BUILDING AN **MPN DISEASE PROGRESSION REGISTRY**

ADVANCING THERAPEUTIC RESEARCH THROUGH REAL-WORLD DATA

Co-written by
Kapila Viges, MPN Research Foundation
& Harvey Jenner, IQVIA

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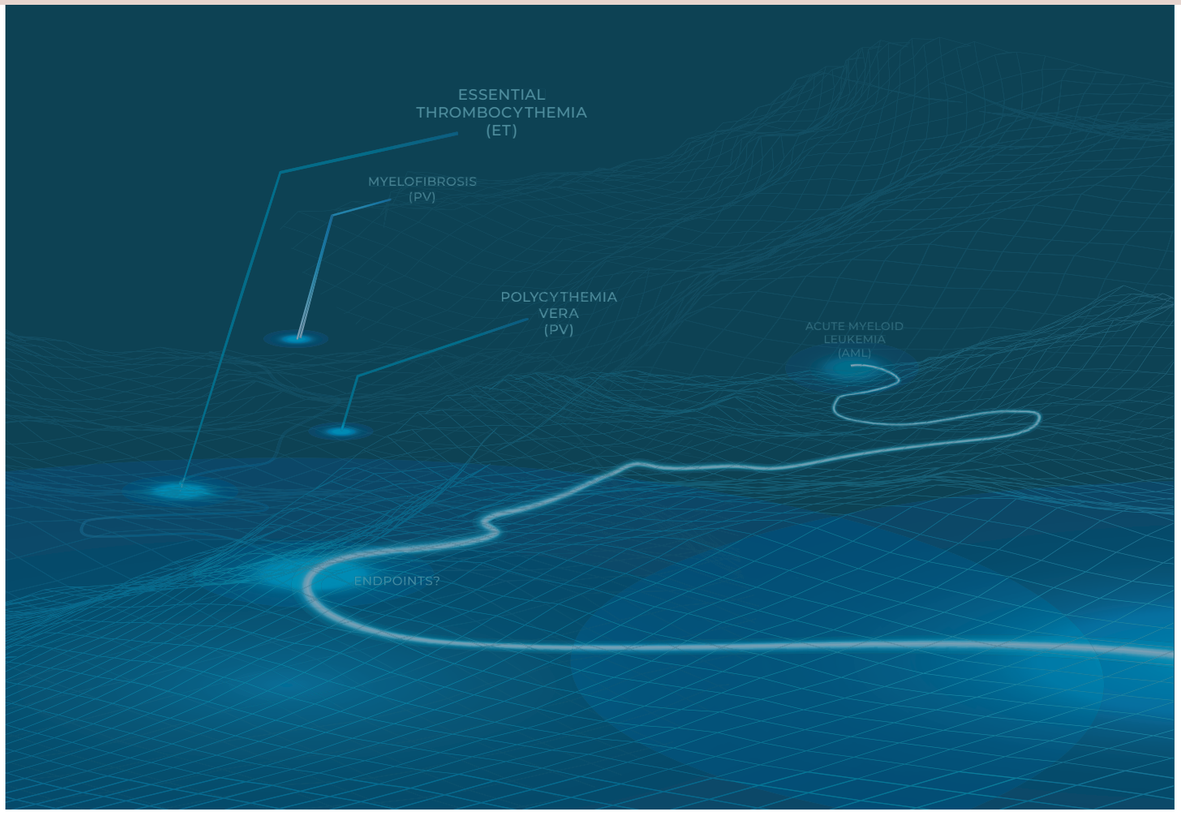
MPN RESEARCH FOUNDATION (MPNRF)

HAS BEEN CALLED TO ACTION BY THE MYELOPROLIFERATIVE NEOPLASMS (MPN) COMMUNITY, INCLUDING PATIENTS, CLINICIANS, AND INDUSTRY STAKEHOLDERS, TO FURTHER THE STUDY OF MPN DISEASE PROGRESSION.

MPNRF is actively pursuing this goal by building a patient registry that captures the full scope of MPN disease progression.



MPN BACKGROUND

and why we need a registry

Myeloproliferative neoplasms (MPNs) are a group of rare blood cancers estimated to affect approximately 300,000 people in the United States.[1,2] MPNs are comprised of essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF).

In each of the cancers, a patient's bone marrow typically overproduces an element of the blood that leads to elevated platelets (ET), elevated red blood cells (PV), or scarring of bone marrow (MF). There is a significant genetic component to MPNs, largely driven by mutations in the *JAK2, CALR*, or *MPL* genes.[3] MPNs can progress, either from ET or PV to MF, or from MF to acute leukemia, often leading to worse outcomes for patients.

Not much is known about the reasons for disease progression, although it is hypothesized that clinical, genetic, and physiological components are involved.[4] Identifying clinical risk factors and surrogate endpoints for MPN progression has the potential to improve clinical prognostication abilities and patient outcomes.

Disease foundations such as MPNRF have a unique role as a neutral body with access to all stakeholders through a trusted and mission-driven model. When embarking on a challenging initiative, foundations in this position are either too ambitious with their initial approach and fall under the weight of the task at hand, or they start too small and find they need more resources and data to affect change.

MPNRF acknowledges the ambitious nature of any project addressing MPN progression and has adopted a meticulous and balanced strategy to navigate potential pitfalls, ensuring sustainable progress and substantial contributions to MPN research and patient care.

After several attempts at exploring tissue banks, a patient reported outcomes (PRO) program, a consortium of institutions to share data, and funding small-scale studies, **MPNRF has landed on building a sustainable, large-scale patient registry anchored by the study of disease progression that can expand to meet life sciences and clinician needs.**

Real-world data is now essential for bringing novel therapies to patients, especially in rare diseases such as MPNs. A registry focused on determining risk factors for disease progression in patients with MPNs has the potential to not only identify patients at risk for MPN progression, but to also aid in developing therapies that delay or inhibit disease progression. Drug discovery and development is increasingly dependent on federated data collection and analysis, going well beyond the historical laboratory approach.

CHALLENGES IN BUILDING A REGISTRY

Building an MPN patient registry is a lofty goal that requires a clear vision to address challenges inherent to this patient population.

Anticipated challenges with building an MPN patient registry include:

- Complexity of the patient and care journey
- Irregular adherence to standard treatment guidelines
- Varied documentation practices across institutions and physicians

Patients with ET, PV, and MF experience a complex healthcare journey with frequent touchpoints across institutions and specialists. For example, a patient may see a hematologist/oncologist in their local community every other month and travel to visit an MPN specialist at a major academic hospital system on a less frequent basis. It is crucial the registry captures each healthcare interaction throughout a patient's journey to support research objectives focused on understanding patient experiences and the use of healthcare resources.

An additional challenge in building an MPN patient registry is the variation across MPN care because patients are not always treated to clinical recommendations. This means that certain procedures or tests, such as gene sequencing or bone marrow biopsies, may not be conducted as standard, especially outside of a clinical research setting, and thus some key clinical data will be unknown. Inconsistent adherence to treatment guidelines, such as the National Comprehensive Cancer Network (NCCN) guidelines, results in incomplete patient data and poses a challenge for data completeness in the registry.

There are also inconsistent charting and documentation standards across sites. Data is stored in different locations and in varied structures between electronic health records (EHR) systems, and even between individual providers in the same department. Therefore, even though EHR may contain highly valuable and detailed clinical data, the data may be nearly impossible to access without significant time and effort. For example, clinical symptoms of MPNs, such as fatigue or bone pain, may be stored in multiple places in the patient's chart and captured as either structured, semi-structured, or unstructured variables. The registry depends on proper data collection. While access to records and technology may have advanced, data capture at the source remains inconsistent.

REGISTRY FEASIBILITY ASSESSMENT AND FINDINGS

Given the inherent risk of building a registry in this space, MPNRF partnered with IQVIA and took a stepwise approach to validate feasibility and make strategic investments in the project. The registry feasibility assessment involved breaking this complex project into smaller activities, providing an opportunity to better understand the task at hand and generate a rigorous plan to build the registry prior to making a large investment.

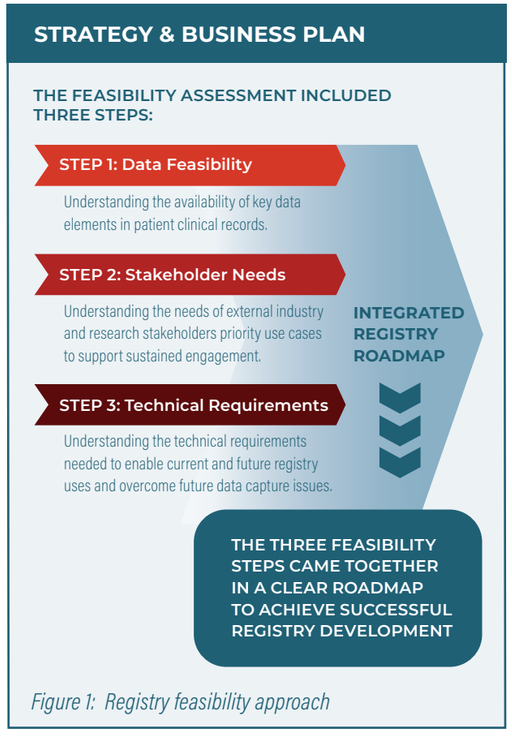


Figure 1: Registry feasibility approach

Approach to data feasibility assessment

Working collaboratively, MPNRF and MPN clinical experts identified key data elements to include in the registry. The process involved developing a data dictionary comprised of desirable variables that may be crucial to understanding MPN progression. This data dictionary was foundational for the rest of the registry feasibility assessment.

After developing the data dictionary, the next step in the registry feasibility assessment was determining the feasibility of capturing the desired variables. Capturing data elements from a patient's chart is dependent on whether the care is provided and documented, and if the data is accessible.

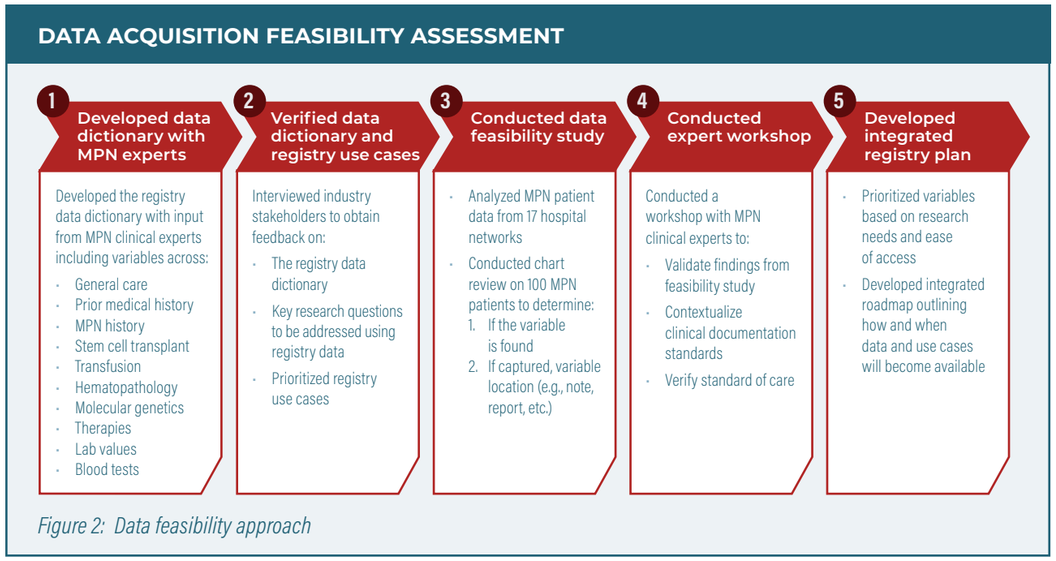


Figure 2: Data feasibility approach

Data availability was assessed in three ways. First, we analyzed existing patient data from over 40,000 patients across academic, community, and integrated delivery network health systems. Second, we conducted a chart review of 100 MPN patients across community and academic sites to evaluate data elements that were not captured in the existing patient data set. Finally, we validated these findings with MPN physician experts.

The goal of these data availability exercises was to assess if variables in the data dictionary were present in the patient's medical record, and if so, where the data was located (e.g., free-text note, lab report, etc.).

We categorized our findings into three variable groups, indicating ease of data capture:

1) **Generally available variables.** These variables included data that is routinely captured in clinical practice in structured and unstructured formats (e.g., demographics, healthcare interactions, medications, procedures). They are largely comprised of data mandated to be collected by U.S. Core Data for Interoperability (USCDI) standards.
2) **Inconsistently documented variables.** These variables are not as consistently captured as the generally available variables and are documented in a variety of places in the patient's chart (e.g., MPN symptoms, date of death, genetic mutations in *JAK2, CALR*, or *MPL* genes).
3) **Inconsistently collected variables.** These variables are not routinely assessed in clinical practice (e.g., quantitative splenomegaly measurement, hematopathology cytokine profiling, non-driver genetic mutations).

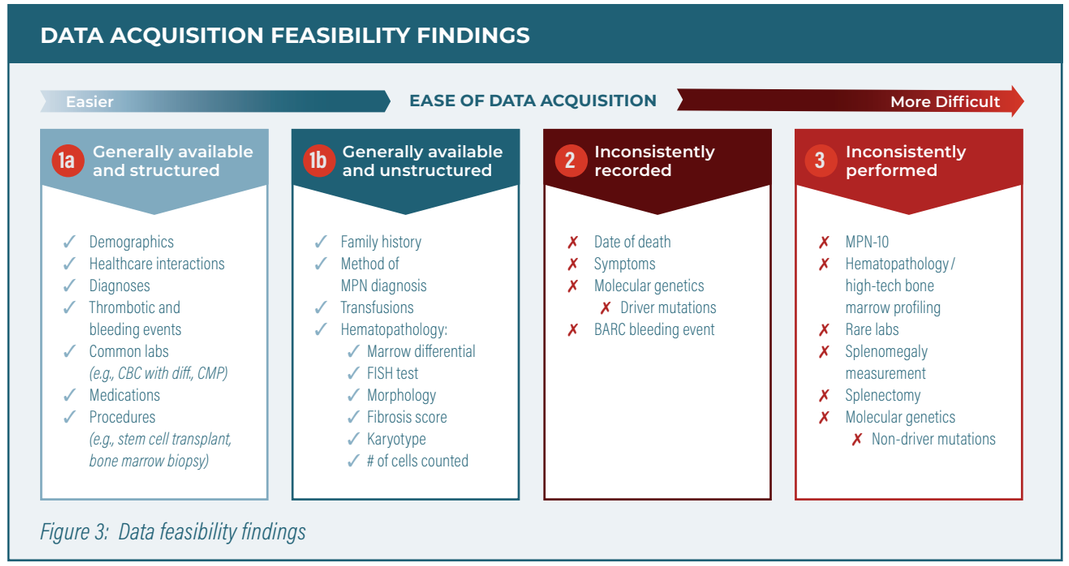


Figure 3: Data feasibility findings

Outcomes of the feasibility assessment

The data feasibility assessment findings revealed that variables in the data dictionary could be split into three tiers, informed by ease of capture (i.e., the three variable groups mentioned above) and value-add to the registry.

All variables in tier 1 were identified by MPN physician experts as required to make the registry useful from day 1 and should be prioritized. As tier 2 and 3 variables are collected, the utility of the registry will increase. However, these variables can be collected over time, as they are difficult to assess and require more time and resources to curate than tier 1 variables.

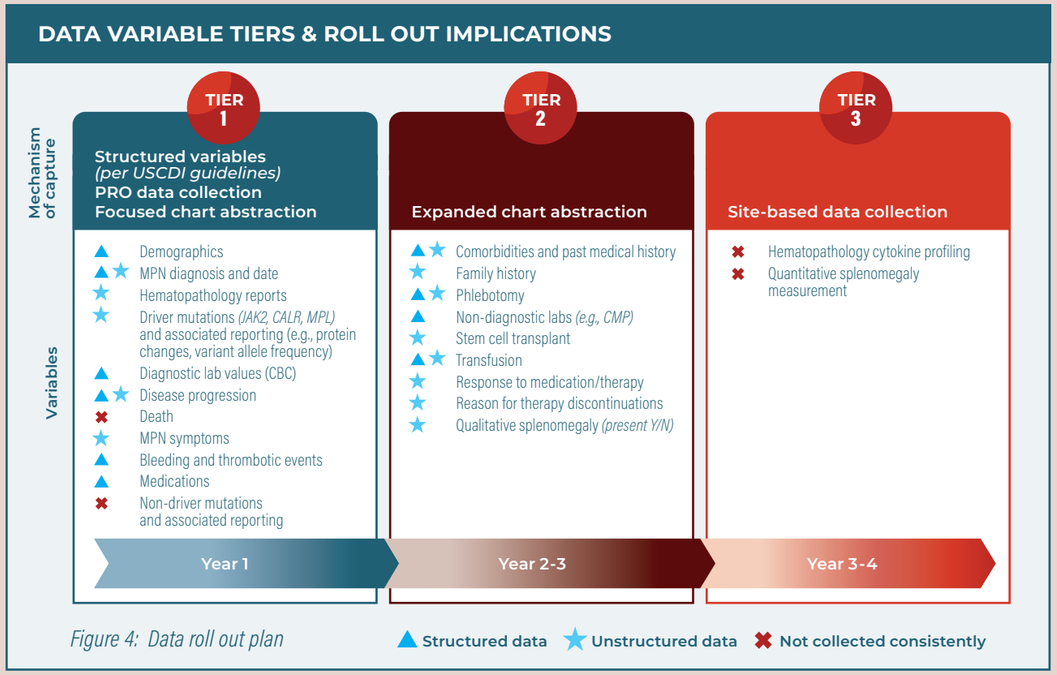


Figure 4: Data roll out plan

Research community engagement assessment

Understanding stakeholder needs allowed us to design an MPN progression registry that will provide sustained value to patients and the research community. The external community engagement workstream included interviews with MPN experts from pharmaceutical companies and academic institutions to identify key unmet needs and determine how the registry would be used over time to help scope the short-, medium-, and long-term build.

These opinions are important as they impact:

1) Patient consent and enrollment at scale
2) Researcher registry leadership, input, and dissemination
3) Industry's registry use cases for therapeutic program advancement

Conversations with MPN stakeholders resulted in identifying key research questions and registry use cases that the MPN registry should support. Research questions ranged from straightforward, such as *What genetic testing is done in routine clinical practice?*, to complex, *How can disease modification prevent MPN progression?*

By tailoring registry data collection efforts and capabilities to key research questions, use cases, as well as the needs of the MPN community, MPNRF can secure early support and ongoing engagement from industry sponsors and research leaders. This approach allows MPNRF to remain dedicated to its mission of stimulating original research for new treatments and, ultimately, a cure for MPNs.

KEY USE CASES FOR COMMUNITY STAKEHOLDERS

Example registry use case	Description overview
Natural history studies	Collect prospective and retrospective patient clinical and non-clinical data to support further understanding of the natiural disease progression of MPN patients across a range of sub-populations. This can include patient diagnostics, treatment journey, etc.
Health economics	Service utilization and cost of care pathways to feed into payer negotiations. This can include healthcare utilization, cost of care, etc.
Trial matching services	Use patient network to advertise potential trial opportunities. Matching services can be targeted/enhanced with data.
Patient insights / market research	Leverage network and patient relationships to ensure that patients' experience, needs, priorities, and collective voice are incorporated into the drug development and evaluation process.
External comparator development	Ability to use patient network to identify, recruit, and enroll patient cohorts and sub-populations to use as control groups for clinical trials based on similar characteristics to the intervention group.
Post-marketing studies	Follow up on MPN patients for safety and effectiveness for regulatory requirements.

Figure 5: Key use cases for registry

Technical needs assessment

After identifying priority data elements and industry use cases, the final step in the feasibility assessment was to create a roadmap for the technical capabilities required to capture and store registry data, with a vision for up-scaling to collecting tier 2 and 3 data.

Data acquisition considerations

To meet the needs of the entire MPN community, the MPN patient registry will pursue a direct-to-patient approach as a first step to obtain data. Thanks to new federal regulations that promote patient access to their health data, patients have the power to choose whom to share it with. Participants can quickly and easily connect their health record portal through a registry platform. The registry automatically removes and replaces personally identifying information with a participant ID, providing a secure and streamlined approach to health data collection.

Once a patient opts to share their data with the registry, we will have a record of their entire care journey, no matter where they received care. This technology also enables MPNRF to re-contact patient and:

- collect information missing from their charts, such as patient-reported outcome (PRO) surveys
- connect clinical data with their care experiences and quality of life
- provide opportunities for patients to participate in new research studies

Interoperability initiatives, such as USCDI, open the door to standardizing contents of patient charts, creating more useful EMR data. Variables that are unstructured and not included in the USCDI initiative will require manual abstraction from patient records. MPNRF will start manual chart abstraction with tier 1 data with an eye towards future automation using natural language processing (NLP) to decrease time and cost.

There are several variables that are not routinely collected in clinical care that are desirable to include in the registry. MPNRF has several opportunities to address this issue and enhance registry data by linking to external data sources (e.g., mortality data), conducting PRO surveys, facilitating deep dive cohort studies, or improving care standards through educational efforts.

MPNRF will use direct-to patient data gathering, new federal data guidelines, and innovative technologies such as artificial intelligence (AI) and NLP to create an agile, growth-oriented, and future-proof registry.

NEXT STEPS

Now that MPNRF has completed the registry feasibility assessment, we are focusing our efforts on the design phase of the registry build. Immediate next steps include finalizing the governance model, securing research partnerships, and building the direct-to-patient infrastructure to support tier 1 data collection.

Our goal is to have the first patient active in the registry in year 1. We are looking forward to continuing to support the patients, clinicians, and researchers of the MPN community by building and scaling this registry, always with an eye towards improving patient outcomes.

REGISTRY ROADMAP

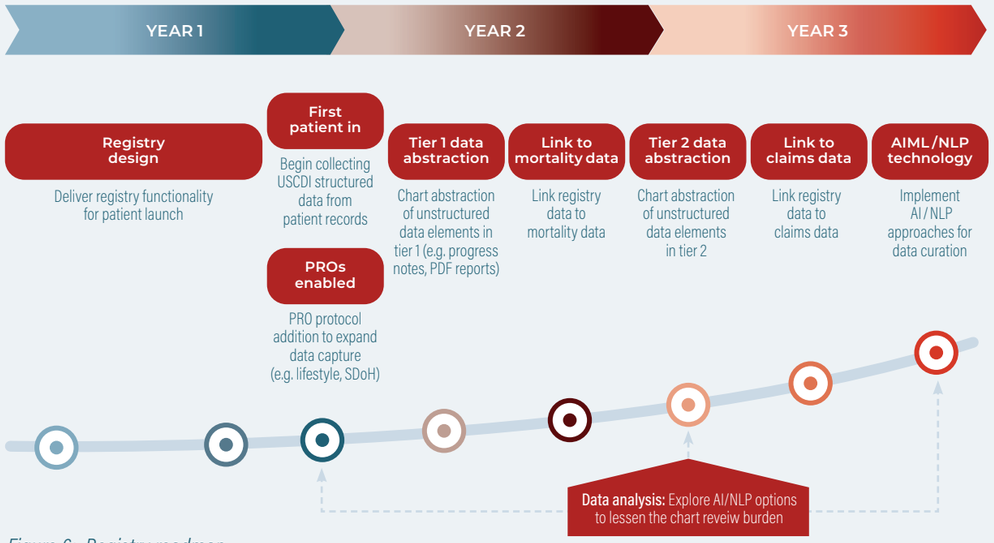


Figure 6: Registry roadmap

CONCLUSIONS

MPNRF's patient registry has been thoughtfully designed to address the significant challenges associated with the endeavor.

By approaching data collection in tiers, it is possible to address the challenges of inconsistent clinical care and data collection. Partnerships with MPN stakeholders are designed to stimulate sustained engagement and meet stakeholders' key research needs, ensuring the registry has the resources to collect longitudinal patient data and enable additional registry uses over time. The tech-enabled, direct-to-patient data collection and abstraction models will allow us to capture robust patient data across multiple care settings. By taking an iterative and collaborative approach to registry building, MPNRF will address some of the most important questions surrounding MPN care and disease progression, as well as identify "quick win" areas to improve patient and disease understanding as soon as possible.

KEY USE CASES

Example research question	Estimated Timeline: Short term	Medium term	Long term
What clinical assessments are routinely done to diagnose MPNs?	Fully addressed		
In what sequence are therapies given?	Fully addressed		
What genetic testing is done in routine clinical practice?	Fully addressed		
What are provider behaviors around patient monitoring?	Fully addressed		
How are patients being maintained on current treatment dose?	Fully addressed		
What influences treatment initiation or modification decisions?	Partially addressed	Fully addressed	
How are rescue phlebotomies used?	Partially addressed	Fully addressed	
How do specialists and non-specialists recognize disease progression?		Partially addressed	Fully addressed
How does the patient journey change over time?	Fully addressed		
What is the relationship between thrombotic events and treatments?	Partially addressed	Fully addressed	
What is the relationship between need for rescue phlebotomies and disease progression?		Partially addressed	Fully addressed
What are the characteristics of patients who progress vs. those who do not progress?		Partially addressed	Fully addressed
What is the profile of patients likely to respond to treatment?	Partially addressed	Partially addressed	Fully addressed
How should disease progression be defined?		Partially addressed	Fully addressed
What is the relationship between allele burden and disease progression?		Partially addressed	Fully addressed
Can overall survival be linked with genetic mutations?	Partially addressed	Partially addressed	Fully addressed
What is the perceived burden and benefit of current therapies?	Partially addressed	Fully addressed	
How does disease and treatment affect health-related quality of life?	Partially addressed	Fully addressed	
What are patients' experiences with anxiety and MPN treatment?	Partially addressed	Fully addressed	
What are patients' experiences with fatigue and MPN treatment?	Partially addressed	Fully addressed	
How can disease modification prevent MPN progression?		Partially addressed	Fully addressed
How to prevent progression/mitigate mutations through earlier treatment with specific therapies?		Partially addressed	Fully addressed
What is the cost and burden of MPNs?		Partially addressed	Fully addressed

Figure 7: Research questions enablement

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References

1. Titmarsh GJ, Duncombe AS, McMullin MF, et al. How common are myeloproliferative neoplasms? A systematic review and meta-analysis. *American Journal of Hematology.* 2014;89(6):581-587. doi:10.1002/ajh.23690

2. Shallis RM, Wang R, Davidoff A, et al. Epidemiology of the classical myeloproliferative neoplasms: The four corners of an expansive and complex map. *Blood* Rev. 2020;42:100706. doi:10.1016/j.blre.2020.100706

3. Hermouet S, Bigot-Corbel E & Gardie B. Pathogenesis of Myeloproliferative Neoplasms: Role and Mechanisms of Chronic Inflammation. *Mediators of Inflammation.* 2015;2015:145293. doi:10.1155/2015/145293

4. Baumeister J, Chatain N, Sofias AM, et al. Progression of Myeloproliferative Neoplasms (MPN): Diagnostic and Therapeutic Perspectives. *Cells.* 2021;10(12):3551. doi:10.3390/cells10123551

ABOUT **MPNRF**

MPN Research Foundation is dedicated to funding and advancing original research in pursuit of new treatments — and eventually cures — for essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF), blood cancers that are known collectively as myeloproliferative neoplasms (MPN).

Founded in 1999, MPNRF was the first organization in the MPN space and is the primary one focused on advancing research. From its unique position at the intersection among key stakeholders — patients and caregivers, researchers and clinicians, and the biotech and pharmaceutical industry — MPN Research Foundation facilitates a collaborative approach to research that elevates the patient voice in research and drug development, brings disease experts together, and accelerates the industry's understanding of an extremely complex group of diseases.

To learn more about MPN Research Foundation and join our community, contact us at communications@mpnrf.org.

ABOUT **IQVIA**

IQVIA is a leading global provider of advanced analytics, technology solutions, and clinical research services to the life sciences and healthcare industry. IQVIA creates intelligent connections across all aspects of healthcare through its analytics, transformative technology, big data resources, and extensive domain expertise.

Our goal in working with patient organizations is to empower these organizations to accelerate advancements to improve patient outcomes and quality of life. Through comprehensive, tailored advisory support, technology and data solutions, and long-term strategies, we enable our customers to achieve their organizational health data and treatment outcome goals.

To learn more about how IQVIA can help you, contact us at pr-contact@iqvia.com.

MPN Research Foundation would like to thank Sobi for their support as the first sponsor of the forthcoming patient progression registry.

Sobi's backing will help move the registry forward, and drive clinical and patient care improvements for people living with these rare blood cancers.

MPN Research Foundation
PO Box 2690
Carol Stream, IL 60132- 2690

mpnresearchfoundation.org