Canada's Drug and
Health Technology Agency

CADTH Methods and Guidelines

User Guide for the Budget Impact Analysis Tool

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Methods Review

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Abbreviations

BIA	budget impact analysis
FNHA	First Nations Health Authority
NIHB	Non-Insured Health Benefits
ODB	Ontario Drug Benefit
RDI	relative dose intensity

Introduction

The purpose of this user guide is to outline how to use the budget impact analysis (BIA) tool built by Canada's Drug Agency. The user guide will also outline restrictions with the tool in its current form and when a more bespoke de novo tool may be warranted. The expectation is that this tool will be usable for the majority of epidemiological BIAs; however, certain reviews and decision problems will have unique nuances that cannot be addressed by the tool. This tool is not a requirement for drug reimbursement reviews submitted to Canada's Drug Agency.

A key consideration when using this tool is that it is based on an epidemiological estimation of the budget impact. An alternative approach, known as a *claims-based approach*, is based on prescribing data to determine market share and population size. The decision for the tool to only consider an epidemiological approach was made for various reasons. First, a retrospective analysis of all submitted BIAs showed that epidemiological BIAs comprise more than 85% of submissions. The goal for this tool was to capture the majority of typical cases (comprehensive in approach), without being overly complex. A tool that is flexible enough to consider both epidemiological- and claims-based approaches would increase the complexity of the tool. Second, in many instances, claims-based approaches do not provide sufficient detail to ensure only patients within a specific indication are identified and included in the analysis, which can limit the validity of the results. If the user has accurate claims data, these can be used to derive more accurate estimates of prevalence and market shares, for example, which can be incorporated into this tool. However, if the user wishes to build a BIA using a claims-based approach, a bespoke analysis is required.

The remaining sections of this guide pertain to each Excel worksheet of the tool. Throughout this document, reference will be made to specific cells or rows. These pertain to the specific worksheet identified in each section.

1. Worksheet: Cover

The Cover worksheet provides an overview of how to use the tool, including a model legend that identifies the types of cells in the tool. There are numerous cells within the tool that provide further notes and comments regarding how to enter data.

Macros

Users should enable macros to ensure the full functionality of the tool. However, the main use of macros is limited to hiding rows and columns for easier navigation in the tool based on user inputs. The Scenario Analyses worksheet also uses macros to enable the user to store results from certain analyses; however, this function can be replicated by the user without using macros. The Inputs–Subgroup worksheet also requires a macro to enter data, although this is a simple copy-and-paste macro that can be easily replicated by the user. No results are generated using macros; if they are not enabled, the tool can still operate.

2. Worksheet: Assumptions

The Assumptions worksheet provides a high-level overview of assumptions, by input type, used in the BIA tool. These assumptions are fixed and cannot be edited within the tool. Each assumption is further explained in the relevant input worksheet.

Row 42 onward: The user may have applied additional assumptions beyond the ones specified in this sheet — these can be added here.

3. Worksheet: Inputs–Market Size

For some parameters in the Inputs–Market Size worksheet, users can either enter a pan-Canadian input value or, if a parameter is expected to vary by jurisdiction, a jurisdiction-specific value. If both pan-Canadian and jurisdiction-specific values are entered, the jurisdiction-specific value will override the pan-Canadian value. All cell references provided in this guide refer to the pan-Canadian estimate. Jurisdiction-specific values can be entered beside these values.

3.1. Drug Characteristics

Cell F16: Users should enter whether the drug under review is an oncology or non-oncology product.

Cell F18: Users should enter whether the product is an oral or take-home product (e.g., prefilled pens for subcutaneous injections) or IV therapy.

These inputs are only used to inform the population size information for a Non-Insured Health Benefits (NIHB)–adjusted population because the size of the NIHB population is dependent on whether a drug is an oncology or non-oncology product as well as whether it is a take-home or IV product (refer to Appendix 1 for further details).

3.2. Default Population Inputs

Default population inputs for the baseline year (current year before drug funding) of the BIA are prepopulated based on the inputs in the drug characteristics section. Default population size estimates for provinces are sourced from Statistics Canada Table 17-10-0005-01 Population Estimates for 2023.[1] Default NIHB population size is based on the annual report.[2] Provincial population estimates are adjusted for the NIHB population because individuals with NIHB coverage are removed from jurisdictional population size estimates if appropriate (refer to Appendix 1 for details).

Default population growth estimates are based on Statistics Canada Table 17-10-0005-01 and were calculated based on the average percent change in population each year between 2019 and 2023.[1] For NIHB, population growth was based on the percent change in eligible clients from March 2022 to March 2023 based on the 2022–2023 Annual Report.[2]

3.3. Prevalence- Versus Incidence-Based Models

Cell F24: The user can choose an incidence, a prevalence, an incidence plus prevalence bolus, or incidence derived using a prevalence approach when estimating the eligible population size. *Incidence* refers to the percentage of the population who are diagnosed with the disease or condition each year. *Prevalence* refers to the percentage of the population who are living with the disease or condition; therefore, prevalence includes incidence. The following information can be used to help the user decide which approach is more appropriate for their review.

3.3.1. Incidence-Based Models

In a BIA, an incidence-based model only looks at new (incident) cases. These are individuals who become eligible for the drug under review each year. This does not only reflect new diagnoses; for example, a treatment may require the individual to have progressed to "severe" disease. At the point of progression, they would be considered an "incident patient" when considering eligibility for the new treatment. Individuals who are already eligible before the BIA time horizon (existing patients) are not included in an incidence-based–only model.

Incidence-based models should be used when the natural history of the condition suggests there is not a large existing cohort of people with the disease or condition who would be considered for the drug under review.[3] This is common in conditions that have a short life expectancy, when treatment is only considered at the point of diagnosis, or when it is unlikely that a patient will switch treatments. In these cases, new incident cases would represent most patients being considered for new therapies. Some examples of conditions in which an incidence-based approach to estimating population size may be more appropriate include the following:

- acute exacerbations of iron deficiency anemia
- COVID-19 infection
- end-stage, refractory, or metastatic cancer with a short life expectancy
- therapies that are only given at or near diagnosis (e.g., adjuvant treatments in the oncology space).

3.3.2. Incidence-Based Models Derived Using Prevalence

In some cases, the number of prevalent patients is required to derive incidence. For example, a drug may be used to treat metastatic cancer. If we look at all new cancer diagnoses within a year (incident patients), some will be diagnosed with metastatic cancer. However, existing patients who have been diagnosed with cancer in years prior will be at risk of developing metastatic cancer which may be relevant to consider in the BIA population. When accurately deriving epidemiological filters, the user may wish to apply different filters to the patients diagnosed with metastatic disease versus those who develop it over time. In this case, the user can select the incidence derived using prevalence option. This allows the user to treat new diagnoses and existing diagnoses differently.

Note this is still an incidence-based model because only patients who become eligible each year are considered in the analysis. If a patient became eligible before the BIA time horizon (e.g., their cancer metastasized before the baseline year of the BIA), they would not be included in the calculations.

3.3.3. Incidence-Based Models With a Prevalence Bolus

In some cases, an incidence- plus prevalence-based modelling approach may be appropriate. In these cases, users should consider the newly diagnosed (i.e., incident) patients who will appear during the time horizon of the BIA as well as the current pool of patients (i.e., prevalent bolus) already eligible for the drug under review if it were reimbursed.[3]

Using this framework, the prevalent bolus cohort is fixed. Any new cases would be covered in the incident cohort. In the current version of the tool, the bolus of prevalent patients is only considered in the analysis in the first year of the BIA. The main example of when this approach may be appropriate is when a new drug is recommended in an early line of therapy (e.g., first or second line). Patients who are currently receiving third or later lines of therapy will have missed the initial opportunity to receive this treatment but might be considered now. Over time, as all patients will receive the therapy in an early line setting, very few patients will receive it in the third or later lines.

For simplicity, the tool does not allow different market shares to be applied to the prevalent bolus and incident patients. A more sophisticated approach may be warranted to consider both a large prevalent and incident population with different and dynamic market shares and population sizes. If the sizes of the prevalent and incident populations are both relevant to the decision problem **AND** market uptake is equal in both, then a prevalence-based approach may be appropriate.

3.3.4. Prevalence-Based Models

A prevalence-based model is one that includes both incident and existing patients. In this case, the user assumes the market shares for all treatments, including the drug under review, are equal for new patients (i.e., incident cohort) as well as existing patients. If the user assumes that the prevalence rate remains constant, this means any number of patients "leaving" the prevalent cohort (due to death or other reasons of ineligibility) are balanced by those "entering" the prevalent cohort. The impact of this assumption will be less influential for diseases in which new diagnoses make up a small percentage of the prevalent cohort.

The main limitation with the prevalence-based approach is, unlike the incidence-based approach, it is difficult to track patients using a standard BIA framework. In an incidence-based approach, it is known when a patient starts any therapy, and when the therapy stops can be easily accounted for. In a prevalence-based model, it can be challenging to gather data on how long the individual has had the condition before the start of the BIA. This could have a large influence on drug costs if the costs in the first year of treatment are substantially different from those in subsequent years (i.e., due to dose titration or changing treatment schedules).

Prevalence-based models also do not explicitly differentiate market uptake in incident patients versus prevalent patients. When a new therapy comes to market, it may displace current therapies if the treatment benefit is substantially improved. However, in some cases, there may be a reluctance to switch patients who are tolerating their current therapy; therefore, the main cohort of patients considered for new therapies would be incident patients.

If the annual mortality rate is low for a condition and rates of treatment discontinuation are low, the limitations associated with a prevalence-based approach will likely not have a large influence on the results.

Some examples of conditions for which a prevalence-based approach may be appropriate include:

- diabetes
- asthma.

If an accurate estimation of the BIA requires sophisticated tracking of incident and existing patients, a more complex analysis is required that is beyond the scope of this tool.

3.4. Market Expansion

Cell F30: The user is asked to consider whether the prevalence or incidence rate is expected to remain constant or increase over time. The tool will permit both a static BIA, in which the population size only increases due to population growth across the time horizon, and a dynamic BIA, in which the incidence or prevalence of a condition can change over time. Users are asked whether the prevalence or incidence rates (depending on selection) are expected to remain constant over the BIA time horizon.

If "Yes" is selected, the rate is assumed to be constant, meaning the size of the incident or prevalent population as a percentage of the population remains unchanged.

Cell F31: The user may specify the expected annual percentage change in the incidence or prevalence rate if "No" is selected in cell F30. For example, a condition with an incidence of 2% that grows by 50% each year will be 2% at baseline, 3% in year 1, 4.5% in year 2, 6.75% in year 3, and so on.

3.5. Companion Diagnostic Testing

Cell F34: The user is asked whether a test is required to receive the drug under review.

An important filter for determining the size of the eligible population is whether a companion diagnostic is needed to fund the drug under review. A companion diagnostic is a test that is conducted for the sole purpose of identifying whether an individual is eligible for receiving the drug under review. If this is not relevant, the user should select "No." For example, a diagnostic test may be required to diagnose individuals with the disease, but further testing is not required to consider which treatment to then give individuals.

Cell F65: The user is required to specify what percentage of the incident cohort will be considered for a test. Note this cell is not relevant if the user has selected a prevalence model in cell F24. If a companion diagnostic test is required, then the user must specify what percentage of incident patients will be eligible to receive a test. The user will have entered various epidemiological filters (refer to Section 3.6: Epidemiological Filters) to derive the size of the population. Some of these filters will be applied to derive the size of the population eligible for testing. Others will only apply after the test has been conducted.

Cell F66: The user is required to specify what percentage of the prevalent cohort will be considered for a test; note this cell is not relevant if the user has selected an incidence-based–only model in cell F24.

Cells F68:F73: The user is required to specify what proportion of eligible patients will be tested each year, including the baseline year (current practice), under the assumption the drug under review is funded. Testing uptake will be influenced by patient preference, clinicians, and access to testing.

Cell F75: The user is required to provide an input for the probability of a positive test result. If the test is perfectly accurate, the probability of a positive test will equal the probability of the test being a true positive. If the test is inaccurate, some individuals who should test positive will test negative (false negative), which will decrease the size of the eligible population. Alternatively, the test could falsely identify individuals who are not eligible (false positive), which will expand the size of the eligible population.

3.6. Epidemiological Filters

In many cases, it is necessary to "funnel down" the initial population to align the population with the Health Canada indication and/or reimbursement request.

According to the *Procedures for Reimbursement Reviews*, "If a sponsor is requesting reimbursement for a specific subgroup of the indicated population or if there are any relevant subgroups, these must be provided as scenario analyses."[4] In these cases, the user can use the Scenario Analyses worksheet to conduct these analyses (refer to Section 15: Scenario Analyses).

Cells B40:B49: Users should enter a description of the epidemiological filter they are applying to the incident cohort.

Cells F40:F49: Users should enter the percentage of incident patients that meet that criterion.

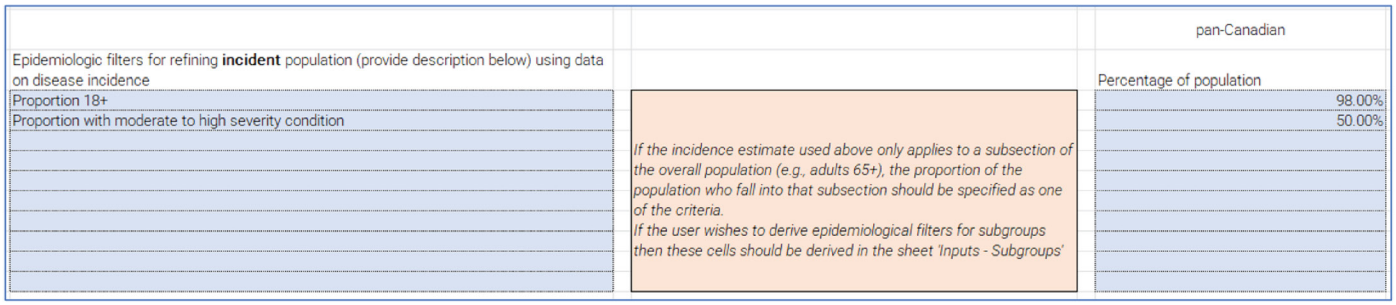
Cells B53:B62: Users should enter a description of the epidemiological filter they are applying to the prevalent cohort.

Cells F53:F62: Users should enter the percentage of prevalent patients that meet that criterion.

The rates should correspond to the population they are being applied to. Therefore, the first filter should apply to the full incident or prevalent cohort. The second filter should apply to patients who meet the criteria for the first filter and so on.

For example, consider an incidence-based model for a first-line treatment used to treat adult patients with disease (alpha) with a moderate to high severity condition. Prior to applying the epidemiological filters, we have specified that 0.01% of the population is diagnosed with the disease (alpha) every year. This rate is assumed to remain constant over time. Using the epidemiological filters, we can restrict the size of the population to only those who are eligible for treatment. Of those diagnosed, the data show that 50% have a moderate to high severity condition. Based on the Health Canada indication, the treatment is only indicated for patients older than 18 years.

Figure 1: Inputs–Market Size Screen — Epidemiological Filters for Refining Incident Population



		pan-Canadian
Epidemiologic filters for refining **incident** population (provide description below) using data on disease incidence		Percentage of population
Proportion 18+		98.00%
Proportion with moderate to high severity condition		50.00%
	If the incidence estimate used above only applies to a subsection of the overall population (e.g., adults 65+), the proportion of the population who fall into that subsection should be specified as one of the criteria. *If the user wishes to derive epidemiological filters for subgroups then these cells should be derived in the sheet 'Inputs - Subgroups'*	

The user should not consider the proportion of patients who are untreated in the epidemiological filters if they meet the criteria to be considered eligible for treatment. The proportion of untreated patients should be included in the market shares calculations (refer to Section 7: Inputs–Market Shares). This is because there may be treatment uptake from patients currently untreated. If the number of untreated patients is not affected by funding the new drug, then the user may add "treated patients" as an epidemiological filter. In this case, when the user completes the Inputs–Market Shares worksheet, they must assign the comparator "untreated" a market share of 0%.

Finally, the user should not enter any filters as they pertain to testing (testing uptake or diagnostic accuracy) because these filters are covered in cells F65:F75 (refer to Section 3.5: Companion Diagnostic Testing).

3.7. Subgroups

Cell F36: The user is asked if they want to consider subgroups.

When deriving epidemiological filters, the user may want to consider subgroups. This may be relevant when there are 2 distinct patient populations eligible for treatment. In these cases, epidemiological filters may be different for different subgroups. If the user wishes to enter filters for subgroups individually rather than for the whole cohort, the user should enter the epidemiological filters in the Inputs–Subgroups worksheet (refer to Section 4: Inputs–Subgroups).

3.8. Age Distribution

Rows 78:80: Users should enter the distribution of eligible patients who are younger than 25 years, between 25 and 64 years, and 65 years and older. This breakdown is required to estimate public drug plan coverage. The rationale for the age categories is based on the observation that public drug plan coverage rates may differ by these categories. For example, in Ontario, OHIP+ provides drug coverage for those aged 24 years and younger without private drug plan coverage.[5] In addition, some public drug plans may provide full coverage for those aged 65 years and older.

3.9. Coverage Rates

Rows 84:86: Users must enter the public coverage rate for each of the age categories.

The tool allows for input of age-dependent coverage rates. Because public coverage of drugs can vary depending on drug and disease characteristics, no default coverage rates are provided. When selecting coverage rates, users should consider factors such as whether the drug is for an oncology or a non-oncology indication, whether it is a take-home drug or IV treatment, as well as other factors that may influence coverage of the drug (e.g., does the indication influence the likelihood that the individual will be enrolled in third-party private insurance plans).

Based on the distribution of patients across ages entered in the previous steps and the public coverage rates by age entered in this step, the tool will multiply these to derive an overall public coverage rate that is weighted by age.

3.10. Population Outputs

The remainder of the rows in the Inputs–Market Size worksheet present population estimates (outputs) based on the inputs entered. No further inputs are required from the user for this worksheet. Cells F131:F136 outline the total size of the population considered for treatment. Cells F139:F144 outline the total size of the population eligible for public funding. If these numbers do not match user expectations, the user should check that the previously mentioned inputs have been correctly imputed. The user can also view the patient flow in the Outputs–Patient flow worksheet, which gives a more detailed breakdown of how these numbers were generated (refer to Section 5: Outputs–Patient Flow for more details).

4. Worksheet: Inputs–Subgroups

This section is only relevant if the user wishes to derive epidemiological filters for subgroups rather than the whole incident or prevalent cohort.

Cells D12:D13: The user is requested to enter the name of the 2 subgroups they wish to consider if they are conducting an incidence-based–only model.

The tool only allows the consideration of up to 2 subgroups for an incidence- or prevalence-based model and up to 4 if the user is conducting an incidence-derived using a prevalence-based or an incidence plus bolus–based model (2 subgroups to derive the incident cohort and 2 subgroups to derive the prevalent cohort).

Cells D18:E18: The user must enter the percentage of the population who comprise the subgroup.

If the 2 subgroups are mutually exclusive, meaning patients cannot be eligible for both subgroups, these 2 percentages should sum to 100%. If they do not sum to 100%, the assumption is the remaining cohort is ineligible for the drug under review. If the subgroups are not mutually exclusive, the user must verify there is no double counting when estimating the epidemiological filters.

Rows 23:32: Once the 2 subgroups are identified, the user must select the epidemiological filters that apply. The user enters a filter and then inputs the percentage of each cohort the filter applies to. If the filter only applies to 1 cohort, leave the cell blank. **If 0% is entered, the tool will produce erroneous results**.

The following is an example of how subgroups work.

In this example, the drug under review is indicated for patients who are low to moderate or high risk. Of these, 10% of patients are considered high risk and the remainder are considered low to moderate risk. This condition is only diagnosed when symptoms are present; this is very common in patients who are high risk and less common in those who are not. Therefore, the rate of diagnosis differs between the 2 groups: 95% of patients who are at high risk are diagnosed and 70% of those who are at low to moderate risk are diagnosed. Upon diagnosis, individuals considered at high risk are eligible for the drug under review so no more filters are applied. For those who are at low to moderate risk, patients are eligible only if current practice fails. In this case, current practice fails in only 20% of patients who are at low to moderate risk. Figure 2 shows how these data are entered into the tool.

Figure 2: Inputs–Subgroups Screen — Epidemiological Filters for Refining Incident Population

Name of subgroup 1 user wishes to derive epidemiological filters for:	High risk		
Name of subgroup 2 user wishes to derive epidemiological filters for:	Low/Moderate risk		
The user must specify what percentage of the cohort the subgroup applies to. If the subgroups are mutually exclusive (meaning a patient cannot be considered in both subgroups) then the percentages should sum to 100%. If they sum to less than 100% then the user assumes any patients not covered by these subgroups are ineligible for treatment. If the subgroups are not mutually exclusive the user must ensure no double counting occurs when deriving data for the epidemiological filters.			
	High risk	Low/Moderate risk	
Percentage of the population who comprise the subgroup	10.00%	90.00%	
The user must enter all the epidemiological filters that apply below. If a filter only applies to one subgroup then leave the cell blank in the subgroup it does not apply to (do not set to 0%).			
Epidemiological filter	Percentage applied to patients who meet the criteria for subgroup: High risk	Percentage applied to patients who meet the criteria for subgroup:	Weighted average
Diagnosed	95.00%	70.00%	73%
Failed current practice		20.00%	30%
			100%
			100%
			100%
			100%
			100%
			100%
			100%
			100%

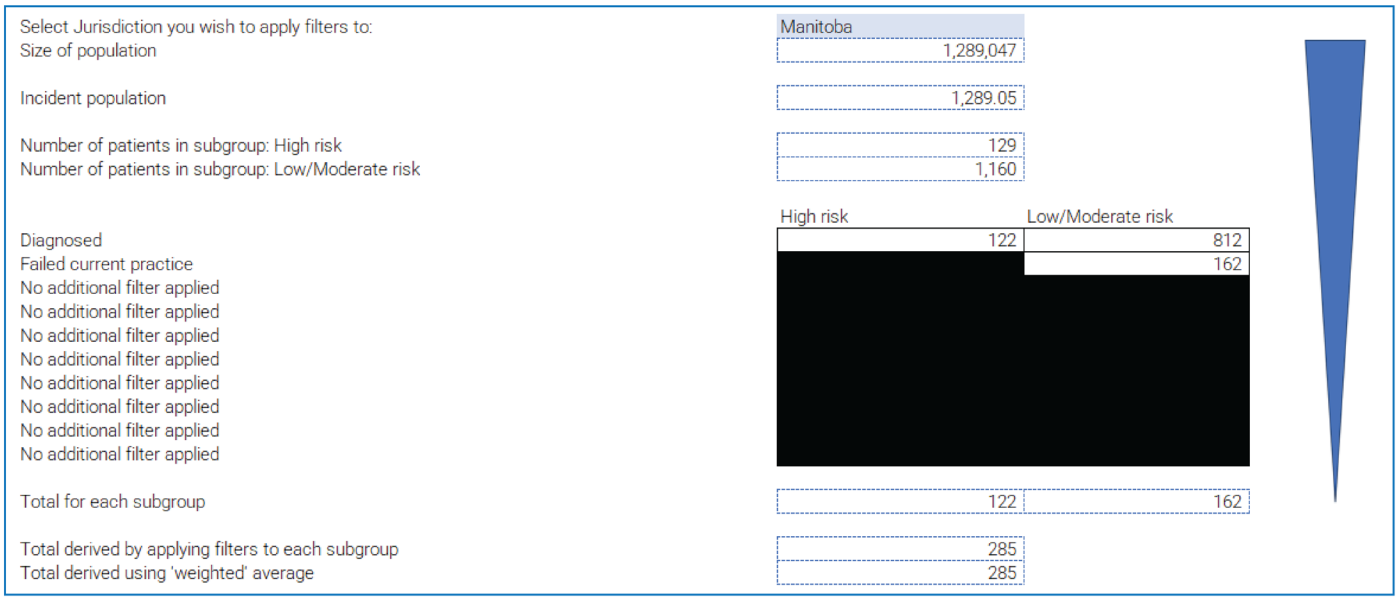
Once the user has finalized this step, they must click the **Apply Epi Weights (incidence)** button. This is a simple copy-and-paste macro that pastes the weighted average filter percentages (cells F23:F32) with their description (cells B23:B32) to the Inputs–Market Size worksheet (cells F40:F49 and B40:B49, respectively).

Figure 3: Inputs–Subgroups Screen — Apply Epi Weights (Incidence) Button

Once the epidemiological filters have been applied above and the user is satisfied the results are valid by checking the patient flow below, click the button to enter these into the market size sheet		Apply Epi Weights (incidence)

To validate the approach, a patient flow chart is provided. The user can select the jurisdiction the filters should be applied to. Continuing with the previous example, Figure 4 shows the patient identification process for Manitoba. This is assuming incidence for the disease of interest is 0.1% (which the user will have specified in cell F28 on the Inputs–Market Size worksheet). By applying the weighting separately to each subgroup, 122 patients who are at high risk will be eligible for the drug under review and 162 patients at low to moderate risk will be eligible. Summed together, this equals 285 patients. If we apply the weighted average filters to the full population, the same result occurs. If cell D62 does not equal cell D63, an error has occurred, and the user should recheck the previously imputed values.

Figure 4: Inputs–Subgroups Screen — Patient Flow (Incidence)



The remainder of the worksheet is a repeat of the first section except it applies to models for which the prevalent cohort is relevant to the decision problem.

5. Worksheet: Outputs–Patient Flow

The Outputs–Patient Flow worksheet presents patient flow in the analysis, meaning how the full population is filtered down to include only those patients eligible for the drug under review. This worksheet is for validation purposes only and does not require any inputs used to calculate the BIA.

Cell D8: The user must select which jurisdiction they want patient numbers for.

6. Worksheet: Inputs–Drug Names

Cell E10: The user must enter the name of the drug under review.

Cell E12: The user must specify the number of comparators. The current tool allows for 10 comparators. If users require more comparators, it is suggested they either consolidate certain comparators if appropriate (e.g., combine all generics of 1 drug) or build a bespoke tool. If there are no active therapies in this space, then 0 can be selected; this means "untreated" will be the only comparator in the analysis.

Cells E14:E23: The user must enter the names of all comparators.

7. Worksheet: Inputs–Market Shares

Throughout the Inputs–Market Shares worksheet, users can enter either pan-Canadian market shares or, if market shares are expected to vary by jurisdiction (e.g., if certain comparators are not listed in some jurisdictions), a jurisdiction-specific value. If both pan-Canadian and jurisdiction-specific values are entered, the jurisdiction-specific value will override the pan-Canadian value.

7.1. Time Horizon (3 to 5 Years)

Cell F14: The user must specify the time horizon of the analysis.

The *Procedures for Reimbursement Reviews*[4] specify that 4 years of data should be presented: 1 baseline year (i.e., the year before the drug under review enters the market) and a 3-year forecast period. Note the time horizon selected here excludes the base year, so if the user wishes to view a 3-year time horizon plus baseline year, 3 years should be selected. The procedures also recommend that if full implementation is expected to extend beyond 3 years, a longer time horizon may be submitted as a scenario analysis.[4] For example, if the introduction of a new drug does not result in stable market shares at 3 years, a longer time horizon should be considered (refer to Section 8: Outputs–Market Dynamics for examples of what constitutes a stable market).

If full implementation is expected to take longer than 3 years, users can select a 4- or 5-year time horizon.

7.2. Reference Scenario

Cell F19: The user must specify the market shares for the baseline year and each year of the specified time horizon in a scenario in which the drug under review is **not** funded.

Market shares are the distribution of patients across each available treatment (i.e., percentage receiving drug A; percentage receiving drug B). Entries for market shares can be jurisdiction specific or pan-Canadian.

For an incidence-based model, the market share relates to the distribution of treatments patients receive upon becoming eligible for the drug under review. Each year in the BIA, new patients enter the model (incident patients) and the market share determines which treatment they will receive.

For a prevalence-based model, market share relates to the distribution of treatments at a given point in time. For example, there are 2 treatments, A and B, and the market share is 50% and 50%. This means at any point throughout the year we expect 50% of patients to be receiving treatment A and 50% to be receiving treatment B. This would assume uptake and the likelihood of remaining on treatment is the same. If after a year the

distribution changed to 40% and 60% for A and B, respectively, this means at least 10% of patients receiving B will be receiving it for the first time and 10% less of the cohort will be receiving treatment A. This is considered when calculating time-varying costs, as detailed in Section 9: Inputs–Drug Costs User Worksheet.

In the reference scenario, market shares represent the **current** distribution of all eligible patients across all available treatments in a scenario in which the new drug is **not** available. Untreated is included as a comparator in market shares. *Untreated* represents patients who meet the criteria for the Health Canada indication but do not receive treatment.

7.3. New Drug Scenario

Cell G35: The user must specify the market shares for the baseline year and each year of the specified time horizon in a scenario in which the drug under review **is** funded.

In the new drug scenario, the market shares of the currently available treatments change (i.e., there is a change in current use) according to the anticipated proportion of the patients who will use the newly available drug. Therefore, this scenario outlines the market shares for which the new drug **is** available.

8. Worksheet: Outputs–Market Dynamics

No user input is required in this worksheet; output is provided to allow the user to validate their numbers provided in market shares (refer to Section 7: Inputs–Market Shares).

When deriving market shares, it is important to determine where market capture for new treatments will likely come from and whether it is stable at the end of the BIA time horizon. Based on the market shares the user entered in Inputs–Market Shares, this worksheet allows the user to assess the impact treatment has on market dynamics. This gives the user information to validate the impact of their market share assumptions in terms of where the market capture comes from. The percentages in each column outline what proportion of a drugs market share is allocated to the new drug based on the input from the user under the new drug scenario in the Inputs–Market Shares worksheet. An example of this output is provided in Figure 5. For example, in year 1, the inputs for the new drug scenario imply that the new treatment captures 50% of the market occupied by drug 1 and 25% of the market occupied by drug 2. In year 2, the new treatment captures the remainder of the market occupied by drug 1, no further market capture from drug 2, but now the new drug also captures 16.7% of the market occupied by drug 3. In year 3, the new treatment does not capture any further market from drugs 1, 2, or 3 but now captures 25% of the market from drug 4.

Figure 5: Outputs–Market Dynamics Screen — Example Inputs

Reference scenario		pan-Canadian			
	If market shares are expected to be jurisdictionally specific, fill in columns M to CC. If market shares are the same across	Baseline	Year 1	Year 2	Year 3
New Drug		0%	0%	0%	0%
Untreated		0%	0%	0%	0%
Drug 1		10%	10%	10%	10%
Drug 2		20%	20%	20%	20%
Drug 3		30%	30%	30%	30%
Drug 4		40%	40%	40%	40%
Total		**100%**	**100%**	**100%**	**100%**
New drug scenario					
			Year 1	Year 2	Year 3
New Drug			10%	20%	30%
Untreated			0%	0%	0%
Drug 1			5%	0%	0%
Drug 2			15%	15%	15%
Drug 3			30%	25%	25%
Drug 4			40%	40%	30%
Total		**0%**	**100%**	**100%**	**100%**

Figure 6: Outputs–Market Dynamics Screen — Example Outputs

Implied Capture Rates for NewDrug

	Year 1	Year 2	Year 3
Untreated	0.0%	0.0%	0.0%
Drug 1	50.0%	100.0%	0.0%
Drug 2	25.0%	0.0%	0.0%
Drug 3	0.0%	16.7%	0.0%
Drug 4	0.0%	0.0%	25.0%

The capture rate for New Drug from Drug 4 is greater in the final year than the previous

For market uptake to be considered stable, capture rates in the final year of the BIA should be small and not increase from previous years. If capture rates are high (> 25%) or larger than previous years in the final year of the BIA, this **may** indicate that the new treatment has not fully penetrated the market, therefore the market share is unstable. These cases are flagged to the user **as prompts** to potentially consider a longer time horizon. In the example presented in Figure 6, the large increase in market capture from drug 4, which was unimpacted in years 1 and 2, would indicate the market shares may not be stable.

9. Worksheet: Inputs–Drug Costs User Worksheet

This Inputs–Drug Costs User Worksheet is used for calculating drug costs to be used in the BIA. Currently, the tool does not have a prespecified formula to calculate annual drug costs. This gives users flexibility when it comes to estimating drug costs because of the many permutations for how drugs can be delivered.

Any cells in this worksheet can be edited or deleted to suit the user's needs. For transparency, an example is included in the tool to demonstrate how to estimate total drug costs. This is for illustrative purposes only and can be removed, edited, or expanded upon.

Although the tool allows for full flexibility, the following must be adhered to for a robust validation:

- Information on the unit cost (to 4 decimal places) per lowest dispensable unit and the per unit amount per lowest dispensable unit must be transparently detailed in the tool.
- All calculations should be transparently laid out.
- All assumptions must be clearly stipulated (e.g., those pertaining to relative dose intensity [RDI], time on treatment, dose titration, and compliance).
- If total costs are taken directly from the submitted economic evaluation, the user must list the assumptions used in the economic evaluation to derive drug costs.
- Please refer to Appendix 2 for considerations when estimating drug costs for this tool.

10. Worksheet: Inputs–Total Drug Costs

10.1. Average Per-Patient Annual Costs

The Inputs–Total Drug Costs worksheet is where the annual drug cost estimates are entered.

Cell F12: The user is required to specify whether drug costs are expected to remain constant. If the answer is "Yes," first-year drug costs are used to populate all years of the BIA. If drug costs are not expected to remain constant over time, "No" should be selected and the user should specify drug costs for each year of the analysis.

There are 2 ways to estimate annual drug costs within the tool.

Option 1: Manually estimate annual drug costs (refer to Section 9: Inputs–Drug Cost User Worksheet) and link annual drug costs to the relevant cells specified in the tool.

Option 2: Extract drug costs from an economic model (this applies to incidence-based models only).

As part of a submission, except for tailored reviews, a sponsor is required to also submit an economic evaluation. Part of this economic evaluation requires a sophisticated estimation of drug costs. The economic model should be flexible enough to report disaggregated total costs, such that drug costs can be easily extracted and used in the BIA.

- **Step 1:** Set discounting rate to 0%.
- **Step 2:** Run the model with a 1-year time horizon. From this, extract **only** the costs associated with the drug(s) of interest. This should be provided in the disaggregated results. Call this parameter **$A**.
- **Step 3:** Run the model with a 2-year time horizon. Again, extract only the costs associated with the drug(s) of interest. Call this parameter **$Y**.

- **Step 4:** Run the model with a 3-year time horizon. Again, extract only the costs associated with the drug(s) of interest. Call this parameter **$Z**.

With this information, the user can estimate what drug costs are for individuals who are diagnosed in years 1, 2, and 3 of the BIA.

When an individual enters the BIA in the first year, drug costs are expected to be **$A**. In the second year, we would expect additional drug costs to be **$B** (**$Y** – **$A** = **$B**). Finally, in the third year we would expect additional drug costs to be **$C** (**$Z** – **$Y** = **$C**). If a time horizon of greater than 3 years is used, then the model will need to be run for a 4- and 5-year time horizon with the same process repeated.

This information can be directly inputted into the BIA tool. In the Inputs–Total Drug Costs worksheet for the drug under review, the user should enter 1-year costs ($A) into cell **F17**, second-year costs ($B) into cell **F33**, and third-year costs ($C) into cell **F49**.

This process is repeated for each comparator.

The advantage of this approach is it ensures the BIA and economic evaluation are aligned. Likewise, an economic evaluation can use sophisticated techniques to estimate drug costs (e.g., by conducting survival analysis to extrapolate long-term treatment discontinuation).

If this approach is conducted, the user should still specify the unit cost, dosing, and assumptions (e.g., RDI, time on treatment, dose titration over time) used in the economic evaluation in the **Inputs–Drug Cost User Worksheet** for transparency. Alternatively, the user can use the economic model to extract information to estimate drug costs, such as average time on therapy or, at minimum, validate the numbers derived using option 1.

An important consideration is that drug cost estimation in the economic evaluation must be sufficiently flexible and transparent.

11. Worksheet: Inputs–Subsequent Therapy Costs

Cell F10: The user is asked if they want to consider subsequent therapy costs in the analysis.

If a therapy is effective at delaying or negating the need for the next line of treatment, then there may be cost savings to the drug plans. These may be important costs to consider when conducting a BIA.

Calculation of subsequent therapy costs can be challenging because of the number of assumptions required; for example, how many patients discontinue a therapy each year, what proportion go on to receive a subsequent therapy, what type of subsequent therapy is received, are subsequent therapies equivalent across drug plans, and how long the individual spends on that subsequent therapy. Due to these issues, no standardized template is provided for the calculation of these costs because of the sophisticated techniques required to estimate them.

Instead, on this worksheet the user will enter the average per-patient subsequent therapy costs.

11.1. Estimating of Subsequent Therapies — Incidence-Based Model

For an incidence-based model, the user will enter subsequent therapy costs for each year of the BIA. For example, for year 1, the user enters what they expect the average per-patient costs associated with subsequent therapy to be for patients who started each therapy. For year 2, the user enters what additional subsequent therapy costs are expected to occur in that year. This is repeated for the length of time the user wishes to conduct the BIA for.

One method of estimating subsequent therapy costs is to use results from an economic evaluation (this applies to incidence-based models only).

- **Step 1:** Set discounting rate to 0%.
- **Step 2:** Run the model with a 1-year time horizon. From this, extract only the costs associated with subsequent therapies. This should be provided in the disaggregated results. Call this parameter **$A**.
- **Step 3:** Run the model with a 2-year time horizon. Again, extract only the costs associated with subsequent therapies. Call this parameter **$Y**.
- **Step 4:** Run the model with a 3-year time horizon. Again, extract only the costs associated with subsequent therapies. Call this parameter **$Z**.

When an individual enters the BIA in the first year, we would expect them to incur **$A** of subsequent therapy costs. In the second year, we would expect them to incur (**$Y** – **$A** = **$B**) in subsequent therapy costs. Finally, in the third year, we would expect them to incur (**$Z** – **$Y** = **$C**) of subsequent therapy costs.

If a time horizon of greater than 3 years is used, the model will need to be run for a 4- and 5-year time horizon with this process repeated. This information can be directly inputted into the BIA tool.

Cell F16: For drug under review, enter first-year costs ($A).

Cell F32: For drug under review, enter second-year costs ($B).

Cell F48: For drug under review, enter third-year costs ($C).

An option is provided to make subsequent therapy costs specific to each jurisdiction. This may be appropriate when availability of subsequent therapies varies across jurisdictions.

11.2. Estimating of Subsequent Therapies — Prevalence-Based Model

In a prevalence-based model, the market share incorporates what proportion of patients are receiving therapy at a given point in time. If a drug has a high rate of discontinuation relative to all the comparators, this will reduce the market share. This makes estimating subsequent therapy costs in a prevalence-based model challenging. If the patient moves on to a comparator therapy considered in the BIA, this should not be captured in subsequent therapy use but rather changing market shares. Because we do not know when patients started the comparator therapies, we can only apply an average subsequent therapy cost for all years of the BIA. If the expectation is a high rate of treatment failure and movement between multiple lines of therapy, the assumptions of a prevalence-based model limit the accuracy with which you can estimate subsequent therapy costs.

Using a prevalence-based model, the user must assume, every year, the percentage of patients who experience treatment failure and therefore require a subsequent therapy. Then multiply this percentage by the average annual cost of the subsequent therapy received. These calculations can be conducted in the Inputs–Unit Drug Costs worksheet. For calculations to be accurate, the percentage of patients failing and thereby requiring a subsequent therapy each year must be similar across all treatment options included in the BIA.

Overall, accurate estimation of subsequent therapies using a prevalence-based model is challenging because the user would need to create a dynamic model that can track every patient entering and leaving the BIA.

12. Worksheet: Inputs–Administration Costs

Cell F12: The user is asked to consider the costs associated with administering medications. This applies for any drug administered by a health care professional. If "No" is selected, the rest of this worksheet can be skipped.

There are 2 components considered in this tool:

Cells F16:F27: First, the user must enter the cost of administration for the drug under review and each comparator. Depending on how drugs are administered, this may vary by comparator. An oral therapy, for example, will have no to minimal administration costs, whereas an IV will require health care professional time to administer.

Cells F31:J42: The user must enter the frequency of administration for the drug under review and each comparator.

- In an **incidence-based model,** this equates to the number of administrations expected per year on treatment. This accounts for treatment discontinuation, dose skipping, and so on. For example, if the therapy was a one-time therapy, such as chimeric antigen receptor (CAR) T-cell therapy, the administration rate would be 1 in year 1 and 0 in subsequent years.
- In a **prevalence-based model** for drugs that are already funded, it is not known when patients started their therapy. This means time-varying administration estimates are not usable. Instead, an average must be applied based on the average length of time patients are expected to have been on therapy. For the drug under review, it is assumed the drug is not currently funded. Therefore, all patients starting therapy represent a patient's first year on therapy. The tool then allows for changing administration rates in subsequent years.

13. Worksheet: Inputs–Companion Diagnostic

In the Inputs–Market Size worksheet, the user is required to specify if a companion diagnostic is used to identify patients eligible for the drug under review. If testing is not relevant (the user selects "No"), no information will display on this worksheet, and it can be skipped.

In the Inputs–Market Size worksheet, the user enters inputs related to testing eligibility, uptake, and percentage testing positive (refer to Section 3.5: Companion Diagnostic Testing).

Cells F21:F25: The user must specify what proportion of the patients eligible for testing will be tested if the drug under review is **not** funded. In some jurisdictions, the test may already be part of routine care but, in others, it may not be. If the drug under review is **not** funded, will testing rates remain static or will they increase?

In a prevalence-based model, the assumption is individuals will be tested once. If testing is 50% in year 1 and 60% in year 2, that means an additional 10% of the population is tested in year 2. If testing rates hit 100%, although individuals may not be retested, new diagnoses would have not been tested before and should be accounted for. Because this BIA tool does not track individuals entering and leaving a prevalence-based model, if the testing rate hits 100%, this tool will underestimate testing costs in a prevalence-based model.

In any incidence-based model (incidence, incidence with bolus, incidence derived through prevalence), new patients enter the model every year and these patients are eligible for testing.

Cell F27: The user is required to specify the cost of the test.

14. Worksheet: Results

The Results worksheet provides users with results based on the inputs they have entered in the input worksheets of the tool.

Cell C6: Users may select the jurisdiction they want results for (i.e., pan-Canadian results or any individual jurisdiction).

Cells C8:C11: Users can flexibly select the types of costs they would like reported. As a default, only drug costs are considered (i.e., drug costs and subsequent drug costs).

The first table provides a high-level result of total drug costs in the reference and new drug scenarios. These results are disaggregated by year, with the number of years presented reflecting the time horizon selected in the Inputs–Market Shares worksheet. The total column sums costs across years (3, 4, or 5 years, depending on time horizon) in the reference and new drug scenario. The budget impact is calculated in the bottom row by subtracting the reference scenario costs from the new drug scenario costs.

The subsequent tables provide more detailed results. First, the **Patient Numbers** tables provide the number of patients receiving each treatment, by year, in both the reference and new drug scenarios. The total patient numbers are then summed to provide the total number of patients in the analysis by year.

The detailed **Drug Costs** tables (**Cells C40** and **L40**) provide detailed results of drug costs disaggregated by treatment, year, and scenario (reference and new drug). This shows total expenditures associated with a specific drug (e.g., to understand expected sales of the drug under review in the new drug scenario).

The Budget Impact–Drug Costs Only table (**cell C55**) presents detailed budget impact results by treatment and year.

The tables at the bottom of the worksheet (**cells C73, L73, C80**) present an overview of the user-selected costs. For example, if users entered administration or testing costs and selected these to be displayed in the users' inputs rows of the Results worksheet, these costs will be displayed disaggregated by year and scenario.

15. Worksheet: Scenario Analyses

The Scenario Analyses worksheet allows the user to inspect the effect of different assumptions and parameter changes to the results of the analysis. First, the user is required to finalize the base case. This is the set of results that the user feels reflects the best estimate of what the budget impact will be. These results will be used to compare the results of all scenario analyses.

Once the base case is finalized, the user must click the **Save base case** button. This hard codes the results so the user can make changes to the BIA and refer to these base-case results. This simple macro just copies data from cells C10:I27 and pastes it into cells C23:I27 as values.

For scenario analysis 1:

Cells B36:B43: The user must transparently lay out what parameters they want to change.

Cells D36:D43: The user must specify the worksheet the change is being made in.

Cells E36:E43: The user must specify the cell reference within the worksheet where the change is being made.

Cells E36:E43: The user must specify what the new parameter is.

Once the user has made the change(s) to the relevant parameters, they can click the **Save Scenario Analysis 1** button. This hard codes the results so the user can make changes to the BIA and refer back to the scenario analysis 1 results.

If the user wants to conduct further scenario analyses, this same process can be repeated for scenario analyses 2 to 5.

If the Health Canada indication differs from the proposed reimbursement request, the user should include the reimbursement-requested population as 1 of the scenario analyses.

16. Worksheet: References

The user can enter a numbered reference throughout the tool. In the References worksheet, the user can enter the full reference relating to each of the numbers.

17. Worksheets: Newfoundland and Labrador to NIHB

According to *The Procedures for Reimbursement Reviews*,[4] results should be calculated individually by jurisdiction then summed to provide a pan-Canadian estimate. Calculations of budget impact are calculated for each jurisdiction on separate worksheets.

The name of the jurisdiction being calculated is presented in cell B4. A high-level presentation of the market size by year follows.

Each jurisdiction-specific calculation worksheet can estimate the budget impact using either a prevalence or incidence approach, depending on the user's selection. The tool will not display calculations for the approach not selected because these are irrelevant and may be misleading.

The first set of results calculated are those applicable to a prevalence-based approach (rows 2:163). If an incidence or incidence with prevalence bolus or incidence derived through prevalence approach is selected, these results are calculated in rows 165:325.

The results shown in rows 327:424 in the jurisdiction calculation worksheets selects either the prevalence- or incidence-based calculations (depending on the approach selected). These are the "live" results that are used in the Results worksheet.

These worksheets are not user modifiable.

18. Worksheet: Drop-Downs

The Drop-Downs worksheet stores drop-down lists used throughout the tool and is not user modifiable.

19. Worksheet: Data Store

The Data Store worksheet contains the final adjusted population size estimates, adjusted for the NIHB population size, considering whether a drug is an oncology versus non-oncology treatment and an oral or a take-home versus an IV medication.

20. Worksheet: StatsCan Population Size

The StatsCan Population Size worksheet contains the raw Statistics Canada population data used in the tool.

21. Worksheet: NIHB Population Data 2023

The NIHB Population Data 2023 (NIHB Pop Data 2023) worksheet contains NIHB population data from 2023.

22. Worksheet: NIHB and Population Calculations, Sequential

The NIHB and Population Calculations (NIHB and Pop Calcs) worksheet contains the calculations used to calculate the NIHB population size and to adjust the size of jurisdiction population estimates to account for people within the jurisdiction who will have NIHB coverage (i.e., to avoid double counting).

A full explanation of the approach to calculating this population size is provided in Appendix 1.

23. Worksheet: Growth Rate

The Growth Rate worksheet contains the calculations used to estimate the population growth rate for each jurisdiction.

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Appendix 1: NIHB Population Size Calculations

A1. Objective and Aims

The aim of this Appendix is to assist sponsors conducting BIA submissions by providing instructions on how to appropriately derive the Non-Insured Health Benefits (NIHB) program population size when an epidemiological-based approach is used. In deriving this population, it is important to consider certain subgroups of the NIHB-eligible population that receive pharmacy benefit coverage through other jurisdictions. This means that both the NIHB population size (derived from NIHB annual reports[2]) and jurisdictional population sizes (derived from Statistics Canada data[6]) may require adjustments to ensure the population sizes are accurate.

Considerations that influence the size of the NIHB and jurisdictional populations include the following:

- Ontario pharmacists must coordinate drug benefits and pursue payment through the Ontario Drug Benefit (ODB) program before billing the NIHB Program for all NIHB clients living in Ontario who are eligible for drug coverage under the ODB Program, including OHIP+.[7,8] This means that NIHB clients with ODB coverage (i.e., those younger than 25 years and those aged 65 years and older) must be subtracted from the NIHB population and kept in Ontario population estimates.
- Oncology BIA submissions only: Alberta[9] and Saskatchewan[10] provide universal cancer treatment coverage for patients registered with their respective cancer agencies. All requests received for oncology products, take-home or otherwise, for clients in Alberta or Saskatchewan are redirected back to the provincial cancer agency for coverage and reimbursements, meaning that NIHB clients in these jurisdictions receive their coverage from the provincial cancer agencies, not NIHB.[9,10] Therefore, when conducting a BIA for oncology products, NIHB clients in Alberta and Saskatchewan should not be subtracted from the provincial populations, but instead from the NIHB population.
- The NIHB does not fund non–take-home oncology products.[7,8,11,12] When the drug under review and its comparators and subsequent therapies are all IV oncology products, the NIHB should not be included as a budget holder within the submitted BIA and NIHB clients should remain within provincial population estimates. When the drug under review and all comparators and subsequent therapies are take-home oncology products, the NIHB should be included as a budget holder and population adjustments should occur as usual (i.e., both ODB age group adjustments as well as Alberta's and Saskatchewan's universal oncology coverage apply). At the current time, and for simplicity, when regimens are part take-home and part IV, or when some comparators are take-home and some are IV, the user should follow the procedure for take-home oncology products when the drug under review is take-home and IV products when the drug under review in IV. This method may evolve in the future.
- First Nations Health Authority (FNHA)[13] assumed responsibility for the design, management, delivery, and the funding of the delivery of health services to First Nations residing in British Columbia. First Nations residing in British Columbia receive their health benefits through the FNHA's Health Benefits Program, which replaced the NIHB Program in British Columbia.[14] Current NIHB population estimates account for this; as a result, there are relatively fewer NIHB clients in British Columbia compared

to the other provinces. Since 2017, FNHA Health Benefits for prescription medications have been administered through British Columbia PharmaCare's Plan W.[15,16] Because FNHA clients are administered through British Columbia PharmaCare, no further population adjustments are required.

Because the approach to derive the population size differs depending on whether the submission is an oncology or non-oncology submission, the following sections present the method to derive the population size based on the type of submission.

A2. Approach to Derive NIHB Population and to Adjust Jurisdictional Population Estimates

Typically, population data from Statistics Canada[6,17] is used for determining population sizes when employing an epidemiological-based approach. Often, the NIHB population is then added to the populations of the participating provincial jurisdictions to estimate the pan-Canadian population. However, this leads to double counting of some or all the NIHB population because NIHB clients are already counted within provincial population data from Statistics Canada. Several steps are required to avoid such double counting and to ensure NIHB clients are assigned to alternate jurisdictional budgets when appropriate.

The overall size of the NIHB population within each province can be found within NIHB annual reports,[2] with the exception of the Atlantic provinces (New Brunswick, Newfoundland and Labrador, Nova Scotia, Prince Edward Island), which are grouped together. For the purposes of budget impact analyses submitted to Canada's Drug Agency, the NIHB population within each Atlantic province may be estimated by multiplying the overall Atlantic NIHB client population by the proportion of the total population of the Atlantic provinces residing within each Atlantic province.

Typically, NIHB clients within each province are then subtracted from the provincial population to avoid double counting. However, as noted in section A1, there are several circumstances in which all or part of the NIHB client population within a province should remain within provincial budgets and instead be subtracted from the NIHB population. These circumstances differ based on client age and whether the drug under review is an oncology or non-oncology product.

A2.1 Non-Oncology Drugs

A2.1.1 Step 1: Start With the Full NIHB Population and the Full Provincial Populations

The base NIHB population should be derived from "Section 2: Client Population" of the latest NIHB Annual Report.[2] This section includes overall eligible client population counts; client population changes by region over time; growth rates over time; client population by age group, gender, and region; and other analyses.

Provincial population sizes can be derived from Statistics Canada population estimates (typically Table 17-10-0009-01 or 17-10-0005-01).[6,17]

A2.1.2 Step 2: Adjust Provincial Populations by Removing NIHB Clients

For non-oncology BIAs, the populations of British Columbia, Alberta, Saskatchewan, and Manitoba can be adjusted simply by subtracting NIHB clients from provincial population counts.

Example 1: Manitoba 2023, non-oncology BIA

- Manitoba provincial population (source: Statistics Canada Table: 17-10-0005-01[1]): **1,454,902**
- Manitoba NIHB client population (source: NIHB annual report, 2022–2023[2]): **165,855**
- Manitoba BIA population = [Manitoba population] – [Manitoba NIHB population] = 1,454,902 – 165,855 = **1,289,047**

Similarly, the populations of New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador can also be adjusted by simply subtracting NIHB clients from provincial population counts. However, because the NIHB annual reports combine these 4 provinces into a single Atlantic NIHB client population, an extra step must be performed to estimate the NIHB client population within each Atlantic province. For the purposes of BIAs, this estimate can be achieved by assuming the proportion of NIHB clients within each Atlantic province is the same as the proportion of the total population of the Atlantic province residing in each one:

Example 2: Nova Scotia 2023, non-oncology BIA

- NS provincial population: **1,058,694** (Source: Statistics Canada Table: 17-10-0005-01)[1]
- Atlantic province population (NL + PE + NS + NB): (538,605 + 173,787 + 1,058,694 + 834,691) = **2,605,777** (Source: Statistics Canada Table: 17-10-0005-01)[1]
- Atlantic province NIHB client population: **69,589** (Source: NIHB annual report, 2022–2023).[2]
- [NS BIA population] = [Population NS] – ([Atlantic NIHB Population] × [Population NS] / [Population Atlantic Provinces]
- [NS BIA population] = 1,058,694 – (69,589 × [1,058,694 / 2,605,777]) = **1,030,421** (rounded to nearest person)

However, in Ontario, ODB covers all publicly funded Ontario residents aged 24 years or younger and those aged 65 years and older, including those who are otherwise NIHB clients. NIHB clients in Ontario within these age ranges (≤ 24 years and ≥ 65 years), derived using section 2 of the annual report, **should be subtracted from the NIHB population**, while NIHB clients in Ontario who are aged 25 to 64 years should be subtracted from the Ontario population:

Example 3: Ontario, non-oncology BIA

- ON provincial population: **15,608,369** (Source: Statistics Canada Table: 17-10-0005-01)1
- ON NIHB population 25 to 64 years (sum 25 to 29, 30 to 34, 35 to 39, 40 to 44, 45 to 49, 50 to 54, 55 to 59, 60 to 64 age groups): **125,838** (Source: NIHB annual report, 2022–2023).[2]
- [ON BIA population] = [Population ON] – [ON NIHB population 25 to 64]

- [ON BIA population] = 15,608,369 – 125,838 = **15,482,531**

A2.1.3 Step 3: Adjust the NIHB Population by Removing Clients Who Are Funded by Ontario

For non-oncology BIAs, the NIHB client population must be adjusted by removing clients in the age ranges covered by ODB (i.e., those aged 24 years and younger as well as those aged 65 years and older). For brevity, this is often internally referred to as the "Ontario subset."

Example 4: NIHB 2023, non-oncology BIA

- NIHB client population: **936,006**[2]
- Ontario NIHB population < 25 years (sum 0 to 4, 5 to 9, 10 to 14, 15 to 19, 20 to 24 years age groups): **70,160**[2]
- Ontario NIHB population ≥ 65 years: **32,704**[2]
- [Ontario subset] = [Ontario NIHB population < 25 years] + [Ontario NIHB population ≥ 65 years]
- [Ontario subset] = 70,160 + 32,704 = **102,864**
- [NIHB BIA population] = [NIHB population] – [Ontario subset]
- [NIHB BIA population] = 936,006 – 102,864 = **833,142**

A2.1.4 Summary Tables

Table 1 presents the size of the NIHB population for non-oncology drug submissions for the 6 most recent NIHB annual report years.

Table 1: NIHB Population Size for Non-Oncology Drug Submissions

Annual report year	2017–2018	2018–2019	2019–2020	2020–2021	2021–2022	2022 –2023
NIHB total client population	867,749	873,312	887,518	898,839	915,895	936,006
Ontario subset (aged < 25 and ≥ 65 years)[a]	96,748	96,876	98,067	98,716	100,551	102,864
NIHB Non-oncology total	**771,001**	**776,436**	**789,451**	**800,123**	**815,344**	**833,142**

NIHB = Non-Insured Health Benefits.

[a]The Ontario subset includes those aged 24 years and younger plus 65 years and older. The eligible client population by age group, gender, and region can be found in section 2 of each year's annual report.

Source: NIHB Annual Reports.[2]

Table 2 presents an example adjusted BIA population size for non-oncology products for all jurisdictions (2023) as well as the appropriate total population relevant to the pan-Canadian analysis required for submissions. Note that although the jurisdictional populations of Quebec, Yukon, the Northwest Territories, and Nunavut are not included within the pan-Canadian BIA population, NIHB clients living within those jurisdictions are included together with the rest of the NIHB BIA population.

Table 2: Jurisdictional Population Size Estimates for Non-Oncology Drug Submissions (2023 Example)

Jurisdiction	Jurisdiction population size[a]	NIHB clients for non-oncology products[b]	Adjusted population size[c]
Newfoundland and Labrador	538,605	14,384	524,221
Prince Edward Island	173,787	4,641	169,146
Nova Scotia	1,058,694	28,273	1,030,421
New Brunswick	834,691	22,291	812,400
Quebec	8,874,683	83,279	8,791,404
Ontario	15,608,369	125,870	15,482,499
Manitoba	1,454,902	165,855	1,289,047
Saskatchewan	1,209,107	165,347	1,043,760
Alberta	4,695,290	131,796	4,563,494
British Columbia	5,519,013	17,897	5,501,116
Yukon	44,975	7,852	37,123
Northwest Territories	44,972	28,233	16,739
Nunavut	40,673	37,418	3,255
TOTAL	40,097,761	833,142 [d]	**39,264,625**
Pan-Canadian BIA population[e] (NL, PE, NS, NB, ON, MB, SK, AB, BC, NIHB)			**31,249,246**

AB = Alberta; BIA = budget impact analysis; BC = British Columbia; MB = Manitoba; NB = New Brunswick; NIHB = Non-Insured Health Benefits; NL = Newfoundland and Labrador; NS = Nova Scotia; ON = Ontario; PE = Prince Edward Island; SK = Saskatchewan.

[a]Source: Statistics Canada Table: 17-10-0005-01 (2023, accessed May 2024).[1]

[b]Source: NIHB annual report 2022–2023 Table 2.3.[2] Note the number of NIHB clients in Ontario has been adjusted from the value in the annual report (228,734) by removing the Ontario subset (102,864). Because the annual report only provides the number of clients in Atlantic Canada (69,589), the number of clients in each Atlantic province was estimated by weighting the population size of each Atlantic province by the total Atlantic population.[6]

[c]The adjusted population size was calculated by taking jurisdictional population estimates and subtracting the number of NIHB clients in each jurisdiction.

[d]The sum of the NIHB clients for non-oncology products within each province or territory is 833,136. However, the overall total number of NIHB clients from the NIHB annual report includes 119 people who selected a gender that was not male or female, of whom 6 do not otherwise appear in regional subgroup data from NIHB. Therefore, the total here is reported as 833,136 plus 6, or 831,142, to ensure all NIHB clients are included. The effect on individual jurisdictional budgets is expected to be minimal. Note that when age- or sex- and gender-based subgroup data are used, all individuals who selected an alternate gender are absent.

[e]The pan-Canadian analysis population consists of the adjusted totals of 9 provinces (i.e., excluding Quebec) and the NIHB. The adjusted jurisdictional populations of Quebec and the 3 territories should not be included in the pan-Canadian BIA population.

A2.2 IV Oncology Drugs

NIHB does not fund IV oncology products.[12] Ideally, if any part of the regimen under review, relevant comparators, or subsequent treatments are funded by NIHB (i.e., are take-home oncology products or non-oncology products), costs for the varying products would be appropriately assigned to the relevant budget according to mode of administration and status as an oncology or non-oncology drug so that the effect on each jurisdictional budget holder could be accurately assessed.

However, at the current time, methods to appropriately distribute clients to the jurisdictional budgets based on individual treatment choice or regimen component mode of administration have not been fully developed.

As such, for simplicity, the choice of budget holder for all comparators within a BIA should be based on the mode of administration of the drug under review.

Therefore, if the drug under review is an IV oncology product, all NIHB clients should remain within their respective provincial budgets for all comparators because the NIHB does not fund IV oncology products and the NIHB should not be included as a budget holder within the pan-Canadian analysis. This is a simplifying assumption and may evolve in future.

A2.3 Take-Home Oncology Drugs

NIHB does fund take-home oncology products.[12] If the drug under review is a take-home oncology product, NIHB should be included as a budget holder and the BIA populations of all jurisdictions should be adjusted as if all comparators, individual products within a regimen, and subsequent therapies are take-home oncology products. This simplifying assumption is likely to evolve in the future.

A2.3.1 Step 1: Start With the Full NIHB Population and the Full Provincial Populations

For non-oncology products, the base NIHB population should be derived from "Section 2: Client Population" of the latest NIHB Annual Report.[2] This section includes overall eligible client population counts; client population changes by region over time; growth rates over time; client population by age group, gender, and region; and other analyses.

Provincial populations can be derived from Statistics Canada population estimates (typically Table 17-10-0009-01 or 17-10-0005-01).[6,17]

A2.3.2 Step 2: Adjust Provincial Populations by Removing NIHB Clients as Appropriate

For take-home oncology BIAs, the populations of British Columbia and Manitoba can be adjusted simply by subtracting NIHB clients from provincial population counts (refer to example 1), while those of Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador can be adjusted by estimating the NIHB clients within each Atlantic province and subtracting them from provincial population counts (refer to example 2).

Alberta and Saskatchewan provide universal cancer treatment coverage for patients registered with their respective cancer agencies. All requests received for take-home oncology products for clients in Alberta or Saskatchewan are directed to the provincial cancer agency for coverage and reimbursements. As such, the populations of Alberta and Saskatchewan should not be adjusted to remove NIHB clients, while the NIHB population should be adjusted to remove clients from Alberta and Saskatchewan.

For Ontario, as for non-oncology BIAs, ODB covers all publicly funded Ontario residents aged 24 years or younger and those aged 65 years and older, including those who are otherwise NIHB clients. NIHB clients in Ontario who are aged 25 to 64 years should be subtracted from the Ontario population (refer to example 3).

A2.3.3 Step 3: Adjust the NIHB Population by Removing Clients Who Are Funded by Alberta, Saskatchewan, and Ontario

For take-home oncology BIAs, the NIHB client population must be adjusted by removing clients in the age ranges covered by ODB (i.e., those aged 24 years and younger and those aged 65 years and older, the "ODB subset") as well as all clients in Alberta and Saskatchewan:

Example 5: NIHB 2023, take-home oncology BIA

- NIHB client population: **936,006**
- Ontario NIHB population < 25 years (sum 0 to 4, 5 to 9, 10 to 14, 15 to 19, 20 to 24 years age groups): **70,160**
- Ontario NIHB population ≥ 65 years: **32,704**
- Alberta NIHB population: **131,796**
- Saskatchewan NIHB population: **165,347**
- [Ontario subset] = [Ontario NIHB population < 25 years] + [Ontario NIHB population ≥ 65 years]
- [Ontario subset] = 70,160 + 32,704 = **102,864**
- [NIHB BIA population] = [NIHB population] – [Ontario subset] – [NIHB Alberta population] – [NIHB Saskatchewan population]
- [NIHB BIA population] = 936,006 – 102,864 – 131,796 – 165,347 = **535,999**

A2.3.4 Summary Tables

Table 3 presents the size of the NIHB population for take-home oncology drug submissions for the 6 most recent NIHB annual report years.

Table 3: NIHB Population Size for Take-Home Oncology Drug Submissions

	Population					
Annual report year	2017–2018[b]	2018–2019	2019–2020	2020–2021	2021–2022	2022–2023
NIHB total client population	867,750	873,312	887,518	898,839	915,895	936,006
Ontario subset (aged < 25 and ≥ 65 years)[b]	96,748	96,876	98,067	98,716	100,551	102,864
Alberta NIHB population	123,812	125,209	127,098	128,230	129,657	131,796
Saskatchewan NIHB population	152,324	154,323	157,162	158,785	161,518	165,347
NIHB take-home oncology total	**494,866**	**496,904**	**505,191**	**513,108**	**524,169**	**535,999**

NIHB = Non-Insured Health Benefits.

[a]There appears to be an error or other discrepancy in the total NIHB annual report of 2017–2018; the total client population is reported as 867,750, whereas the sums of the total client population by jurisdiction is 867,749. We have assumed 867,750 to be correct.

[b]The Ontario subset includes those aged 24 years and younger + 65 years and older. The eligible client population by age group, gender, and region can be found in section 2 of each year's annual report.

Source: NIHB Annual Reports.[2]

Table 4 presents an example of an adjusted BIA population size for take-home oncology products for all jurisdictions (2023) as well as the appropriate total population relevant to the pan-Canadian analysis required for submissions. Although the jurisdictional populations of Quebec, Yukon, the Northwest Territories, and Nunavut are not included within the pan-Canadian BIA population, NIHB clients living within those jurisdictions are included within the NIHB BIA population.

Table 4: Jurisdictional Population Size Estimates for Take-Home Oncology Drug Submissions (2023 Example)

Jurisdiction	Jurisdiction population size[a]	NIHB clients for take-home oncology products[b]	Adjusted population size[c]
Newfoundland and Labrador	538,605	14,384	524,221
Prince Edward Island	173,787	4,641	169,146
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Ontario	15,608,369	125,870	15,482,499
Manitoba	1,454,902	165,855	1,289,047
Saskatchewan	1,209,107	0	1,209,107
Alberta	4,695,290	0	4,695,290
British Columbia	5,519,013	17,897	5,501,116
Yukon	44,975	7,852	37,123
Northwest Territories	44,972	28,233	16,739
Nunavut	40,673	37,418	3,255
TOTAL	**40,097,761**	**535,999[d]**	**39,561,768**
Pan-Canadian BIA population[e] (NL, PE, NS, NB, ON, MB, SK, AB, BC, NIHB)			**31,249,246**

AB = Alberta; BC = British Columbia; MB = Manitoba; NB = New Brunswick; NIHB = Non-Insured Health Benefits; NL = Newfoundland and Labrador; NS = Nova Scotia; ON = Ontario; PE = Prince Edward Island; SK = Saskatchewan.

[a]Source: Statistics Canada Table 17-10-0005-01 (2023, accessed February 2024).[1]

[b]Source: NIHB annual report 2022–2023 Table 2.3.[2] Note the number of NIHB clients in Ontario has been adjusted from the value in the annual report (228,734) by removing the Ontario subset (102,864). Because Alberta and Saskatchewan fund all oncology medications, the NIHB BIA population within these 2 provinces has been adjusted to 0. Because the annual report only provides the number of clients in Atlantic Canada (69,589), the number of clients in each Atlantic province was estimated by weighting the population size of each Atlantic province by the total Atlantic population.[6]

[c]The adjusted population size was calculated by taking jurisdictional population estimates and subtracting the number of NIHB clients for take-home oncology products in each jurisdiction.

[d]The sum of the NIHB clients within each province or territory is 535,993. However, the overall total number of NIHB clients from the NIHB annual report includes 119 people who selected a sex or gender that was not male or female, of whom 6 do not otherwise appear in regional subgroup data from NIHB. The total here is therefore reported as 535,993 plus 6, or 535,999, to ensure all NIHB clients are included. The effect on individual jurisdictional budgets is expected to be minimal due to the small number of NIHB clients affected. Note that when age- or gender-based subgroup data are used, all individuals who selected an alternate gender are absent.

[e]The pan-Canadian analysis population consists of the adjusted totals of 9 provinces (i.e., excluding Quebec) and the NIHB. The adjusted jurisdictional populations of Quebec and the 3 territories should not be included in the pan-Canadian BIA population.

A3. Tips When Considering Subpopulations for Review-Specific Reasons

- Age data from Statistics Canada can be retrieved by individual year of age; however, the NIHB reports age data in 5-year categories that may not exactly correspond to the indicated population of the drug under review. In this case, the NIHB client population within the required age group may be approximated by adding all age categories that are clearly within the indicated age range, and then assuming that one-fifth of patients within the borderline category or categories are each age within that category. For example, if the relevant population for a submission is adults aged 18 years or older, the corresponding NIHB client population can be estimated by adding together all age groups from the 20 to 24 years age group to the 65 years and older age group, inclusive, and then adding two-fifths of clients in the 15 to 19 years age group, thus approximately including those who are aged 18 or 19 years and excluding those aged 15, 16, or 17 years.
- NIHB annual reports have included clients who selected an alternate gender (not male or female) since 2021–2022. However, due to the small number of clients currently doing so, for privacy reasons, they are often not reported within regional and age group data from NIHB, as well as not reported within binary gender data. Care should be taken to ensure that NIHB clients who selected an alternate gender are still represented in overall population totals.

Appendix 2: Considerations When Estimating Drug Costs

How Does the Use of Treatments (Dose and Frequency) Change Over Time?

Incidence-based model: Some medications have an induction period, in which the dose is titrated up, and a maintenance period in which the dose is then maintained. This means drug costs in the first year will be different than those in subsequent years. In an incidence-based model, we know when patients start therapy, so we can estimate first-year and subsequent-year costs.

Prevalence-based model: In a prevalence-based model when looking at drugs that are already available to patients, some individuals will have been on therapy for years and others will just be starting. If there is a difference in first-year and subsequent-year costs, then the "average" annual drug cost must be derived. This will require making assumptions about what proportion of the cohort are receiving therapy for the first year versus subsequent years. For the drug under review, if the treatment was not previously funded, every new patient receiving the drug under review will be receiving it for the first time. The tool assumes minimal discontinuation; therefore, if there is a high rate of discontinuation, the proportion of patients in their second year of therapy in years 2 and 3 will be overestimated.

Will There Be Wastage?

If the vial is single use, even if a patient does not receive the full amount of content within the vial, the full cost of the vial is still incurred. If vial sharing is possible, an assumption must be made regarding how much of a vial can be shared.

Will All Patients Receive the Treatment as per the Product Monograph? (Relative Dose Intensity)

RDI estimates the proportion of received dose in relation to the optimal or recommended dose in the product monograph. For example, if the recommended dose is 100 mg per week and, on average, a patient receives 90 mg, the RDI would be 90%. There are many factors that can impact RDI:

- **Dose adjustment.** A patient may have their dose titrated above or below the recommended dose. This may or may not have an impact on drug costs depending on wastage. For example, if vials are single use, a lower dose may mean a patient receives less medicine from a single vial, but this does not affect costs if the same number of vials is used.
- **Skipped doses (compliance).** A patient may miss or skip a dose. In this case, the dose is not administered, and this will likely have a direct reduction in drug costs, especially when the therapy is administered in a health care setting as opposed to being self administered. It is assumed the patient will not eventually make up for the missed dose.
- **Delayed dose.** A patient may miss a dose; however, they may be put on an accelerated administration schedule to make up for the missed dose. If RDI is measured before the patient has "made up"

the dose, it may inaccurately estimate that the patient receives a lower dose than what they eventually receive.

When incorporating RDI into a BIA, the reasons for an RDI not equating to 100% must be considered separately and the impact each factor has on cost must be explored.

How to Incorporate Treatment Discontinuation?

Incidence-Based Model

Over time, a patient may discontinue the therapy due to death, toxicity, patient choice, or lack of efficacy. When a patient discontinues the therapy, the cost of the therapy will no longer be incurred so this must be captured in the BIA. There are several ways this is done:

- **Take the median time on treatment from the trial**. This assumes that patients discontinue therapy **at a constant rate over time**. This approach is inappropriate if the data are skewed. For example, there are 5 patients who receive drug A, and this treatment costs $1,000 a month. Information regarding time on therapy is provided in the Table 5.

Table 5: Example for Incorporating Time on Treatment Into a BIA

Patient	Time on treatment A (months)	Total cost ($1,000 × time on treatment)
1	1	$1,000
2	1	$1,000
3	2	$2,000
4	10	$10,000
5	11	$11,000
	Total	**$25,000**

In the example in Table 5, the total drug cost is $25,000. The median time on treatment is 2 months. If we conducted a BIA and assumed the average time spent on therapy is 2 months (using the median), the average cost per patient is $2,000 (2 × $1,000). Multiplying this by the number of patients (5) means we expect to spend $10,000 on this treatment. This is a large underestimation because the skewness in the data has been ignored. Although, on average, most patients remain on therapy for a very short period, there are a few patients who remain on therapy much longer. Depending on the skewness of data, using the median may also lead to an overestimation of the budget spent on a particular therapy. The median is only appropriate if there is no skewness in the data (a patient is as likely to discontinue therapy at 1 month as they are 12 months).

- **Take the mean time on treatment from the trial**. The mean incorporates the skewness in the data. In the example in Table 5, the mean time on treatment is 5 months. Using this estimation, we expect the budget impact to be $5,000 (5 months × $1,000) per patient. Therefore, with 5 patients, the expected budget impact is $25,000, which matches the data provided. In this example, all patients have discontinued therapy. If some patients remained on therapy at the end of the trial data cut and the

time horizon of the trial does not match the BIA, the mean will be inappropriate. If the mean is used, it must be taken from data that cover the time horizon of the BIA. For example, if the BIA is 3 years, then the mean data must be taken each year over the first 3 years on treatment or when all patients discontinued treatment, whichever comes first.

- **Extrapolate time to treatment discontinuation from the trial**. If the trial duration is less than the time horizon of the BIA, and it is expected that individuals will remain on therapy after the trial period, extrapolation of treatment discontinuation over time may be required. For example, conducting survival analysis on these data will enable the user to extrapolate what discontinuation rates may be beyond the available data. This method also has the advantage of specifying when drug costs are expected to occur. This gives a more accurate estimation of costs in years 1, 2, and 3. If an economic evaluation is conducted, this information will be generated to produce costs for the economic evaluation.

Prevalence-Based Model

A prevalence-based model assumes a static population, meaning the number of new individuals entering the analysis (due to new diagnoses) replace individuals who leave the cohort (e.g., due to death). Therefore, the assumption is that at any given point in time during the year, a patient is on a treatment specified as part of the market share. For example, a prevalence of 500 patients means at any given point throughout the year, 500 people will be on the therapy. If an individual leaves the cohort, they are replaced by a new diagnosis. It may not be that the same 500 patients are on therapy throughout the year, but the number does not fall above or below 500. This means for prevalence-based models, the only cost that needs to be estimated is the average annual drug cost. No considerations need to be made regarding treatment discontinuation due to death because the assumption is new diagnoses will replace individuals who die. Likewise, treatment discontinuation is considered using the market share assumptions. If a treatment has a high rate of discontinuation, all else being equal, the market share will be lower because at any given point in time fewer patients will be on that therapy relative to others.

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Questions or requests for information about this report can be directed to **Requests@CADTH.ca**.