12, 24]. In Manitoba, BIA should be reported for the Manitoba Health, Seniors and Active Living Pharmacare program and additional information may be requested for drugs that significantly impact other Manitoba Provincial Government-sponsored drug programs [10]. In Alberta, an Alberta Health-sponsored drug programs’ perspective should be taken for all BIAs [11] (e.g., not the entire health care system). Inclusion of the patients’ perspective in addition to the primary payer’s perspective (in the case of co-payment) is recommended in the PMPRB BIA guidelines as a supplement to the base-case analysis [7, 24] as per the drug plan’s requirement (i.e., Alberta and Quebec).

##### 3.1.2 Time Horizon

The recommended time horizon in the PMPRB and F/P/T and private BIA guidelines is 3 years [7, 9–12].

##### 3.1.3 Modeling

The Ontario, British Columbia and 2007 PMPRB BIA guidelines [7, 9, 24] provided an Excel-based template for reporting BIA results. Only the PMPRB 2007 BIA guidelines [7, 24] recommended testing the face, internal and external validity of the structured BIA model.

##### 3.1.4 Target Population

The target population is defined as “all drug plan beneficiaries who are expected to be diagnosed and treated for the conditions of interest and are eligible to use the new drug” [9–12]. For the target population estimation, there are two
| BIA primary elements | BIA secondary elements | Canada PMPRB (2007) | British Columbia | Alberta | Manitoba | Ontario | Quebec | CADTH (pCODR) | Medavie Blue Cross |
|----------------------|------------------------|---------------------|------------------|---------|----------|---------|--------|---------------|------------------|
| Perspective          |                        | Yes                 | Yes              | Yes     | Yes      | Yes     | Yes    | Yes           | Yes              |
| Co-payment:          | Inclusion of the patients’ perspective is complementary to the base-case analysis | Yes                 |                   |         |          |         |        |               |                  |
| Population size and characteristics |                          | Yes                 | Yes              | Yes     | Yes      | Yes     | Yes    | Yes           | Yes              |
| Definition of patient population (defined as individuals insured by drug plans of interest and have the condition of interest) | Yes (epidemiologic approach) | Yes (epidemiologic approach) | Yes (epidemiologic approach) | Yes (epidemiologic approach) | Yes (epidemiologic approach) | Yes (epidemiologic approach) |
| Top-down population approach: Estimation of the number covered by the locally approved indications for the new technology which needs to reflect uptake, and changes in patterns of use | Yes (claim-based approach) | Yes (claim-based approach) | Yes (claim-based approach) | Yes (claim-based approach) | Yes (claim-based approach) | Yes (claim-based approach) |
| Bottom-up approach: This starts from the number of individuals likely to avail themselves of the technology. It includes the number of individuals who will switch from an existing technology and the number of newly treated patients. These estimates may be informed by existing claims-based data | Yes                       | Yes (claim-based approach) | Yes (claim-based approach) | Yes (claim-based approach) | Yes (claim-based approach) | Yes (claim-based approach) |
| Access restrictions | Unit of analysis (per patient or episode) | Yes                 | Yes              |         |          |         |        |               |                  |
| Off-label indications in the eligible population may also be included | No (only in sensitivity analysis) | No (only in sensitivity analysis) |                   |         |          |         |        |               |                  |
| BIA primary elements | BIA secondary elements | Canada PMPRB (2007) | British Columbia | Alberta | Manitoba | Ontario | Quebec | CADTH (pCODR) | Medavie Blue Cross |
|----------------------|------------------------|----------------------|------------------|---------|----------|---------|--------|---------------|-------------------|

**Comparators**

- **Degree of implementation of the new intervention (substitution, combination and expansion)**
  - **Yes**
  - **Yes**
  - **Yes**
  - **Yes**

- **Comparators**
  - **Yes** (two scenarios, reference and new drug scenario, should be compared for the treatment strategy)
  - **Yes**
  - **Yes**
  - **Yes**
  - **Yes**

- **Current intervention mix for the eligible population (forecasted version of the current market without the new drug)**
  - **Yes**
  - **Yes**
  - **Yes**
  - **Yes**
  - **Yes**

- **New intervention mix (new drug scenario is forecasted version of the current market with introduction of the new drug)**
  - **Yes**
  - **Yes**
  - **Yes**
  - **Yes**
  - **Yes**

**Costs and outcomes**

- **Cost of the current and new intervention mix: Is determined by multiplying the budget holder’s price for each intervention by proportion of the eligible population using that intervention and by the number of people in the eligible population**
  - **Yes** (treatment strategy-based approach)
  - **Yes** (treatment strategy-based approach)
  - **Yes**
  - **Yes**
  - **Yes**
  - **Yes**

- **Actual acquisition cost of the intervention for the budget holder (including any discounts, rebates, or other adjustments that may apply)**
  - **Yes**
  - **Yes**
  - **Yes**
  - **Yes**
  - **No** (markups and dispensing costs should be excluded)

- **The costs included should be limited to direct costs associated with the technology that will accrue to the relevant payer(s)**
  - **Yes** (direct drug cost)
  - **Yes** (direct drug cost)
  - **Yes** (direct drug cost)
  - **Yes** (direct drug cost)
  - **Yes** (direct drug cost)

- **Cost of clinical outcomes and disease complication**
  - **No**
  - **No**
| BIA primary elements | BIA secondary elements | Canada PMPRB (2007) | British Columbia | Alberta | Manitoba | Ontario | Quebec CADTH (pCODR) | Medavie Blue Cross |
|----------------------|------------------------|---------------------|------------------|---------|----------|---------|----------------------|-------------------|
| **Cost of health care utilization** (e.g., hospital days or physician visits) | No | No | Yes [significant impact on health care services (e.g., laboratory testing, diagnostic testing, etc.)] |
| **Indirect costs**: The impact of the new intervention on productivity, social services, and other costs outside the health care system | No | No | Yes (in the sensitivity analysis) |
| **Cost of supplies**: The analytic framework should allow for cost-relevant details of how accompanying devices for the proposed medication are used | | | Yes (cost adjustment is recommended if the duration of use is less than 30 days) |
| Proposed drug cost based on unit drug price and average dose for average duration of time | Yes | Yes | Yes (cost adjustment is recommended if the duration of use is less than 30 days) |
| Least cost alternative (LCA) price for relevant drug comparators is recommended | | Yes | Yes |
| Drugs which require reconstitution or dose preparation, the method of dose preparation, dose stability and specifics around potential drug wastage | | Yes | |
| Time horizon | BIAs should be presented for the time horizons of relevance to the budget holder | 3 years | 3 years | 3 years | 3 years | 3 years | 3 years | 3 years |
| Modeling | The computing framework for a BIA can be a simple cost calculator programmed in an Excel-based spreadsheet | Yes | Yes | Yes |
Table 3 (continued)

| BIA primary elements | BIA secondary elements | Canada PMPRB (2007) | British Columbia | Alberta | Manitoba | Ontario | Quebec | CADTH (pCODR) | Medavie Blue Cross |
|----------------------|------------------------|---------------------|------------------|---------|----------|---------|--------|----------------|-------------------|
| Handling uncertainty and scenario analyses | | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Sensitivity analysis: Parameter uncertainty in the input values | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| One-way and/or multi-way sensitivity analysis, analysis of extremes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Probabilistic sensitivity analysis (PSA) is recommended in BIA | No | No | | | | | | | |
| Scenario analysis: Structural uncertainty introduced by the assumptions made in framing the BIA | | | | | | | | Yes | |
| Important parameters to be assessed in the sensitivity and scenario analyses have been provided in the guidelines | Yes | Yes | | | Yes (drug dosage and duration) | Yes (cost of supplies) | | | |
| Discount rate | | Yes | Yes | | | | | | |
| An attempt should be made for forecasting changes in the value of the currency used the BIA over the time horizon | Yes | Yes | | | | | | | |
| Discounting is generally not required | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Validation | | Yes | Yes | | | | | | |
| The computing framework and input data used for a BIA must be sufficiently valid to credibly inform the budget holder’s decisions | Yes | Yes | | | | | | | |
| The process of the validation is required | No | No | | | | | | | |
| Value of the information analyses (the cost of extra data collection vs improved model precision) | Yes | Yes | | | | | | | |
Table 3 (continued)

| BIA primary elements | BIA secondary elements | Canada PMPRB (2007) | British Columbia | Alberta | Manitoba | Ontario | Quebec | CADTH (pCODR) | Medavie Blue Cross |
|----------------------|------------------------|---------------------|------------------|---------|----------|---------|--------|--------------|-------------------|
|                      | The programming created by the developer of the budget impact model to perform the analysis (source code) should be made available for review (on the condition that property rights are respected) | Yes | Yes | |
|                      | Model code should be provided to reviewers | Yes | Yes | |
|                      | Post-market re-assessment: The observed costs in a health plan with the current interventions should be compared with the initial-year estimates from a BIA | Yes | Yes | |
|                      | Quality assurance and publication | | | |
| Inputs and data sources | Recommended data sources | Yes | Yes | |
|                      | Use data from another jurisdiction where the intervention has been introduced | Yes | Yes | Yes | Yes | |
|                      | Use estimates of expected market share from the manufacturer | Yes | Yes | Yes | Yes | |
|                      | Extrapolate from experience on product diffusion with similar interventions in the budget holder’s setting | Yes | Yes | |
|                      | Data could be sourced from clinical trials | Yes | Yes | |
|                      | Unpublished data sources, such as expert panels | Yes | Yes | |
| Presenting results | The estimated annual total and incremental budget impacts should be reported separately for each year of the time frame | Only incremental impact | Only incremental impact | Yes | Yes | Yes | Yes |
Table 3 (continued)

| BIA primary elements | BIA secondary elements | Canada PMPRB (2007) | British Columbia | Alberta | Manitoba | Ontario | Quebec | CADTH (pCODR) | Medavie Blue Cross |
|----------------------|------------------------|---------------------|------------------|---------|----------|---------|--------|----------------|--------------------|
| Gross and net impact on the budget [the anticipated sales of the drug of interest for each of the first 3 years after the coverage is granted for it (gross impact) and the net impact] | Yes (not described in details) | Yes (not described in details) | | | | | | Yes | |
| Introduction, study design and methods, results, conclusions and limitations | Yes (results should be presented in a disaggregated manner) | Yes (results should be presented in a disaggregated manner) | | | | | Yes | Yes | Yes |
| All results should be presented in their disaggregated and aggregated forms for each year of the timeframe | Yes | Yes | | | | | | |
| Inclusion of graphics and figure of the analytical framework, schematic representation of uncertainty analyses | | | | | | | Yes | Yes | |
| Table of assumptions, tables of inputs and outputs, appendices and references | Yes | Yes | | | | | | |

BIA budget impact analysis, CADTH Canadian Agency for Drugs and Technologies in Health, F/P/T federal, provincial and territorial, pCODR pan-Canadian Oncology Drug Review, PMPRB Patented Medicine Prices Review Board

*British Columbia BIA guidelines are consistent with the PMPRB BIA guidelines.
broad approaches: top-down or epidemiologic and bottom-up or claims-based (market-share) analyses. An epidemiologic approach is usually preferred if the submission indicates a superior therapeutic conclusion in clinical studies, whereas a market-share approach might be preferred if the submission indicates a non-inferior therapeutic conclusion.

The private payer whose BIA checklist was included in the review did not explicitly mention anything about the analysis for target population assessment. Private payers who use the US AMCP template adopt ISPOR BIA guidelines which apply only a top-down population assessment approach. In Canada, public plans accept both approaches. In Alberta, in the absence of epidemiologic data (e.g., disease prevalence), claims data could be applied with justification for calculating prevalence in this manner and necessary assumptions and sources appropriately cited [11]. In the epidemiologic analysis, disease severity shifts, incidence, and prevalence are required, and it is usually inevitable to use data from different sources [7, 24]. In Manitoba, the prevalence of the disease state and/or indication for which the medication is intended for the total Manitoba population and for the population covered by the Manitoba Pharmacare program should be provided [10]. A list of all new and currently covered indications for the proposed new medication and information on shifts in the target population or market expansion are recommended in the Alberta, Ontario and Manitoba BIA guidelines [9–11].

3.1.5 Comparators

According to the PMPRB 2007 BIA guidelines, the reference scenario is the current market share distribution of all comparators without the new drug, whereas the new drug scenario is the forecasted market share of the same comparators with the inclusion of the new drug [7]. One should note that comparator mix does not necessarily always match the comparator mix in the utilization (real world) of the different comparators that private payers see in their databases, and that could be due to differences in the public versus private formularies. Choice of comparators is important, and is sometimes consistent with the economic evaluations and sometimes not.

3.1.6 Costing

Clear costing methods description is required in all provincial guidelines, and the inclusion of cost items is directly related to the chosen perspective [9–12, 24]. The costs associated with changes in outcomes, disease complications, adverse drug reactions and resource utilization (e.g., hospitalization and emergency room admission) are excluded from BIA [9–12]. Manitoba requires reporting any significant impact on health care services (e.g., laboratory testing and diagnostic testing) if applicable [10]. The BIA should clearly state which unit of analysis is adopted in measuring the outcomes [9–11]. According to Ontario and Manitoba BIA requirements, in the case of medications where the recommended duration of use is less than 30 days (e.g., antibiotics), this should be specified and the cost calculated accordingly [9, 10]. All provincial guidelines require reporting on the total and incremental impact on the budget in BIAs. For drugs which require reconstitution or dose preparation, information should be provided on the method of dose preparation, dose stability and specifics around potential drug wastage [22]. INESSS and pCODR require the cost of supplies to the manufacturer and the payer, and any cost of companion diagnostic tests or medical devices should be reported [12, 22].

Some of the BIA guidelines recommend that the cost of the treatment should be adjusted to consider the markups [25], discounts, inventory charges, business-related costs to the pharmacy covered by the drug plans, dispensing fees and/or patient co-payments, as requested by drug plans [7, 10, 12, 24]. Regulations for covering markups (caps) are different across Canadian provinces. For instance, in Ontario, there is a provincial 8% markup cap (6% for high-cost drugs) [25]; however, markups and dispensing fees should be excluded in BIA reports [9]. In contrast, in Alberta, effective May 2018, the Manufacturer List Price (MLP) is the price published in the Alberta Drug Benefit List plus the wholesaler (3%) and pharmacy (7% up to $100) allowable upcharges and the dispensing fee ($12.50), and if applicable, the least cost alternative (LCA) price for relevant drug comparators is recommended [11]. Also, in Manitoba, the total drug cost/patient/month should be based on the actual acquisition cost (AAC) of the medication, which includes the whole cost borne by the pharmacy; therefore, the AAC may include a wholesaler markup if applicable [10]. The PMPRB BIA guidelines [7, 24] and those for Ontario [9] provide Excel-based templates for reporting BIAs. Other provinces request submission of BIA results with accompanying methods of calculation (spreadsheets).

Only in the PMPRB BIA guidelines and those for British Columbia [7, 24] is the use of inflation rates permitted if there is justification for these to be included (e.g., confirmed information on pricing policy, implementation of an approved new policy rule shortly or price changes after patent expiration).

Inflation and discount rates are not applied; however, in the Canadian guidelines, they are permitted in certain circumstances if there is justification for them being included (e.g., confirmed information on pricing policy, 3 “Markup” and “upcharge” are used interchangeably.  

△ Adis
implementation of an approved new policy rule in the near future or price changes after patent expiration).

### 3.1.7 Modeling and Model Validity

All submitted models should be transparent, simple and include confidential prices at the same time. Excel-based electronic models would be preferred if they have the ability to express results in either contract or fiscal years. In addition, it is recommended that the incident and prevalent patients and patients coming off the excess (if there is one) be shown in the model separately (e.g., in the case of biologics). Face, internal and external validity are recommended to be checked and documented. The model validity and transparency could be assessed using recommendations provided by ISPOR and the Society for Medical Decision Making task force report [26]. The detailed process of the validation is not required in Canadian BIA. The programming code should be documented, annotated, and undergo quality assurance and control methods for software engineering. The program created by the developer of the budget impact model to perform the analysis (source code) should be made available for review (on the condition that property rights are respected).

### 3.1.8 Handling Uncertainty

One-way (univariate) deterministic sensitivity analysis or scenario analysis (multivariate) is acceptable for the most critical variables such as prices, population, and market shares. Alberta and Manitoba recommend one-way and/or multi-way sensitivity analyses for direct prescription costs and incremental prescription costs (savings), and an explanation of the methods used to calculate the sensitivity analyses must be included as well as the assumptions used in calculating the values [10, 11]. Sensitivity analysis of drug dosage and duration [9] and cost of supplies for manufacturers [12] are also recommended. Scenario analysis is recommended in Quebec [12].

### 3.2 Input and Data Sources

Based on our analysis, regarding clinical safety and efficacy and market data (e.g., degree of implementation in the market), it is acceptable to use data from other jurisdictions in the case of a lack of real-world information for a specific disease/new drug (e.g., rare disease). Epidemiologic data should be captured from Canadian statistics as much as possible. Cost transfers from other jurisdictions are not accepted. In most of the reviewed guidelines, including the PMPRB BIA guidelines [7, 24], epidemiologic data (e.g., disease prevalence and incidence) has to be obtained from national and provincial statistics and registries. In Manitoba, data should ideally be Manitoba specific and not simply an extrapolation of Canadian national data or data from other provinces to the Manitoba population. If Manitoba specific data are not available, a justification for why this is so must be provided [10].

The best sources for the claims-based and market research information are the payer database and the manufacturer’s marketing department [7, 8]. In the PMPRB, Alberta, and Manitoba BIA guidelines data from foreign markets are accepted if local data are not available [7, 10, 11, 24]. The BIA reports from manufacturers with clear supporting data could also be helpful in the PMPRB, Alberta, and Manitoba guidelines [7, 10, 11, 24]. Consensus expert opinion is an option when market intelligence for forecasting the new drug market share is not available [7, 8, 24].

### 3.3 Presenting Results

There are a few specific requirements for reporting the results mentioned in the reviewed guidelines. In general, total and incremental impact on the primary payer’s budget should be presented [9, 10]. Results should be both aggregated and disaggregated in each year of the time horizon [7, 10, 12, 24]. A table of assumptions, inputs, and outputs, a schematic representation of any uncertainty analyses (e.g., tornado diagram), appendices, references [11] and net\(^4\) and gross\(^5\) impact [12] should be included.

### 4 Discussion

We conducted a comparative review amongst the Canadian BIA guidelines available from the PMPRB, F/T/P jurisdictions and private drug plans. A comprehensive list of recommendations was abstracted from seven reviewed guidelines. Table 3 summarizes the similarities and differences between the 2007 PMPRB, F/P/T and private payers BIA requirements.

The similarities amongst the different BIA guidelines include a time horizon of 3 years, terminologies used for defining current and new scenarios, the epidemiologic data requirements for the proposed indications, the real-world market analysis information, the market share or market capture estimates for the new drug and comparators, and the direct drug costs to be used in the BIAs. Limited information was available regarding private payers’ BIA requirements.

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\(^{4}\) Net impact: the incremental cost associated with coverage of the drug of interest.

\(^{5}\) Gross impact: the anticipated sales of the drug of interest for each of the first 3 years after coverage is granted for it.
There are differences among provincial BIA guidelines in terms of the nature and number of the recommendations provided for analysts to conduct comprehensive BIA reports based on the provincial drug plan’s requirements (e.g., the AAC including or not including markups and dispensing fees, a supplementary patients’ perspective, cost of supplies, cost of health care utilization, a scenario analysis, and provision of Excel-based templates for cost analysis). To address these differences that were evident also in 2007 [7], the PMPRB BIA guideline was supplemented by an interactive Excel-based template and provided general rules for conducting a BIA that could help policymakers with formulary and reimbursement decisions [7, 8]. The most likely explanation for differences amongst the provinces is that provinces have different inclusion criteria for the coverage eligibility (target population), different access to the new drug, different pricing regulations for generic and brand drugs, and different allowable markups (upcharges), dispensing (professional) fees, and patient co-payments [25].

There are also differences among the updated provincial and 2007 PMPRB guidelines, for which the most suitable explanation is the passage of time and the development of more sophisticated BIA guidelines in which the later guidelines capture the following: inclusion of the patients’ perspective as supplementary to the base-case analysis, in the case of co-payment [11]; a clear description of the unit of analysis in the population and cost analyses [9–11]; the degree of implementation of the new intervention (i.e., substitution, combination and expansion) [9–12]; any significant impacts on health care services (e.g., laboratory testing and diagnostic testing) [10]; cost of supplies [12]; the LCA price for relevant drug comparators [11]; a scenario analysis [12]; the gross and net impact on the budget [12]; and detailed recommendations regarding inclusion of graphics and figures of the analytical framework, a schematic representation of uncertainty analyses, a table of assumptions, tables of inputs and outputs, appendices and references [10, 11].

There are literature reviews as part of the Canadian [7], Belgian [16] and French [18, 27] BIA guidelines. Our review is an update to the literature review published by Marshall et al. in 2008 [7]. They made a side-by-side comparison between the PMPRB 2007 BIA guidelines [8] and the Canadian provincial, other national and transnational BIA guidelines of the time, i.e., those of Alberta (2006), Manitoba (2003), Ontario (2006), Poland (2004), Australia (2002) and ISPOR (2007). In their review, they highlighted differences in the BIA costing approach, perspective, time horizon, opportunity cost, definition of target population and methods for performing sensitivity analysis between the PMPRB 2007 BIA guidelines and the others [7]. When comparing the results obtained in this review with BIA guidelines around the world (Australia [14], UK [15], Belgium [16], Ireland [17], France [18], Poland [19], Brazil [20] and ISPOR [21]), we identified that a considerable number of recommendations related to BIA key elements, including the open (dynamic) population, subgroup analysis in the target population assessment, catch-up effect (for chronic conditions and treatment switch), off-label indications in the eligible population assessment, opportunity costs, cost of clinical outcomes and disease complications, indirect costs, capital costs, staff training costs, applicable tax, patient adherence, total and incremental budget impact for the different health care payers, complicated modeling methods, probabilistic sensitivity analysis (PSA) and scenario analysis for handling the uncertainty, were not included or discussed differently in the 2007 PMPRB guidelines. Most of the Canadian provincial recommendations were in line with other reviewed guidelines, except for the following recommendations: (1) LCA price for relevant drug comparators is only mentioned in Alberta [11], (2) sensitivity analysis for drug dosage and duration in Ontario [9], (3) reporting gross impact on the budget is recommended in Quebec [12], and (4) for drugs which require reconstitution or dose preparation, the method of dose preparation, dose stability and specifics around potential drug wastage [22].

There were two important limitations to the current study: (1) only six (out of 15) F/P/T drug plans had published their template for BIA on their website and (2) there was limited information for private payers, which were found online. Thus we had to contact some private payers to get the required information.

The output from the present Canadian study has been used in conducting a qualitative research project in order to obtain stakeholders’ feedback and opinion on the relevance and applicability of the recommendations that were not included or were discussed differently in the PMPRB 2007 BIA guidelines. The next step will be developing a proposal for updating the guidelines.

5 Conclusion

The present study has provided a review of the current BIA guideline environment in Canada. It also identified where the PMPRB 2007 BIA guidelines might not have kept pace with the evolution of BIA guidelines over the past decade. The study has provided a foundation for updating those guidelines, which will occur after conducting a qualitative study to obtain Canadian stakeholders’ feedback and opinions. Future work will also need to address the diversity of BIA needs across the different provincial and territorial programs.

6 For designing the interview guide and a closed survey.
Author Contributions All authors contributed to the conception and planning of the work. Naghmeh Foroutan conducted the database search, data abstraction and the final descriptive analysis with input from Mitchell Levine. She also led the writing of this manuscript and was supervised by Mitchell Levine. All authors participated in the discussion that led to this paper and in the revision of all drafts. All authors approved the final version submitted for publication.

Compliance with Ethical Standards

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Conflict of interest Naghmeh Foroutan, Jean-Eric Tarride, and Feng Xie have no conflicts of interest that are directly relevant to the contents of this article. Mitchell Levine is the chair of the Patented Medicine Prices Review Board (PMPRB), and Fergal Mills is a director at Innomar Consulting.

Data Availability Statement We have provided the required data as much as possible (in a summarized format), and there are no additional data to be shared.

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Appendix 1

Provincial and Territorial Requirements for Manufacturers’ Submissions for Budget Impact Analysis

Alberta (Prescription Drug Programs): There is a budget impact assessment form provided for manufacturers7 [11].

British Columbia (Pharmacare): A provincial budget impact analysis (BIA) for British Columbia that is consistent with the standards published by the Patented Medicine Prices Review Board (PMPRB) [24].

Atlantic Common Drug Review (ACDR): BIAs for all four provincial plans (Nova Scotia, New Brunswick, Newfoundland and Labrador, and Prince Edward Island) have to be also submitted to ACDR. Submissions to the individual Atlantic provincial drug plans only require their own BIA.

Note: The ACDR assesses the clinical and cost effectiveness of drugs that do not fall under the mandates of the national Common Drug Review (CDR) or the pan-Canadian Oncology Drug Review (pCODR), and provides formulary listing recommendations to the provincially funded drug plans in Atlantic Canada (e.g., new single-source products that do not fall under the CDR mandate, line extensions, resubmissions for products not previously reviewed by CDR and currently listed drugs) [28, 29].

Ontario (Drug Benefit Program): There is a BIA template for new drug submissions on their website [9].

Manitoba (Pharmacare Program): The BIA for Manitoba Health, Seniors and Active Living should be prepared in accordance with the template supplied on their website [10].

Northwest Territories: In terms of formulary decisions, the Government of the Northwest Territories (GNWT) follows the Non-Insured Health Benefits (NIHB) formulary [30].

Saskatchewan: No information regarding specific requirements for BIA was found on the website [31].

Nunavut: No information regarding specific requirements for BIA was found on the website [32].

Yukon: No information regarding specific requirements for BIA was found on the website [33]. According to expert opinion, Yukon follows the NIHB formulary.

Federal drug plans (Citizenship and Immigration Canada, Correctional Service Canada, NIHB, National Defense, Veterans Affairs Canada): No information regarding specific requirements for BIA was found on the website. According to expert opinion, NIHB has no specific requirements for BIA, and they review BIA reports prepared for other provinces [34].

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