Epiphany

Why MPN Exposes the Limits of Cancer Epidemiology Data and How Epiphany's EpiOncology™ Solves the Problem

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Introduction

MPN epidemiology is complicated due to key factors including treatment patterns, progression, transformation, and survival curves, and requires an augmented patient flow modeling to accurately size the market opportunities. Epiphany's EpiOncology™ is an enhanced, dynamic epidemiology engine, rather than a static market estimate, that gives clients a decision-ready perspective that supports critical market decisions regarding the current treatable MPN patients and how these populations may evolve.

Myeloproliferative Neoplasm Background

Myeloproliferative neoplasms (MPNs) consist of Polycythemia Vera (PV), Essential Thrombocythemia (ET), and Primary Myelofibrosis (PMF, myelofibrosis at diagnosis). These patient subtypes have significant differences in their natural history, treatment patterns, survival curves, risk group progression, and leukemic transformation rates.

There is also progressive Secondary Myelofibrosis (SMF) which occurs post-PV and/or post-ET. While SMF treatment may be similar to PMF, it does have different survival outcomes.

As a result of its composition, MPNs are a challenging market. MPN epidemiology models must capture the structure and dynamics of the patient populations, accounting for much more than incidence. Detailed patient flow models must incorporate treatment patterns, patient progression, leukemic transformation, survival curves, and geographic variations by subtype.

In a complex, evolving market like MPN, the quality of the underlying patient estimates materially influences each important clinical and marketing decision.

Understanding the Limitations of MPN Incidence Data

Some countries, such as the United States, have solid MPN incidence data. The table below presents the 2026 incidence data for PV, ET, and PMF from the National Program for Cancer Registries (NPCR) and estimates from three leading AI models.

2026 INCIDENCE	POLYCYTHEMIA VERA (PV)	ESSENTIAL THROMBOCYTHEMIA (ET)	PRIMARY MYELOFIBROSIS (MF)	TOTAL MPN
NPCR (2023)	6,600	7,800	1,700	16,100
AI Average	5,650	6,700	1,700	14,050

NOTE: NPCR incidence rates for 2023 were applied to the U.S. Census Bureau 2026 estimated populations (middle variant). The AI estimates were requested for the year 2026 via a detailed prompt from three leading LLMs

While the AI average incidence values are close to the NPCR data, the only reason we know these values are rigorous is because we have a clean benchmark for comparison (NPCR). In fact, for most hematologic malignancies, there is a lack of a publicly-available global benchmark dataset. The International Agency for Research on Cancer (IARC)'s GLOBOCAN data set provides no data for most leukemic subtypes, including MPN.

Additionally, MPNs have been, and are currently, often underreported. These underreporting rates can be estimated by comparing MPN data to other myeloid malignancies (like chronic myeloid leukemia (CML)). Because CML incidence is well-documented and its biology is comparable to MPN as a myeloid malignancy, a low MPN:CML ratio in a given country likely reflects MPN underreporting rather than a true epidemiologic difference.

The following table presents 15 country-specific and three regional averages out of a total of 42 countries for which Epiphany provides detailed cancer epidemiology data. The focus was to provide examples of both under-reporting countries compared to countries with rigorous incidence data.

For countries with ratios that fall more than 25% below the regional average, the MPN registry data needs correcting to generate more accurate incidence estimates. About 55% of the 42 countries Epiphany studies require a correction factor, 77% of the Americas, 56% of Asia, 31% of Europe, and 75% of the Middle East. Therefore, using either AI-generated or country-specific patient estimates, in many countries, will result in figures that are low and directionally incorrect.

Ratio of MPN to CML for Selected Countries and Regions

	MALE	FEMALE		MALE	FEMALE		MALE	FEMALE
Americas	**164.54%**	**241.88%**	**Asia**	**161.40%**	**224.25%**	**Europe**	**214.48%**	**295.51%**
U.S	165.26%	272.61%	Japan	80.14%	116.89%	France	162.51%	235.82%
Canada	212.77%	315.07%	China	40.19%	50.32%	Germany	103.65%	150.84%
Argentina	125.69%	144.65%	S. Korea	139.00%	205.64%	Italy	230.49%	313.00%
Brazil	62.69%	80.69%	Taiwan	233.56%	337.55%	Spain	186.56%	280.82%
Colombia	42.88%	62.77%	Australia	140.68%	204.02%	U.K.	240.34%	349.13%

NOTE: Shaded countries have ratios higher than or within 25% of the regional average for both sexes

Source: The ratios were calculated by Epiphany Partners based on incidence data from Cancer Incidence in Five Continents (CI5), Vols. X to XII. Lyon: International Agency for Research on Cancer.

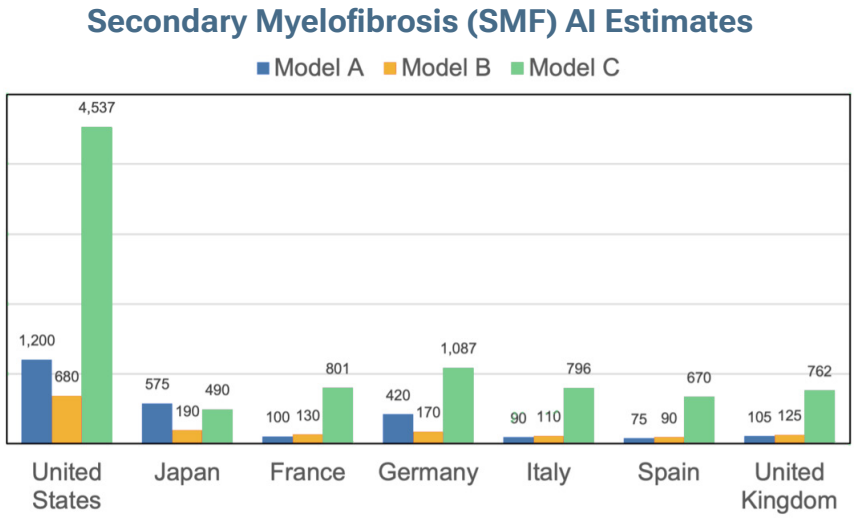
Assessing the Secondary MF Opportunity

Underestimating the rate of progression to SMF (post-PV or post-ET myelofibrosis) can have a substantial impact on the estimate of the total myelofibrosis (PMF and SMF) market.

Unlike PMF, SMF is not an "incident" data set and requires an understanding of the progression process from PV and ET.

Unfortunately, there is no solid benchmark to estimate the actual value of the SMF patient population. Looking at the three AI model estimates, you can see wide variability across each model and across each of the G7 countries. For the incidence estimates, the three models had similar outputs that were close matches to the NPCR benchmark. For SMF, the three models have widely varying estimates illustrating that **without a clear understanding of the patient flow dynamics, selecting a rigorous SMF estimate is difficult**.

Likewise, underestimating the movement of patients into acute myeloid leukemia (AML) via leukemic transformation from all four subtypes (PV, ET, PMF, and SMF) can result in patient overestimates, especially in later lines of treatment.



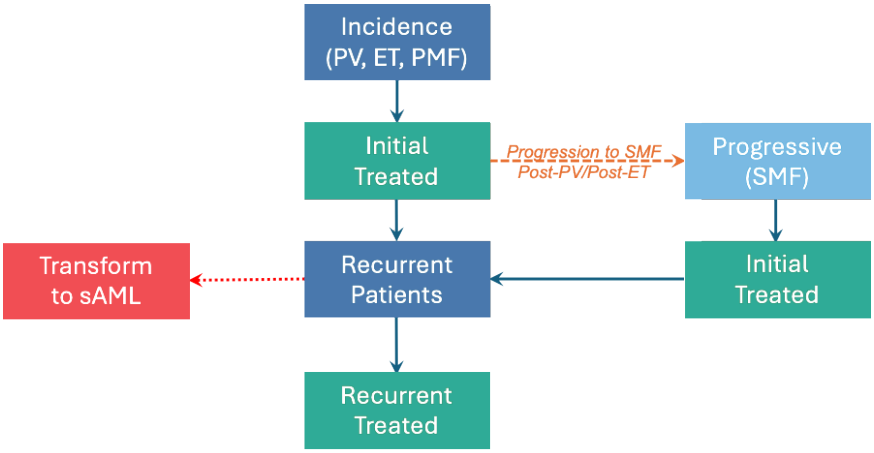
Beyond Incidence: The Need for Dynamic Patient Flow Models

The distinction between patients who are diagnosed with MPN versus those patients who represent a treatable opportunity is crucial. For each MPN subtype, a useful epidemiology data set would quantify the following population types:

- Incident (newly diagnosed PV, ET, and PMF)
- Untreated (both in the year of interest and across multiple years)
- Re-entry patients (following "watch-and-wait" or active surveillance)
- Treatment eligible patients, both initial and recurrent/refractory
- Treatment estimates across key modalities

- Resistant or refractory/intolerant patient groups
- Patients progressing to more advanced disease (SMF from prior-PV/prior-ET)
- Prevalence estimates by subtype and treatment flow
- Candidates for emerging targeted therapies, including "pull through" opportunities (from untreated and remission pools)
- Transformation from all subtypes into secondary AML (leukemic transformation

Dynamic patient flow models are a necessary starting point for assessing the MPN market opportunities. These types of models can account for incidence, incorporate treatment patterns, utilize response and recurrence rates, determine progression and transformation, and assess subsequent treatment opportunities, all united by survival curve data.



Simplified Patient Flow Dynamics for MPN

Understanding how these different patient groups move across the MPN spectrum of subtypes allows for the epidemiology to better inform the forecasting process by focusing on potentially targetable patient groups.

Epiphany's Enhanced Methodologies: Improving the Available Data

In order to correct and enhance the MPN epidemiology data that is currently available, Epiphany's approach is systematic and structured to provide rigorous and unique data.

- Correct underreporting issues in incidence rates for key countries
- Assess subtype estimates to allow for appropriate patient estimates

- Analyze time trends in incidence data by subtype to reflect more accurate future incidence rates
- Apply treatment pattern data from surveys, literature, and available registry data
- Incorporate subtype-specific survival and outcomes measures (response, recurrence, progression, and transformation)
- Utilize detailed patient flow approaches to account for patient movement between lines of therapy, allowing for untreated, response, and recurrence over time

As an example, for Japan, the estimated MPN:CML ratio was well below the regional average (80% vs. 161% for males, and 116% vs. 224% for females). Epiphany applied appropriate correction factors accounting for differences in the MPN:CML ratio by gender and age group. These have different correction factors applied in older age groups, where diagnosis rates should be the highest in this disease. These corrections result in an overall average correction rate of 171% for males and 166% for females. **These corrected incidence rates better reflect the biological rationale, relative to the strong CML incidence data for the country.**

	ORIGINAL REGISTRY RATES		EPIPHANY CORRECTED RATES	
	Male	Female	Male	Female
Polycythemia Vera (PV)	0.856	0.670	1.468	1.112
Essential Thrombocythemia (ET)	1.183	0.926	2.028	1.536
Primary Myelofibrosis (PMF)	0.216	0.169	0.369	0.280

Most epidemiology and forecast models have a key limitation: they can't modulate future assumptions to account for anticipated changes in outcomes, treatment patterns/drug usage, and survival.

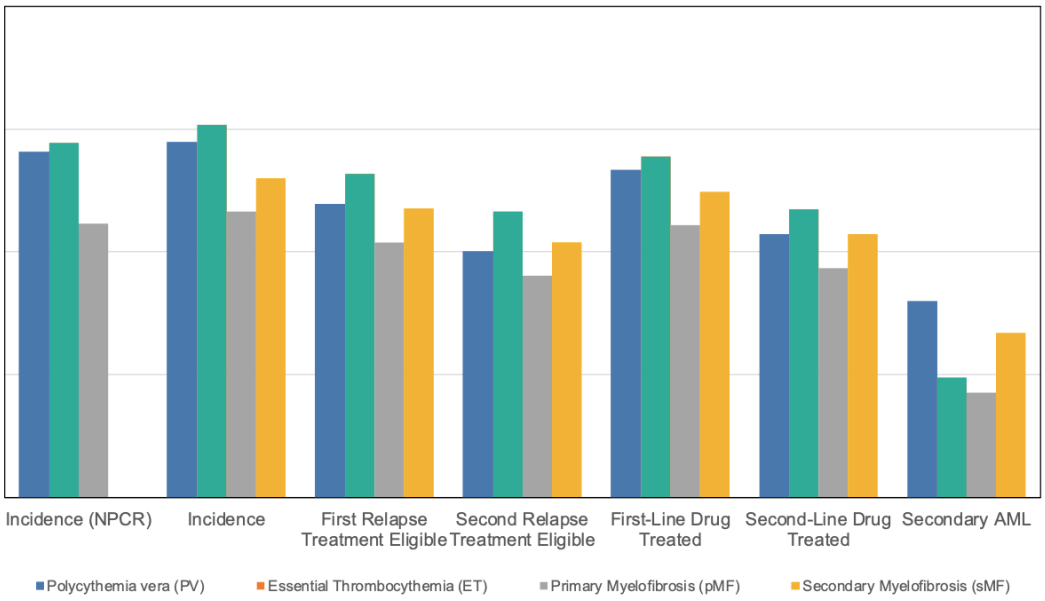
Epiphany's models have been built to allow for customization of most assumptions (incidence, staging/subtypes, survival, outcomes, treatment patterns) on an annual basis. This approach allows users to generate future estimates accounting for anticipated changes in patient outcomes and treatment shifts. By changing these future assumptions as part of the flow model, the output is more useful, as it provides insights into potential outcomes and the driving assumptions, rather than just a static future market estimate.

EpiOncology™: The New Cancer Epidemiology Benchmark

In a complicated market like MPN, the ideal dataset is a **dynamic epidemiology engine** that connects disease burden with treatment patterns, progression, survival, and future assumptions. This type of engine can support decisions throughout product development and lifecycle management.

Epiphany Partners' EpiOncology™ data is a global epidemiology engine that utilizes enhanced methodologies, including more rigorous case definitions, corrections for under-reported incidence rates, better integration of country-specific data, stronger patient flow assumptions, and a transparent view of future market assumptions.

Examples of EpiOncology™ Detailed Flow Model Outputs



This detailed and dynamic approach to patient flows means Epiphany's patient estimates are unique and grounded in actual patient inflows and outflows along the treatment pathway, accounting for changes in outcomes, survival, and future treatment trends.

The MPN market does not need more epidemiology data; it needs corrected, focused, and dynamic data that can support critical market decisions. Epiphany's EpiOncology™ can provide these more rigorous MPN datasets to address market issues and improve product forecasts.