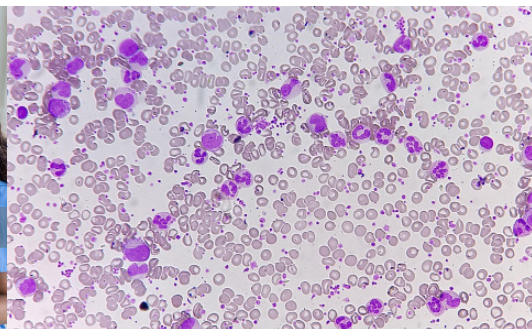
HNHCP
Haematology Nurses & Healthcare Professionals Group







Haematology Nurses and Healthcare Professionals (HNHCP)

Myeloproliferative Neoplasms (MPN)

Polycythaemia Vera | Essential Thrombocythaemia | Primary Myelofibrosis
Learning Program
A Resource for Nurses and Allied Healthcare Professionals

Dear Colleague,

Welcome to the Haematology Nurses and Healthcare Professionals (HNHCP) Myeloproliferative Neoplasms (MPN) Learning Program.

It is with great pleasure that we present this comprehensive educational resource, developed specifically for nurses and healthcare professionals caring for patients with Polycythaemia Vera (PV), Essential Thrombocythaemia (ET), and Primary Myelofibrosis (PMF).

Over the past two decades, our understanding of myeloproliferative neoplasms has evolved dramatically. Advances in molecular biology, particularly the discovery of driver mutations such as JAK2, CALR and MPL, together with the development of targeted therapies, have fundamentally changed the diagnosis, treatment and long-term management of these chronic haematological malignancies. As survival improves and patients live longer with their disease, the need for knowledgeable, highly skilled nurses has never been greater.

Today, nurses are central members of the multidisciplinary team. Their role extends far beyond treatment administration and includes patient assessment, symptom management, treatment monitoring, toxicity recognition, psychosocial support, patient education, care coordination and advocacy. The quality of nursing care has a direct impact on patient safety, treatment adherence, quality of life and clinical outcomes.

This learning program has been developed by an international multidisciplinary faculty of specialist nurses, haematologists, allied healthcare professionals and patient advocates. Our ambition is to bridge the gap between scientific evidence and everyday clinical practice by translating current knowledge into practical guidance that can be immediately applied in daily patient care.

Throughout this program, readers will find:

- Evidence-based reviews aligned with current international recommendations.
- Practical nursing implications integrated within every module.
- Clinical algorithms and case-based examples supporting decision-making.
- Patient education strategies promoting shared decision-making and self-management.
- Key nursing take-home messages summarising the most important learning points.

One of the defining characteristics of this program is its strong nursing focus. Every chapter has been designed not only to explain the scientific background of MPN, but also to highlight the practical challenges nurses encounter every day—from communicating a new diagnosis and supporting treatment decisions to recognising complications early and helping patients manage a lifelong chronic condition.

Education is one of the core missions of the Haematology Nurses and Healthcare Professionals Group. Through international collaboration, we strive to provide independent, high-quality educational resources that are relevant across healthcare systems while remaining practical for daily clinical practice. We firmly believe that investing in nursing education ultimately improves patient outcomes.

Whether you are entering the field of haematology or are an experienced specialist nurse, we hope this program will become a trusted companion throughout your professional development. We encourage you to use it not only as a learning resource, but also as a practical reference that supports evidence-based care and stimulates discussion within your multidisciplinary team.

On behalf of the entire faculty and the Haematology Nurses & Healthcare Professionals Group, I would like to thank all contributors, reviewers and patient advocates who have generously shared their expertise and experience. Most importantly, I would like to thank you—the reader—for your commitment to delivering compassionate, safe and evidence-based care to patients and their families.

This MPN Learning Program was made possible through educational grants from Incyte and GSK.

Together, we can continue to advance haematology nursing through education, collaboration and excellence in patient care.

With best wishes,
Erik Aerts
President
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Haematology Nurses and Healthcare Professionals (HNHCP)

Myeloproliferative Neoplasms (MPN) Learning Program.

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online at

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Disclaimer

This educational resource has been developed for nurses and allied healthcare professionals involved in the care of patients with myeloproliferative neoplasms (MPNs). It is intended for educational purposes only and does not constitute medical advice or replace the clinical judgement of qualified healthcare professionals.

Clinical management decisions should be guided by current local and national guidelines and adapted to the needs of the individual patient. Information on therapeutic agents reflects data available at the time of preparation; licensed indications, dosing and prescribing information may vary between countries.

The views expressed are those of the contributing authors and do not necessarily reflect the official positions of their affiliated institutions or organisations.

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Quick Facts

- Myeloproliferative neoplasms (MPNs) are clonal stem-cell disorders of myeloid lineages; the classical BCR::ABL1-negative (Philadelphia-negative) MPNs are polycythaemia vera (PV), essential thrombocythaemia (ET) and primary myelofibrosis (PMF). These are recognised as blood cancers.
- The World Health Organization (WHO) 5th edition (2022) and the International Consensus Classification (ICC, 2022) place driver mutations and bone-marrow morphology at the centre of diagnosis.
- Janus kinase–signal transducer and activator of transcription (JAK–STAT) pathway activation through driver mutations in JAK2 (Janus kinase 2), CALR (calreticulin) or MPL (myeloproliferative leukaemia virus oncogene) explains the disease in approximately 90% of patients. In essential thrombocythaemia specifically, up to around 10–20% of patients are 'triple-negative' for these drivers (see Table 1).
- MPNs are lifelong conditions; younger PV patients can expect median survival exceeding 35 years, whereas high-risk PMF patients face survival of fewer than five years without haematopoietic stem-cell transplantation. In practice this reflects younger, low-risk patients approaching a life expectancy close to that of the general population; essential thrombocythaemia carries a favourable prognosis, with median survival of around 18–20 years overall (see Section 4.3).
- The principal complications are thrombosis, fibrotic and leukaemic transformation, and a substantial symptom burden — fatigue, pruritus, microvascular events and constitutional symptoms.

Module I: An Introduction to Myeloproliferative Neoplasms

Contents:

A. Definition and Classification
B. Epidemiology and Disease Burden
C. Molecular Pathophysiology
   a. JAK–STAT pathway
   b. Driver mutations: JAK2, CALR, MPL
D. Chronic Nature of MPN
E. Nursing Focus and Key Take-Home Messages
F. References

Learning Objective

By the end of this module, you will be able to describe the defining features, pathophysiology and epidemiology of polycythaemia vera, essential thrombocythaemia and primary myelofibrosis, and explain the impact of a chronic blood cancer diagnosis on patients and their families.

1.1 Definition and Classification

Myeloproliferative neoplasms (MPNs) are clonal stem-cell disorders characterised by the over-production of one or more terminally differentiated myeloid cell lineages (red cells, white cells and/or platelets) and a propensity for disease progression to myelofibrosis and/or transformation to acute myeloid leukaemia.

The classical Philadelphia-negative MPNs comprise polycythaemia vera (PV), essential thrombocythaemia (ET) and primary myelofibrosis (PMF); together with chronic myeloid leukaemia (CML), they form the core of what William Dameshek originally described in 1951 as 'myeloproliferative disorders' (Dameshek, 1951).

Two contemporary classification systems are now in use: the World Health Organization (WHO) 5th edition (Khoury et al., 2022) and the International Consensus Classification (Arber et al., 2022). Subclassification of MPN is broadly similar between the two systems; both retain the disease entities listed above, place molecular driver mutations centrally within the diagnostic criteria, and recognise pre-fibrotic and overt PMF as distinct phases (Arber et al., 2022; Tefferi and Barbui, 2023).

1.2 Epidemiology and Disease Burden

Classical MPNs are uncommon but not rare. A large Swedish population-based study (n=6,281) reported an age-standardised incidence of 4.45 per 100,000 person-years for all MPNs, with PV at 1.48, ET at 1.60 and PMF at 0.52 per 100,000 person-years (Tefferi and Barbui, 2023).

Incidence rises steeply with age; median age at diagnosis is approximately 60–65 years for PV and ET and 65–70 years for PMF, although about 10% of patients are younger than 40 years at diagnosis (Tefferi and Barbui, 2023; Moulard et al., 2014). ET shows a slight female predominance; PV affects men and women equally; PMF affects men slightly more than women (Tefferi and Barbui, 2023; Moulard et al., 2014).

Although MPN survival has improved substantially with current management strategies, disease burden remains considerable. In PV the 20-year cumulative risk of thrombosis, fibrotic transformation and acute myeloid leukaemia is approximately 26%, 16% and 4% respectively (Tefferi and Barbui, 2023). In ET, vascular events (arterial and venous thrombosis, major bleeding) account for the bulk of morbidity. In particular, JAK2 V617F–mutated ET can evolve towards a PV-like, polycythaemic phenotype, whereas CALR-mutated ET carries a comparatively higher risk of progression to myelofibrosis (Rumi et al., 2014).

In PMF, anaemia, transfusion dependence, splenomegaly, profound symptoms and a median overall survival in high-risk groups of less than five years drive a much greater early-life impact (Tefferi, 2023; McLornan et al., 2024a).

Across all three diseases, fatigue, pruritus, microvascular symptoms and psychological distress impair quality of life to a degree comparable with many advanced solid-organ cancers (Mesa et al., 2007). This burden extends to tangible impact on employment and family life; around half of working-age patients report that MPN symptoms affect their ability to work, with additional strain on relationships and caregiving (Harrison et al., 2017).

Entity	Driver mutations (typical frequency)	Defining feature
Polycythaemia vera (PV)	JAK2 V617F (~97%); JAK2 exon 12 (~3%)	Sustained increase in red-cell mass
Essential thrombocythaemia (ET)	JAK2 V617F (~60–65%); CALR (~20–25%); MPL (~3–4%); triple-negative (~10–15%)	Sustained thrombocytosis with megakaryocytic proliferation
Primary myelofibrosis (PMF) — pre-fibrotic and overt	JAK2 V617F (~50–60%); CALR (~25–35%); MPL (~8%); triple-negative (~10%)	Bone marrow fibrosis with leukoerythroblastic film and splenomegaly
Post-PV / post-ET myelofibrosis	Inherits driver from antecedent disease	Secondary fibrosis meeting IWG-MRT criteria

Table 1. The three classical BCR::ABL1-negative myeloproliferative neoplasms (PV, ET and PMF), with characteristic driver mutations and the defining haematological feature of each entity. Post-PV MF and post-ET MF are recognised forms of secondary myelofibrosis rather than separate classical entities, and pre-fibrotic PMF may lack fibrosis, leukoerythroblastosis and splenomegaly.
Sources: Arber et al., 2022; Khoury et al., 2022; Tefferi and Barbui, 2023; Tefferi and Barbui, 2024.

1.3 Molecular Pathophysiology

JAK–STAT Pathway

The Janus kinase–signal transducer and activator of transcription (JAK–STAT) pathway is the dominant signalling axis in classical MPNs. Cytokine receptors for erythropoietin, thrombopoietin and granulocyte colony-stimulating factor signal through paired Janus kinases — chiefly JAK2.

Receptor engagement leads to JAK auto- and trans-phosphorylation, recruitment and phosphorylation of STAT transcription factors (notably STAT5 and STAT3), and translocation of phosphorylated STAT dimers to the nucleus where they drive proliferation, survival and lineage-commitment programmes (Vainchenker and Kralovics, 2017).

In MPN, point mutations or insertions/deletions render this signalling constitutively active in the absence of ligand, producing autonomous expansion of one or more myeloid lineages and the secondary inflammatory milieu that characterises these diseases.

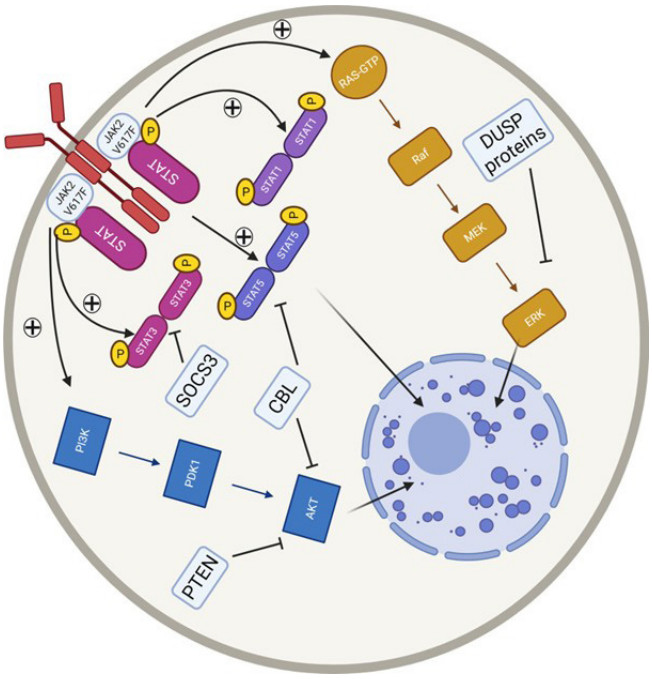


Figure 1. Activated signalling in MPN. Activated signalling pathways in MPN include JAK/STAT signalling, PI3K/AKT and MAPK (RAS/MEK/ERK) cascades. The balance of predominant STAT1/3/5 signalling may impact on ultimate disease phenotype, whilst persistence of activated MAPK or PI3K signalling or STAT serine phosphorylation may occur despite JAK inhibitor therapy. Examples of intracellular negative regulators of JAK/STAT, PI3K/AKT and MAPK signalling with potential roles in MPN pathophysiology are also shown. Source: Greenfield, G. et al. (2021) JAK inhibition and the JAK-STAT pathway in haematological malignancies. Journal of Hematology & Oncology, 14, p.103. Licensed under CC BY 4.0.

Driver Mutations: JAK2, CALR and MPL

Three driver mutations account for the majority of MPN cases. JAK2 V617F, a G-to-T somatic substitution in exon 14 producing a valine-to-phenylalanine change at codon 617, is found in approximately 97% of PV patients, 60–65% of ET patients and 50–60% of PMF patients (Baxter et al., 2005; Tefferi and Barbui, 2023).

In JAK2 V617F-negative PV (~3%), exon 12 JAK2 mutations are usually responsible. CALR (calreticulin) mutations — predominantly type-1 (52-bp deletion) and type-2 (5-bp insertion) frameshifts in exon 9 — occur in approximately 20–25% of ET and 25–35% of PMF and confer a more favourable thrombosis and survival profile, particularly the type-1 variant (Klampfl et al., 2013).

MPL mutations (most often W515L/K) account for around 3–4% of ET and 8% of PMF (Pikman et al., 2006). A small proportion of patients (most commonly with ET) are 'triple-negative' for these driver mutations, and in some of these other JAK2 or non-canonical MPL variants are subsequently identified.

Driver mutation	PV	ET	PMF	Clinical correlate
JAK2 V617F	~97%	~60–65%	~50–60%	Higher haematocrit, leukocytosis, thrombosis risk; allele burden tracks with phenotype
JAK2 exon 12	~3%	–	–	Isolated erythrocytosis; younger age at diagnosis
CALR (type-1 / type-2)	–	~20–25%	~25–35%	Lower thrombosis risk; type-1 favourable in PMF survival. CALR type-2 (5-bp insertion) is less favourable than type-1, with a higher risk of progression to myelofibrosis.
MPL W515L/K	–	~ 3 – 4%	~8%	Older age, anaemia in PMF
Triple-negative	–	~10–15%	~10%	Often poorer prognosis in PMF; germline testing may be considered where clinically indicated. This applies specifically to triple-negative PMF; triple-negative ET instead follows a comparatively benign, indolent course with low thrombosis risk.

Table 2. Frequency of driver and triple-negative mutation status across the three classical MPN entities (PV, ET and PMF), with characteristic clinical correlates.
Sources: Baxter et al., 2005; Klampfl et al., 2013; Pikman et al., 2006; Tefferi and Barbui, 2023; Tefferi and Barbui, 2024; Vainchenker and Kralovics, 2017.

Beyond the driver mutations, 'high molecular risk' (HMR) co-mutations — particularly ASXL1, EZH2, IDH1/2, SRSF2 and U2AF1 — increase the risk of fibrotic and leukaemic transformation and shorten survival; they are now embedded in modern prognostic models such as the MIPSS70+v2.0 (Tefferi et al., 2018).

1.4 Chronic Nature of MPN

MPNs are by definition lifelong conditions. Patients diagnosed in their fifties or sixties may live with the disease for two decades or more, adjusting to changing treatment goals and complications. PV and ET are typically managed for many years with the goal of preventing thrombosis and minimising progression; in younger patients with PV, median survival exceeds 35 years (Tefferi and Barbui, 2023).

By contrast, PMF carries a more variable course: low-risk disease can be observed, while high-risk patients face a median survival of fewer than five years and may need allogeneic haematopoietic stem cell transplantation (allo-HSCT), which is currently the only curative option (McLornan et al., 2024a; Tefferi et al., 2018).

Because the disease can transform — from PV or ET into post-PV/post-ET myelofibrosis (MF), and from any of the classical MPNs to acute myeloid leukaemia (AML) — long-term surveillance is essential. Each clinic visit is an opportunity to track haematological parameters, symptom burden, cardiovascular (CV) risk and treatment-related toxicity.

Nursing Implications for MPN Introduction

Nurse Specialists (such as Clinical Nurse Specialists (CNSs) and Advanced Nurse Practitioners (ANPs) caring for people with MPN play a central role throughout the disease: from explaining the diagnosis and supporting the early shock that often follows, through co-ordinating phlebotomy and cytoreductive treatments, to managing complex symptoms and end-of-life care in the small but important proportion of patients who progress. Nursing input is particularly important across several areas:

- Patient education — explaining 'blood cancer' in terms of a long-term condition, while acknowledging that these are genuine cancers. Well-informed patients demonstrate greater adherence and confidence in self-management; the nurse specialist is pivotal in translating complex clinical information into clear, individualised discussions.
- Psychosocial support — addressing the impact on work, fertility, relationships and family members, and screening for depression and anxiety. Holistic Needs Assessments (HNAs) support early identification of concerns; nurse specialists facilitate referrals to specialist psychological services and signpost patients and families to relevant support organisations.
- Treatment co-ordination — venesection, drug administration and counselling, monitoring for toxicity, and recognising emergencies (thrombosis, haemorrhage, transformation, infection on JAK inhibitors). In some healthcare systems, specialist nurses independently lead venesection clinics and prescribe or adjust cytoreductive therapy under agreed protocols. The nurse specialist promotes treatment adherence, identifies barriers, and ensures monitoring aligns with local and national guidelines and standards.
- Symptom assessment and management — validated tools such as the MPN-SAF enable systematic evaluation of symptom burden; symptoms do not always correlate with haematological parameters, making routine structured assessment essential.
- Fertility and reproductive health — counsel patients on fertility preservation, contraception and the implications of MPN therapies; collaborate with haematology, fertility and specialist obstetric teams.
- Health promotion — cardiovascular risk reduction, including smoking cessation, physical activity, weight management and optimisation of hypertension, cholesterol and diabetes, forms an integral component of holistic MPN care.
- Assessment of health literacy and individual information needs should form part of the first nursing consultation. Patients differ considerably in their understanding of MPNs and their preferred level of information. Tailoring education to the patient's needs improves engagement, adherence and shared decision-making throughout the disease trajectory.

Nursing practice point

- MPN patients are often diagnosed incidentally, on routine blood tests. Many describe the moment of diagnosis as more frightening than the disease itself initially feels. Giving patients a short, clear written summary of what an MPN is — and what it is not — at the first appointment can reduce anxiety and helps patients stay engaged with monitoring.
- Patients newly diagnosed with MPN frequently retain only a limited amount of information discussed during their first consultation. Providing written educational material and arranging an early follow-up consultation with a haematology nurse can improve patient understanding and confidence.

Clinical Nursing Assessment

At diagnosis nurses should assess:

- Physical symptoms
- Psychological wellbeing
- Employment status
- Family support
- Health literacy
- Learning preferences
- Cardiovascular risk factors
- Lifestyle factors
- Current medications
- Vaccination status

Key Nursing Take-Home Messages	
1	MPNs are clonal myeloid neoplasms; PV, ET and PMF share the JAK–STAT pathway as a common driver but differ in clinical phenotype, prognosis and treatment. These are cancers, even though many patients can live for decades with good quality of life.
2	Two complementary classification systems (WHO 5th edition and ICC 2022) inform diagnosis; both place driver mutations and bone-marrow morphology at the centre.
3	Explain that the JAK2, CALR and MPL driver mutations are usually acquired during life and are not directly inherited. Routine testing of family members is generally not required, although familial predisposition to MPN can occur.
4	Encourage patients to keep a written summary of their MPN type, driver mutation, current treatment and emergency contacts and to share this with any healthcare professional they see (including dentists and pharmacists).
5	Provide information on reputable patient organisations and peer-support groups, recognising that patients often seek additional information following diagnosis.
6	Emphasise the importance of attending regular blood tests and clinic appointments — even when they feel well, because subtle changes can be picked up early and acted on.
7	Point patients towards reputable national and international MPN resources and patient organisations (e.g. MPN Voice, MPN Research Foundation) and warn against unreliable websites; encourage patients to bring questions to clinic. Nursing follow-up should also include checking that patients understand their symptoms, discussing workplace adjustments, supporting patients through 'watch and wait', and addressing cardiovascular risk at every visit.
8	Reinforce medication adherence at every visit; proactively explore any barriers to taking prescribed treatments.
9	Signpost to peer-buddy schemes available through patient organisations such as MPN Voice.
10	Encourage an annual cardiovascular risk review with the GP.
11	Advise prompt management of modifiable cardiovascular risk factors — hypertension, raised cholesterol and diabetes — in partnership with the GP.
12	Encourage use of the MPN10 — a validated, patient-reported outcome tool comprising ten key MPN symptoms — to monitor and record symptom burden between clinic visits, supporting structured symptom review at each appointment.

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Quick Facts

- MPN is suspected when an unexplained, persistent abnormality of the full blood count (FBC) is identified — erythrocytosis, isolated thrombocytosis, leukocytosis or a leukoerythroblastic film.
- First-line investigations include FBC and blood film, ferritin, erythropoietin (EPO), JAK2 V617F, and reflex testing for JAK2 exon 12, CALR and MPL where indicated.
- Bone marrow aspirate and trephine biopsy remain central; they confirm morphology, grade fibrosis on the MF-0 to MF-3 (myelofibrosis grade) scale and inform the distinction between true ET and pre-fibrotic PMF.
- Imaging — particularly ultrasound or magnetic resonance imaging (MRI) of the spleen — gives an objective baseline for monitoring response and pre-transplant planning.
- The MPN Symptom Assessment Form (MPN-SAF) Total Symptom Score, often called MPN10, should be obtained at diagnosis as the patient-reported baseline to support assessment of future treatment response. This should be accompanied by a baseline cardiovascular risk assessment (blood pressure, lipids, smoking status, glucose and weight).
- Nurses should introduce the MPN-SAF questionnaire as an important communication tool rather than simply another assessment form. Discussing changes in symptom scores over time helps patients understand treatment response and supports shared clinical decision-making.
- Consider repeating the MPN-SAF at clinically appropriate intervals, particularly following treatment initiation, dose adjustments or when patients report worsening symptoms.

Module II: Diagnostic Workup and Monitoring in MPN

Contents:

A. Laboratory Diagnostics
B. Bone Marrow Examination
C. Imaging and Spleen Assessment
D. Nursing Role in Diagnostics
E. References

Learning Objective

By the end of this module, you will be able to outline the key investigations, diagnostic criteria and prognostic scoring systems used in MPN, and describe the nurse's role in supporting patients through the diagnostic process and ongoing monitoring.

2.1 Laboratory Diagnostics

Diagnosis of an MPN typically begins with a persistent abnormality on a full blood count: erythrocytosis, isolated thrombocytosis, leukocytosis, or a leukoerythroblastic blood film. National guidelines emphasise that an MPN should be considered, and a full work-up arranged, when these abnormalities have no reactive cause and persist on repeat testing (McLornan et al., 2024a; McMullin et al., 2019).

First-line investigations include a full blood count (FBC) with peripheral blood film review, ferritin and iron studies, renal and liver function tests (LFTs), lactate dehydrogenase (LDH), urate, fasting lipids and glucose to characterise cardiovascular (CV) risk, C-reactive protein (CRP) to identify reactive causes, and pregnancy testing where appropriate (Harrison et al., 2010; McLornan et al., 2024a; McMullin et al., 2019).

Serum erythropoietin (EPO) is an essential adjunct to the diagnosis of PV — a low or low-normal value supports a primary erythrocytosis. JAK2 V617F testing should be requested early in any patient with unexplained erythrocytosis or thrombocytosis; a positive result is a major diagnostic criterion for PV, ET and PMF. In JAK2 V617F-negative cases, reflex testing for JAK2 exon 12 mutations (in suspected PV) and CALR / MPL mutations (in suspected ET or PMF) is now standard practice (Arber et al., 2022; Khoury et al., 2022).

Where uncertainty remains — especially in younger patients, triple-negative ET, or unusual presentations — extended myeloid next-generation sequencing (NGS) panels are increasingly used. NGS panels typically cover ASXL1, EZH2, SRSF2, U2AF1, IDH1/2, TET2, DNMT3A, TP53 and SF3B1, among others. These mutations may support diagnosis and are increasingly important for risk stratification and treatment planning (Arber et al., 2022; Tefferi et al., 2018).

2.2 Bone Marrow Examination

Bone marrow aspirate and trephine biopsy remain central to MPN diagnosis. They allow morphological confirmation, fibrosis grading using the European Consensus reticulin score (grade 0–3), karyotyping, and fluorescence in situ hybridisation (FISH) or molecular analyses where local pathways permit (McLornan et al., 2024a; Thiele et al., 2005).

The British Society for Haematology (BSH) guidance recommends bone marrow examination in essentially all suspected cases of ET, PMF and atypical PV, though the WHO 5th edition allows the diagnosis of PV without marrow biopsy in patients with unequivocal JAK2 mutation and very high haemoglobin/haematocrit values (Khoury et al., 2022; McMullin et al., 2019). For ET, marrow morphology is also key in distinguishing true ET from pre-fibrotic PMF — a distinction with important prognostic and therapeutic implications (Tefferi et al., 2018).

Reticulin and collagen fibre grading is reported on a four-point scale:

- MF-0 (normal),
- MF-1 (loose reticulin meshwork without intersections),
- MF-2 (diffuse and dense reticulin with extensive intersections, occasionally with focal collagen),

Test	Purpose	Nursing notes
FBC + film	Detect lineage involvement, dysplasia, leukoerythroblastic features	Repeat to confirm persistence; collect with no tourniquet to avoid pseudo-erythrocytosis
Ferritin / iron studies	Assess iron status and identify iron deficiency that may mask erythrocytosis; guide phlebotomy planning	Iron deficiency may develop with repeated phlebotomy and can be an intended consequence of treatment.
Erythropoietin (EPO)	Differentiate primary from secondary erythrocytosis	Take before any venesection; result interpreted alongside JAK2
JAK2 V617F	Major diagnostic criterion for PV, ET, PMF	Send EDTA peripheral blood; assay requires sensitivity <1%
JAK2 exon 12 / CALR / MPL	Reflex testing where JAK2 V617F negative	Important not to default to 'triple-negative' until full panel assessed
NGS myeloid panel	Identify HMR co-mutations; refine prognosis	Counsel on what genetic testing means; some patients fear 'heritability' Cytogenetic/karyotype analysis on the bone marrow sample, performed alongside NGS, also contributes to prognosis.

Table 3. First-line laboratory investigations for suspected MPN, their diagnostic purpose and nursing considerations at the point of sample collection. Sources: Arber et al., 2022; Harrison et al., 2010; Khoury et al., 2022; McLornan et al., 2024a; McMullin et al., 2019; Tefferi et al., 2018.

- MF-3 (diffuse and dense reticulin with extensive bundles of collagen, often associated with osteosclerosis) (Thiele et al., 2005).

Grade is not in itself diagnostic; clinical, haematological and molecular features must be integrated.

Nursing Role in Bone Marrow Procedures

- Explain the procedure in plain language; many patients have unrealistic fears based on prior experience or hearsay.
- Nurses should proactively assess procedural anxiety, previous experiences with bone marrow biopsies and preferred coping strategies. Individualised psychological support may improve the overall patient experience.
- Confirm coagulation status, platelet count and current antiplatelet or anticoagulant medication before the procedure, in accordance with local guidance.
- Administer local anaesthetic; provide options for anxiolysis (e.g. Entonox or, where available, conscious sedation) and distraction techniques. In many centres this procedure, including administration of local anaesthetic, may be performed independently by trained nurse specialists.
- Post-procedure: monitor for bleeding/haematoma at the iliac crest, advise on analgesia and signs of infection, and ensure follow-up for results — never let a patient leave without knowing when and how results will be communicated.
- Provide patients with written post-procedure advice including expected discomfort, activity recommendations, signs of complications and contact details for urgent concerns.

2.3 Imaging and Spleen Assessment

Splenomegaly is an important clinical sign across all three classical MPNs but most prominently in PMF. Clinical examination should record spleen size by palpation in centimetres below the left costal margin (LCM).

Because clinical assessment is operator-dependent and underestimates true volume — particularly above 5 cm LCM — ultrasound or MRI is preferred for objective measurement and serial monitoring (National Comprehensive Cancer Network (NCCN), 2024; Pan-London Cancer Alliances, 2020). Spleen length on ultrasound (>13 cm in adults) and spleen volume (typically >450 mL) are thresholds used to define splenomegaly or enlargement, not 'massive' splenomegaly, which has no single universally accepted imaging threshold; palpable spleen length is used routinely in practice, with ultrasound for confirmation and CT/MRI volume reserved for trial endpoints and selected treatment/transplant assessments.

In PMF, spleen response to Janus kinase inhibitors (JAK inhibitors, or JAKi) is a key efficacy endpoint. The pivotal trials (COMFORT-I/II for ruxolitinib, JAKARTA for fedratinib, MOMENTUM for momelotinib, PERSIST for pacritinib) used MRI- or computed tomography (CT)-defined spleen volume reduction of ≥35% from baseline (SVR35) at 24 weeks as the primary endpoint (Harrison et al., 2012; Pardanani et al., 2015; Verstovsek et al., 2012, 2023). Imaging should also be considered to investigate splanchnic vein thrombosis, extramedullary haematopoiesis (e.g. paravertebral masses), and pre-transplant splenic assessment, where reduction of marked splenomegaly may be considered as part of transplant planning (Polverelli et al., 2021).

Other imaging considerations include vascular ultrasound or CT in patients presenting with thrombosis (especially atypical sites such as splanchnic veins), and echocardiography where pulmonary hypertension is suspected.

Nursing Implications for Diagnostic Workup and Monitoring

Diagnosis of an MPN is rarely a single moment; it unfolds over weeks of tests, repeat blood counts, biopsy and a multidisciplinary team review. Nurses are often the most stable point of contact during this period and can make this process feel less daunting by:

- Making sure investigations are arranged in the right order without unnecessary delays.
- Providing accurate, paced information about each test — what it shows, what it does not, and how long results take.
- Identifying practical barriers (distance to hospital, work commitments, caring responsibilities) that make attending appointments difficult.
- Supporting the disclosure of the diagnosis — being present at the consultation where possible, and offering a follow-up call within 48–72 hours to revisit information and answer questions.
- Following diagnosis, nurses should offer patients the opportunity for a dedicated follow-up consultation within the first one to two weeks to reinforce key information, answer additional questions and assess psychological adaptation.
- Documenting baseline symptom burden using the MPN-SAF Total Symptom Score (MPN10) — a validated 10-item patient-reported tool that provides a baseline

for subsequent symptom assessment (Emanuel et al., 2012). This should include a baseline vascular risk assessment (blood pressure, lipids, smoking, glucose/weight, personal and family history of thrombosis) and review of modifiable lifestyle risk factors.

Key Nursing Take-Home Messages	
1	MPN diagnosis integrates clinical findings, blood film, EPO, JAK2/CALR/MPL molecular testing, bone marrow morphology and (increasingly) NGS panels.
2	Bone marrow biopsy remains essential in most ET and PMF cases and is the basis of fibrosis grading and the distinction between ET and pre-fibrotic PMF.
3	Where indicated, spleen assessment can be documented objectively by imaging, particularly in PMF, providing a baseline for assessment of JAK inhibitor response.
4	Accurate baseline nursing assessment provides the foundation for future monitoring and early recognition of disease progression.
5	The MPN-SAF Total Symptom Score should be obtained at diagnosis as the patient-reported symptom baseline.
6	Nurses play a central coordinating role throughout the diagnostic pathway, ensuring continuity of care across outpatient clinics, laboratory services and multidisciplinary teams.
7	The nurse's job at this stage is to make a complex pathway feel manageable and humane — and to make sure every test result is communicated.

Red Flag Symptoms Requiring Immediate Medical Review

- Acute neurological symptoms
- Chest pain
- Sudden dyspnoea
- Severe headache
- Visual disturbances
- New significant bleeding
- Fever in patients receiving JAK inhibitor therapy
- Rapidly increasing splenomegaly
- Unexplained weight loss
- Progressive constitutional symptoms

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Quick Facts

- Polycythaemia vera (PV) is a JAK2-mutated MPN characterised by clonal erythrocytosis; almost every patient carries either JAK2 V617F or a JAK2 exon 12 mutation.
- Diagnosis combines a raised haemoglobin/haematocrit (or red cell mass), a JAK2 mutation and characteristic bone-marrow morphology, with a sub-normal serum erythropoietin as a supportive minor criterion.
- Thrombosis is a dominant cause of early morbidity and mortality; risk is stratified primarily by age >60 years and prior thrombosis, with cardiovascular factors and leukocytosis as added modifiers.
- Maintaining a haematocrit <45% via venesection and using low-dose aspirin for all eligible patients are the cornerstone of management. Aspirin may occasionally be reduced or held in specific circumstances, e.g. very high platelet counts with acquired von Willebrand syndrome, or peri-procedurally.
- Cytoreduction with hydroxycarbamide or ropeginterferon alfa-2b may be used as a first-line therapy for high-risk disease; ruxolitinib is the principal second-line option in hydroxycarbamide-resistant or intolerant patients. Routine iron supplementation should generally be avoided, as iron deficiency may be an intended consequence of venesection and iron replacement can worsen erythrocytosis.
- Pregnancy in PV is high-risk; women who are pregnant or considering pregnancy should be referred to a specialist obstetric haematologist for pre-conception counselling and multidisciplinary care throughout.

A. Diagnostic Criteria
B. Clinical Presentation
C. Risk Stratification
D. Treatment Strategies
   a. Phlebotomy
   b. Low-dose aspirin
   c. Cytoreductive therapy
   d. JAK inhibitors
   e. Hepcidin Mimetics
E. Nursing Implications and Key Take-Home Messages
F. References

Learning Objective

By the end of this module, you will be able to describe the clinical features, treatment goals and nursing assessment priorities for patients with polycythaemia vera, including the management of aquagenic pruritus, venesection and cytoreductive therapy.

3.1 Diagnostic Criteria

PV is a JAK2-mutated MPN characterised by clonal erythrocytosis. Other features include leukocytosis, thrombocytosis, splenomegaly, pruritus, constitutional symptoms and microcirculatory disturbances, with an increased risk of thrombosis and progression to post-PV myelofibrosis or acute myeloid leukaemia (Tefferi and Barbui, 2023).

Both the WHO 5th edition and the ICC 2022 retain three major criteria for PV: a raised haemoglobin or haematocrit (or red cell mass), demonstration of a JAK2 mutation (V617F or exon 12), and a characteristic bone marrow biopsy showing age-adjusted hypercellularity with trilineage proliferation. The minor criterion is a sub-normal serum erythropoietin level. The ICC retains the option of using red cell mass; the WHO 5th edition does not (Arber et al., 2022; Khoury et al., 2022).

Diagnosis requires either all three major criteria, or the first two majors plus the minor criterion. In practice, a patient with sustained absolute erythrocytosis at substantially higher values (Hb >18.5 g/dL or Hct 55.5% in men; Hb >16.5 g/dL or Hct 49.5% in women), JAK2 positivity and a low EPO can, in this narrow group only, usually be diagnosed without bone marrow biopsy at presentation, although the BSH still recommends biopsy to provide a baseline fibrosis grade and to detect early progression (McMullin et al., 2019).

Polycythaemia vera (PV) — ICC 2022 Diagnostic Criteria

Major criteria

1. Elevated hemoglobin concentration or elevated hematocrit or increased red blood cell mass*
2. Presence of JAK2 V617F or JAK2 exon 12 mutation†
3. Bone marrow biopsy showing age-adjusted hypercellularity with trilineage proliferation (panmyelosis), including prominent erythroid, granulocytic, and increase in pleomorphic, mature megakaryocytes without atypia

Minor criterion

Subnormal serum erythropoietin level

Diagnosis: All 3 major criteria OR first 2 major + minor‡

Post-PV myelofibrosis (post-PV MF) — ICC 2022 Diagnostic Criteria

Required criteria

1. Previous established diagnosis of PV
2. Bone marrow fibrosis of grade 2 or 3

Additional criteria (≥2 required)

1. Anaemia or sustained loss of requirement for phlebotomy/cytoreductive treatment
2. Leukoerythroblastosis
3. Increase in palpable splenomegaly >5 cm from baseline or new palpable splenomegaly
4. Development of any 2 (or all 3): >10% weight loss in 6 mo, night sweats, unexplained fever (>37.5°C)

* Diagnostic thresholds: haemoglobin: >16.5 g/dL in men and >16.0 g/dL in women; haematocrit: >49% in men and >48% in women; red blood cell mass: >25% above mean normal predicted value.

† It is recommended to use highly sensitive assays for JAK2 V617F (sensitivity level <1%); in negative cases, consider searching for noncanonical or atypical JAK2 mutations in exons 12 to 15.

‡ A bone marrow biopsy may not be required in patients with sustained absolute erythrocytosis (hemoglobin concentrations of >18.5 g/dL in men or >16.5 g/dL in women and hematocrit values of >55.5% in men or >49.5% in women) and the presence of a JAK2 V617F or JAK2 exon 12 mutation.

Figure 2. ICC 2022 diagnostic criteria for polycythaemia vera (PV) and post-PV myelofibrosis.
Source: Arber DA, Orazi A, Hasserjian RP, et al, 2022.

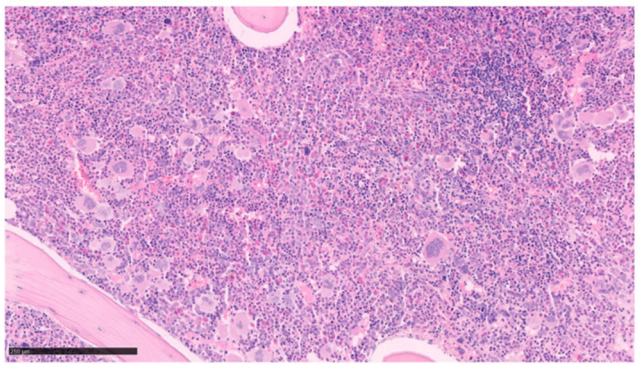


Figure 3. Bone marrow biopsy of polycythaemia vera. Panmyelosis with an increase in pleomorphic mature megakaryocytes. (optical microscopy, May Grünwald Giemsa (MGG), low magnification ×15).

Source: Combaluzier, B. et al. (2023) Cytological diagnosis of classic myeloproliferative neoplasms. Cells, 12(6), 946. © 2023 The Authors. CC BY 3.0.

3.2 Clinical Presentation

Median age at diagnosis is around 61 years; about 10% of patients are below 40 years (Tefferi and Barbui, 2023).

Patients may be asymptomatic, with the diagnosis prompted by an incidental blood count, or may present with microvascular symptoms (headaches, light-headedness, visual disturbance, palpitations, erythromelalgia, distal paraesthesiae), pruritus (particularly aquagenic pruritus, triggered by contact with water, in around 48% of patients) (Tefferi and Barbui, 2023), splenic discomfort, thrombosis (arterial or venous, including atypical sites), or, less commonly, haemorrhage. About 14% of patients have significant constitutional symptoms — fatigue, night sweats, unintentional weight loss — at diagnosis (Tefferi and Barbui, 2023).

Approximately 25% of patients with PV have a history of thrombosis at the time of diagnosis (15–16% arterial, 8–13% venous), making vascular risk assessment a first-line clinical priority (McMullin et al., 2019; Tefferi and Barbui, 2023). Splanchnic vein thrombosis (Budd–Chiari syndrome, portal or mesenteric vein thrombosis) deserves particular vigilance — it is disproportionately associated with JAK2-mutated MPN, often in younger women, and may predate overt blood-count abnormalities (McMullin et al., 2019; De Stefano et al., 2018; Tefferi and Barbui, 2023).

3.3 Risk Stratification

The conventional thrombotic risk model in PV uses two variables — age over 60 years and history of thrombosis — to define 'high-risk' disease (one or both factors present) versus 'low-risk' (neither). High-risk disease generally requires cytoreductive therapy in addition to phlebotomy and aspirin; low-risk disease is treated with phlebotomy and aspirin alone, unless other indications for cytoreduction emerge (McMullin et al., 2019; Tefferi and Barbui, 2023).

More recent prognostic models incorporate cardiovascular risk factors, leukocytosis and JAK2 V617F allele burden for thrombosis risk. While these models have not yet replaced the conventional two-factor system in routine treatment decisions, they help to identify patients who may benefit from earlier consideration of cytoreductive therapy or clinical trial participation (McMullin et al., 2019; Tefferi and Barbui, 2023).

Risk factor	Definition	Implication
Age	>60 years	High-risk → cytoreduction
Prior thrombosis	Arterial or venous	High-risk → cytoreduction; consider anticoagulation if venous thromboembolism (VTE)
Cardiovascular risk factors	Hypertension, smoking, diabetes, hyperlipidaemia	Independent predictor of arterial thrombosis; optimise cardiovascular risk-factor management
Leukocytosis	WBC >11 × 10^9/L (some use >15)	Predicts venous thrombosis; may prompt cytoreduction
JAK2 V617F allele burden	Higher % linked to pruritus, fibrotic transformation	Not yet a routine treatment decision driver

Table 4. Variables used in thrombosis-risk stratification in polycythaemia vera, with the practical implication of each factor for treatment decisions. Sources: Barbui et al., 2015; Marchioli et al., 2013; McMullin et al., 2019; Tefferi and Barbui, 2023.

3.4 Treatment Strategies

The overarching goals of PV therapy are to prevent thrombosis (the dominant cause of early morbidity and mortality), control symptoms, and minimise the risk of fibrotic and leukaemic transformation. Treatment is built on three pillars: phlebotomy, low-dose aspirin and, where needed, cytoreduction, alongside management of the cardiovascular risk factors that compound thrombotic-risk (McMullin et al., 2019; Tefferi and Barbui, 2023).

Phlebotomy

*V*enesection remains the cornerstone of PV management. The CYTO-PV trial established a haematocrit target of <45%, demonstrating a substantial reduction in

cardiovascular death and major thrombosis compared with a target of 45–50% (Marchioli et al., 2013). Initial venesection of 450 mL (300 mL in smaller patients or those with cardiovascular risk) is typically performed weekly until target Hct is achieved, and then as needed — sometimes every 6-12 weeks for low-risk disease (McMullin et al., 2019).

Patients become iron-deficient with repeated venesection; iron restriction, not iron deficiency itself, is the intended mechanism and helps maintain Hct control. Iron supplementation is generally avoided; clinically significant symptoms of iron deficiency should prompt individual clinical assessment. Pre-procedure considerations include hydration status, concurrent anti-platelet therapy and venous access. Venesection should always be performed under trained clinical supervision, with monitoring for vasovagal reactions.

Nursing tip — venesection clinic

- Prior to each venesection, nurses should assess:
    - hydration status
    - blood pressure
    - previous vasovagal reactions
    - anticoagulant or antiplatelet medication
    - venous access
    - symptom burden
    - iron deficiency symptoms
    - anxiety
- Individualising patient preparation contributes to safer and more comfortable procedures.
- Use the largest gauge needle the patient can tolerate, adapting gauge, timing and monitoring to local protocol and individual factors such as frailty, cardiac disease and venous access (typically 16G–17G; 10–15 minutes) rather than as fixed universal standards.
- Monitor pulse, blood pressure and patient comfort throughout; keep the patient warm and offer fluids.
- Document the volume removed and monitor Hct at clinically appropriate intervals to guide venesection frequency.
- Educate that fatigue, headache and 'restless legs' often improve as Hct drops below 45%, but iron-deficiency-related symptoms (mild dyspnoea, hair shedding) can emerge from intentional iron restriction; these should still be assessed rather than dismissed automatically as a treatment failure. Vasovagal reactions (fainting, light-headedness) during or after venesection should be anticipated, especially with difficult venous access; ensure adequate hydration and consider fluid replacement where clinically appropriate.
- Following venesection, patients should receive advice regarding adequate oral hydration, temporary avoidance of strenuous physical activity if symptomatic, recognition of vasovagal symptoms and instructions regarding whom to contact if persistent bleeding or delayed complications occur.

Low-Dose Aspirin

All patients with PV should receive low-dose aspirin (75–100 mg daily) unless contraindicated. The ECLAP trial showed a significant reduction in non-fatal cardiovascular events without an increase in major bleeding (Landolfi et al., 2004). Dosing conventions vary internationally, e.g. 40–100 mg once daily in some countries.

Cytoreductive Therapy

First-line cytoreductive options for high-risk PV are hydroxycarbamide (also called hydroxyurea) and pegylated interferon alfa, including ropeginterferon alfa-2b. Hydroxycarbamide is well-established and inexpensive but is associated with skin side-effects (mucosal ulceration, leg ulcers, skin cancers — particularly squamous cell carcinoma in fair-skinned patients) and concerns about long-term leukaemogenicity in younger patients (Björkholm et al., 2011). Patients should be advised about sun protection and skin self-examination. If future fertility is a priority for the patient, an appropriate haematology and reproductive/obstetric specialist should be involved in discussions about treatment options before starting long-term cytoreductive therapy.

Ropeginterferon alfa-2b is a long-acting pegylated interferon licensed for PV without symptomatic splenomegaly. In the PROUD-PV/CONTINUATION-PV programme, the strict composite primary endpoint (haematological response with normal spleen size) at 12 months did not meet the pre-specified non-inferiority threshold against hydroxycarbamide; however, with longer follow-up, ropeginterferon achieved greater durable haematological response rates and significantly deeper molecular responses (reduction in JAK2 V617F allele burden) at 36 months (Gisslinger et al., 2020). Peginterferon alfa-2a is also widely used in PV, supported by phase 2/3 data (Yacoub et al., 2019; Kiladjian et al., 2016), though used off-label for this indication in most jurisdictions.

Common toxicities include flu-like symptoms (especially during titration), fatigue, transaminase elevation, mood disturbance and autoimmune phenomena.

JAK Inhibitors

Ruxolitinib is licensed for PV in patients who are resistant

or intolerant to hydroxycarbamide, on the basis of the RESPONSE and RESPONSE-2 trials, which demonstrated superior haematocrit control without phlebotomy, spleen volume reduction, and improvement in PV-associated symptoms (especially pruritus) compared with best available therapy (Vannucchi et al., 2015).

Common adverse effects include anaemia, thrombocytopenia, weight gain, hypertension, herpes zoster reactivation and an increased rate of non-melanoma skin cancer (NMSC) — the latter particularly relevant in patients with prior hydroxycarbamide exposure. Lipid profile can also be transiently elevated on ruxolitinib and should be checked at baseline and periodically.

Hepcidin Mimetics

Rusfertide is a novel injectable hepcidin-mimetic peptide that controls erythrocytosis by restricting iron availability for erythropoiesis, reducing or removing the need for phlebotomy. It received FDA approval for PV in August 2026 (as Mimrylo, following the VERIFY trial), representing a new treatment class distinct from cytoreduction and phlebotomy.

Drug	Place in PV therapy	Key nursing considerations
Phlebotomy	All patients; cornerstone for Hct control	Target Hct <45%; expect iron deficiency
Aspirin 75–100 mg	All patients unless contraindicated	Bleeding risk assessment; review with anticoagulants
Hydroxycarbamide	First-line cytoreduction in high-risk PV	Sun protection; annual skin checks; pregnancy contraindicated
Ropeginterferon alfa-2b	First-line alternative; may be preferred in younger patients and when future pregnancy is being considered.	Flu-like symptoms; mood; LFT and TFT monitoring
Ruxolitinib	Hydroxycarbamide-resistant/intolerant	Varicella-zoster virus (VZV) vaccination if possible; herpes zoster vigilance; gradual taper if stopping
Busulfan	Reserved for older patients when other options unsuitable	Late leukaemogenic risk; carefully titrated dose

Table 5. Drugs used in the management of polycythaemia vera: place in therapy and key nursing considerations across the treatment pathway. Across all agents in this table, active management of cardiovascular risk factors — smoking, blood pressure, lipids, glucose, weight — is an essential adjunct to drug therapy.
Sources: Björkholm et al., 2011; Gisslinger et al., 2020; Landolfi et al., 2004; Marchioli et al., 2013; McMullin et al., 2019; Tefferi and Barbui, 2023; Vannucchi et al., 2015.

Nursing Implications for Polycythaemia Vera

Across the PV pathway, nurses contribute to four interconnected areas: cardiovascular risk reduction, phlebotomy delivery, cytoreductive treatment safety, and longitudinal symptom management. Cardiovascular risk should be addressed at every visit — smoking cessation, blood pressure (BP), lipids, glucose and weight. Symptom monitoring with the MPN-SAF (MPN10) at baseline and at clinically appropriate follow-up intervals makes treatment effects measurable and visible to the patient. Pruritus is often under-reported; ask about it routinely and manage it in steps (skin care, selective serotonin reuptake inhibitors (SSRIs), narrow-band ultraviolet B (UVB) and JAK inhibitor consideration).

Nurses play a central role in supporting patients throughout the chronic disease trajectory by combining clinical assessment with patient education, symptom management and coordination of multidisciplinary care. As patients with PV often remain under follow-up for decades, continuity of nursing care is essential to optimise treatment adherence, quality of life and early recognition of disease progression.

What should the haematology nurse assess at every outpatient visit?

At every follow-up consultation, the haematology nurse should perform a structured assessment that complements laboratory and medical evaluation. Particular attention should be paid to changes since the previous visit.

Clinical assessment:

- General condition and performance status (e.g. ECOG)
- Fatigue and its impact on daily activities
- Weight changes
- New constitutional symptoms (night sweats, fever, weight loss)
- Symptom burden using the MPN-SAF (or local validated assessment tool where available)

Disease-related symptoms:

- Headache, dizziness or visual disturbances
- Aquagenic pruritus or other skin symptoms
- Microvascular symptoms (erythromelalgia, paraesthesia)
- Bone pain
- Abdominal discomfort or early satiety suggestive of splenomegaly
- New or worsening bleeding or bruising
- Signs or symptoms suggestive of thrombosis

Treatment assessment:

- Medication adherence
- Adverse events related to treatment
- Tolerance of venesection (where applicable)
- Patient concerns regarding current therapy
- Need for reinforcement of treatment information or additional education

Cardiovascular and lifestyle assessment:

- Smoking status
- Blood pressure (according to local practice)
- Physical activity
- Hydration
- Cardiovascular risk factor management
- Vaccination status where appropriate

Psychosocial assessment:

- Anxiety or emotional distress
- Coping with chronic disease
- Family and caregiver support
- Employment and financial concerns
- Health literacy and educational needs

Patient education

Reinforce:

- recognition of thrombotic and bleeding symptoms
- importance of treatment adherence
- when to contact the haematology team
- healthy lifestyle measures
- upcoming investigations and treatment plan

Escalation

Immediately inform the treating haematologist if the patient reports:

- new neurological symptoms
- chest pain or dyspnoea
- suspected thrombosis or significant bleeding
- rapidly worsening constitutional symptoms
- progressive splenic discomfort
- signs of infection or unexplained fever
- any sudden clinical deterioration

PV in Pregnancy

Pregnancy in PV, as in ET, is high-risk for both maternal thrombosis and adverse fetal outcomes and requires structured pre-conception planning.

A specialist haematology and obstetric team should be involved in all treatment decisions — both before conception and throughout pregnancy. Nurses should ensure patients are aware of the importance of raising pregnancy plans early with their haematology team so that specialist referral can be arranged.

Care should be multidisciplinary — jointly led by obstetrics and haematology — with early plans for monitoring fetal growth and timing of delivery.

Key Nursing Take-Home Messages	
1	Maintaining haematocrit below 45% is a central treatment goal in PV and reduces the risk of cardiovascular and thrombotic events.
2	Venesection remains a cornerstone of treatment and requires regular monitoring of haematocrit, symptoms and tolerance.
3	Low-dose aspirin is commonly used for thrombosis prevention unless contraindicated; adherence and bleeding risk should be reviewed regularly.
4	Cytoreductive therapy may be required according to thrombotic risk, age, disease characteristics, symptoms and treatment tolerance.
5	Nurses should assess for signs and symptoms of both arterial and venous thrombosis at every appropriate patient contact.
6	Cardiovascular risk factors — including smoking, hypertension, diabetes, obesity and dyslipidaemia — should be identified and addressed as part of routine care.
7	Aquagenic pruritus, fatigue, microvascular symptoms and other disease-related symptoms can significantly affect quality of life and should be assessed systematically.
8	Patients receiving long-term hydroxycarbamide require education about skin protection, skin changes and appropriate dermatological surveillance.
9	Patient education should reinforce treatment adherence, recognition of thrombotic and bleeding symptoms, and when to seek urgent medical attention.
10	Regular assessment of symptom burden, treatment tolerance and patient priorities supports individualised, person-centred PV care.
Patient Education	
1	Explain that venesection 'thins' the blood by removing red cells and lowers the risk of stroke and clots — it is one of the most important treatments in PV.
2	Explain that iron deficiency may develop as an intended consequence of repeated venesection; iron supplements or multivitamins containing iron should not be taken unless advised by the haematology team.
3	Stress that patients should take aspirin every day and not stop (for example before a dental procedure) without speaking to the haematology team.
4	During each follow-up consultation, nurses should assess medication adherence, adverse events, patient concerns and potential barriers to treatment. Particular attention should be given to adherence to antiplatelet therapy and cytoreductive treatment.
5	Advise regular skin self-checks, sun protection (SPF 30+, hats) and an annual skin review for patients on long-term hydroxycarbamide, because of the small increased risk of non-melanoma skin cancer.
6	Strongly advise patients to seek urgent medical help for new severe headache, chest pain, shortness of breath, leg swelling, slurred speech or sudden visual disturbance — these may signal thrombosis.

Multidisciplinary Collaboration

- haematologists
- pharmacists
- general practitioners
- cardiologists
- psychologists
- physiotherapists
- dietitians
- social workers

Red Flag Symptoms Requiring Immediate Medical Review

- acute neurological symptoms
- chest pain
- sudden dyspnoea
- unilateral leg swelling
- severe visual disturbances
- uncontrolled bleeding
- persistent fever
- rapidly progressive constitutional symptoms
- sudden severe abdominal pain should also prompt urgent assessment for splanchnic vein thrombosis, and unilateral weakness, facial droop or difficulty speaking should be treated as a possible stroke (FAST assessment) even in younger patients.

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Quick Facts

- Risk is stratified using the Revised IPSET-Thrombosis model, which incorporates age, history of thrombosis and JAK2 mutation status. Cardiovascular risk factors should also be assessed as part of the overall clinical evaluation.
- Essential thrombocythaemia (ET) is the most common classical MPN
- Driver mutation status (JAK2 V617F ~60–65%, CALR ~20–25%, MPL ~3 4%, triple-negative ~10–15%) can shape phenotype, thrombosis risk and prognosis.
- Low-dose aspirin is considered according to thrombotic and bleeding risk (assess for acquired von Willebrand syndrome before starting in extreme thrombocytosis; twice-daily dosing is a specialist decision). High-risk disease receives cytoreduction — hydroxycarbamide first-line, anagrelide and pegylated interferon as alternatives. Pegylated interferon, including ropeginterferon alfa-2b, is increasingly used first-line alongside hydroxycarbamide, particularly in younger patients or those planning pregnancy.
- Bleeding can complicate very high platelet counts (>1500 × 109/L) through acquired von Willebrand syndrome; pregnancy in ET is high-risk and requires structured pre-conception planning. A specialist haematology and obstetric team should be involved in treatment decisions. This risk applies across all three MPNs, not ET alone; the same pre-conception planning principles apply equally to PV (see Module III).

Module IV: Essential Thrombocythaemia (ET)

Contents:

A. Diagnostic Criteria
B. Clinical Presentation
C. Risk Stratification
D. Treatment Approaches
E. Nursing Implications and Pregnancy
F. References

Learning Objective

By the end of this module, you will be able to explain the risk stratification, thrombotic and haemorrhagic complications, and treatment approach in essential thrombocythaemia, and identify nursing priorities for monitoring and patient education.

4.1 Diagnostic Criteria

Essential thrombocythaemia is a JAK2-, CALR- or MPL-mutated MPN characterised by sustained thrombocytosis and proliferation of mature, large megakaryocytes in the bone marrow. WHO 5th edition and ICC 2022 share four major and one minor diagnostic criterion. ET diagnosis requires meeting all four major criteria, or the first three major criteria plus the minor criterion (Arber et al., 2022; Khoury et al., 2022; Tefferi and Barbui, 2024).

Essential thrombocythaemia (ET) — ICC 2022 Diagnostic Criteria

Major criteria

1. Platelet count ≥450 × 10^9/L
2. Bone marrow biopsy showing proliferation mainly of the megakaryocytic lineage, with increased numbers of enlarged, mature megakaryocytes with hyperlobulated staghorn-like nuclei, infrequently dense clusters*; no significant increase or left shift in neutrophil granulopoiesis or erythropoiesis; no relevant BM fibrosis†
3. Diagnostic criteria for BCR::ABL1-positive CML, PV, PMF, or other myeloid neoplasms are not met
4. JAK2, CALR, or MPL mutation‡

Minor criteria

Presence of a clonal marker§ or absence of evidence of reactive thrombocytosisII

Diagnosis: All major criteria OR first 3 major + minor criteria

Post-ET myelofibrosis (post-ET MF) — ICC 2022 Diagnostic Criteria

Required criteria

1. Previous established diagnosis of ET
2. Bone marrow fibrosis of grade 2 or 3

Additional criteria (≥2 required)

1. Anemia and >2 g/dL decrease from baseline
2. Leukoerythroblastosis
3. Increase in palpable splenomegaly >5 cm from baseline or new
4. Elevated LDH above reference range
5. Development of any 2 (or all 3) constitutional symptoms: >10% weight loss in 6 mo, night sweats, unexplained fever (>37.5°C)

* Three or more megakaryocytes lying adjacent without other BM cells in between; in most of these rare clusters ≤6 megakaryocytes may be observed, increase in huge clusters (>6 cells) accompanied by granulocytic proliferation is a morphological hallmark of pre-PMF.

† Very rarely a minor increase in reticulin fibers may occur at initial diagnosis (grade 1).

‡ It is recommended to use highly sensitive assays for JAK2 V617F (sensitivity level <1%) and CALR and MPL (sensitivity level 1% to 3%); in negative cases, consider a search for noncanonical JAK2 and MPL mutations.

§ Assessed by cytogenetics or sensitive NGS techniques.

II Reactive causes of thrombocytosis include a variety of underlying conditions like iron deficiency, chronic infection, chronic inflammatory disease, medication, neoplasia, or history of splenectomy.

Figure 4. ICC 2022 diagnostic criteria for essential thrombocythaemia (ET) and post-ET myelofibrosis.
Source: Arber DA, Orazi A, Hasserjian RP, et al, 2022.

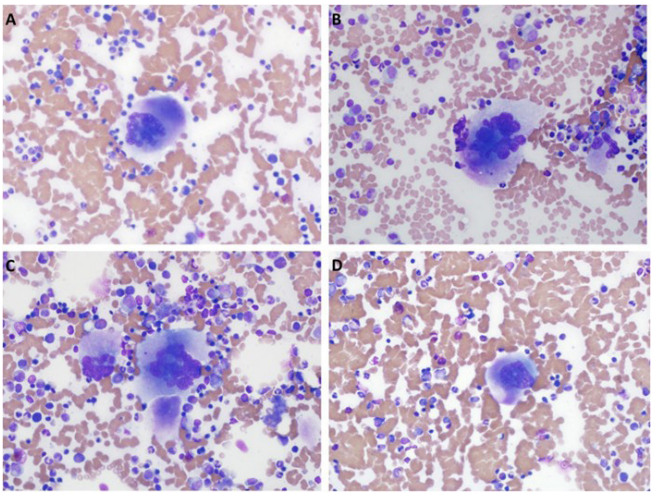


Figure 5. Wright-Giemsa staining of the aspirate demonstrates trilineage hematopoiesis with abnormal megakaryocytes. (A–C) Frequent large and hyperlobated megakaryocytes are present some of which have a vaguely "staghorn-appearing nuclei" (original magnification, 400). (D) Occasional hypolobated megakaryocytes are appreciated (original magnification, 400). Source: Danielson, D.T. and Muir, J.M. (2025) Educational case: essential thrombocythemia. Academic Pathology, 12(1), 100167. CC BY 4.0.

Reactive thrombocytosis should be ruled out — common causes include iron deficiency, infection, inflammation, malignancy, splenectomy/hyposplenism, severe blood loss, recent surgery and rebound after marrow recovery. CRP, ferritin, infection screen and clinical context are important (Harrison et al., 2010).

4.2 Clinical Presentation

Median age at diagnosis is ~60 years (Tefferi and Barbui, 2024).

Presentation varies from incidental thrombocytosis on a routine blood test to vasomotor symptoms (headaches, dizziness, visual disturbance, paraesthesiae, erythromelalgia), thrombosis (arterial more often than venous, including atypical sites such as splanchnic veins), or, paradoxically, bleeding — particularly with platelets >1500 × 10^9/L due to acquired von Willebrand syndrome (acquired vWS, secondary to depletion of large von Willebrand factor (vWF) multimers) (Harrison et al., 2010).

Driver mutation status can influence phenotype: JAK2 V617F-mutated patients tend to have higher haemoglobin, leukocytosis and a greater risk of thrombosis; CALR-mutated patients may have higher platelet counts but a lower thrombosis risk; MPL-mutated patients are older and have a higher rate of fibrotic transformation (Tefferi and Barbui, 2024).

Although many patients with ET remain asymptomatic, nurses should actively assess for symptoms that may indicate microvascular disturbances or evolving disease. Patients often underestimate these symptoms unless specifically asked. Assess:

- headache
- dizziness
- visual disturbances
- tinnitus
- erythromelalgia
- paraesthesia
- concentration difficulties
- fatigue
- pruritus
- constitutional symptoms

4.3 Risk Stratification

A widely used thrombosis model is the Revised International Prognostic Score for ET-Thrombosis (Revised IPSET-Thrombosis), which uses age, prior thrombosis and JAK2 mutation status to assign patients to one of four revised risk categories, with cardiovascular risk factors considered separately (Barbui et al., 2015). This score can inform first-line treatment decisions.

Survival is generally favourable in ET — median is approximately 18–20 years overall (Tefferi and Barbui, 2024) — but the International Prognostic Score for ET (IPSET, for survival) and the Mutation-Enhanced IPSS for ET (MIPSS-ET, integrating SF3B1 and SRSF2) refine survival prediction. Adverse cytogenetics and HMR mutations can help identify patients at higher risk of fibrotic or leukaemic transformation; these patients may warrant closer follow-up and earlier consideration of clinical trials or interferon therapy (Tefferi and Barbui, 2024). This reflects ET's older average age at diagnosis and generally more indolent course, rather than a worse underlying biology than PV; both diseases carry near-normal life expectancy in younger, low-risk patients. HMR mutations are described in Module I, section 1.3.

4.4 Treatment Approaches

Treatment of ET has the same dual goals as PV: prevent thrombosis and bleeding, and control symptoms. Cardiovascular risk factor management — blood pressure, lipids, smoking, glucose — remains a cornerstone. Pharmacological options are tiered to thrombosis risk:

- Low-dose aspirin (75–100 mg daily) is recommended for low-risk JAK2-mutated patients. Once-daily aspirin is recommended when CALR-1/MPL mutations or CV risk factors are present in very low-risk disease (Tefferi and Barbui, 2024).
- Hydroxycarbamide is the first-line cytoreductive agent for high-risk ET. The PT-1 trial demonstrated superiority of hydroxycarbamide plus aspirin over anagrelide plus aspirin for the prevention of arterial thrombosis, although venous thrombosis was lower with anagrelide (Harrison et al., 2005). Genotype-stratified analyses suggest this benefit is concentrated in JAK2 V617F-positive patients, with a less clear advantage in CALR-mutated ET.
- Anagrelide is an alternative or second-line agent, particularly for patients intolerant of hydroxycarbamide, with selective platelet-lowering activity. Adverse effects include headache, palpitations, fluid retention and (uncommonly) cardiomyopathy; an electrocardiogram (ECG) and cardiac history should precede initiation (Birgegård et al., 2018; Harrison et al., 2005).
- Pegylated interferon alfa (including ropeginterferon alfa-2b) is increasingly used as a disease-modifying option — noting that ropeginterferon alfa-2b's licensed European indication is PV without symptomatic splenomegaly, so use in ET may be off-label depending on country/date, and availability, licensing and pregnancy recommendations for any interferon formulation should be checked against Swissmedic/EMA and national guidance, particularly in younger patients, those planning pregnancy, and those with intolerance to hydroxycarbamide. Recent data show durable haematological responses and reductions in JAK2 V617F allele burden (Yacoub et al., 2019).
- Anticoagulation is added in patients with documented venous thrombosis, with the duration and intensity individualised to the bleeding risk.

Nursing Implications for Essential Thrombocythaemia

Nurses are central to the lifelong management of ET. Key contributions include patient education on the nature of the diagnosis; addressing cardiovascular risk; advising on medication safety (especially hydroxycarbamide adherence and skin protection); recognition of thrombosis and bleeding emergencies; and supporting patients before and during pregnancy.

Nursing Assessment

In addition to thrombotic complications, nurses should routinely assess for signs and symptoms of both minor and major bleeding, particularly in patients with extreme thrombocytosis or those receiving antiplatelet or anticoagulant therapy.

Routine assessment should include:

- epistaxis
- gingival bleeding
- easy bruising
- prolonged bleeding from minor wounds
- gastrointestinal bleeding
- heavy menstrual bleeding
- patient concerns regarding bleeding during daily activities

Patients should be educated to report any new or worsening bleeding promptly, particularly before invasive procedures or dental treatment.

Haematology nurses also play an essential role in longitudinal patient assessment, recognising subtle changes in symptom burden and functional status that may indicate evolving disease or treatment-related complications. As patients with essential thrombocythaemia are often followed for many years, each consultation should provide an opportunity to reassess symptoms, reinforce patient education, evaluate treatment adherence and support shared decision-making. A holistic nursing assessment should integrate physical symptoms, psychosocial wellbeing, cardiovascular risk factors and individual patient concerns to optimise long-term outcomes.

ET in pregnancy

Pregnancy in ET is high-risk for both maternal thrombosis and adverse fetal outcomes (early loss, IUGR, placental insufficiency, preterm delivery).

A specialist haematology and obstetric team should be involved in treatment decisions, both before conception and throughout pregnancy. Nurses should ensure patients are aware of the importance of raising pregnancy plans early with their haematology team so that specialist referral can be arranged.

Care should be multidisciplinary — jointly led by obstetrics and haematology — with early plans for monitoring fetal growth and timing of delivery.

Drug	Place in therapy	Common side effects	Monitoring
Aspirin 75–100 mg See 3.4 for a note on international dosing variation.	All except very-low-risk; symptom relief	GI upset, bruising, bleeding	Bleeding history, vWF if very high platelets
Hydroxycarbamide	First-line high-risk	Cytopenias, mucositis, leg/skin ulcers, skin cancer, oligospermia	FBC according to treatment phase and local guidance, LFTs, U&E, skin checks
Anagrelide	Hydroxycarbamide-intolerant or platelet-selective need	Headache, palpitations, fluid retention, cardiomyopathy, anaemia	Baseline ECG, BP, cardiac symptoms
Pegylated interferon / ropeginterferon	Younger patients may be considered when future pregnancy is planned, according to formulation-specific and national guidance	Flu-like symptoms, fatigue, mood, autoimmune phenomena	TFTs, LFTs, mood screen, FBC
Anticoagulation	Following venous thrombosis	Bleeding	Site/duration individualised; review at flares of thrombocytosis

Table 7. Pharmacological options in essential thrombocythaemia: place in therapy, common side effects and the corresponding monitoring requirements.
Sources: Barbui et al., 2015; Birgegård et al., 2018; Harrison et al., 2005; Tefferi and Barbui, 2024; Yacoub et al., 2019.

Key Nursing Take-Home Messages	
1	ET is the most common classical MPN; about half of patients are diagnosed incidentally.
2	Driver mutation status (JAK2 vs. CALR vs. MPL) shapes both phenotype and risk.
3	Use Revised IPSET-Thrombosis to inform first-line therapy; aspirin for most patients and cytoreduction for high-risk disease.
4	Bleeding can complicate very high platelet counts (>1500 × 10^9/L) due to acquired von Willebrand syndrome.
5	Pregnancy planning should begin pre-conception; nurses are well placed to identify and refer patients early.
Patient Education	
1	Explain that ET is a chronic, generally indolent condition and that many patients, particularly those with lower-risk disease, have a favourable long-term outlook.
2	Advise patients to inform both their surgical and haematology teams of any planned procedure in advance, as cytoreductive medication and aspirin may need to be paused and thromboprophylaxis planned.
3	Explain that the driver mutations identified in ET are usually acquired rather than inherited, and routine genetic testing of family members is generally not required.
4	Highlight that very high platelet counts can paradoxically cause bleeding (not just clotting); unusual bruising, nosebleeds or heavy periods should be reported.
5	Emphasise the importance of taking aspirin and/or cytoreductive medication as prescribed and of discussing any interruption or discontinuation with the haematology team.
6	Encourage women of childbearing age to speak to their team BEFORE trying to conceive — pregnancy in ET is high-risk and requires early specialist involvement. A specialist haematology and obstetric team should be involved in pre-conception planning. This applies to male patients too, as some treatments may affect fertility.
7	Reinforce cardiovascular risk reduction: not smoking, healthy blood pressure, managing cholesterol and maintaining a healthy weight all lower thrombosis risk in ET.

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Quick Facts

- Myelofibrosis (primary or secondary to PV or ET) is associated with a substantial clinical and symptom burden; cytokine-driven symptoms — fatigue, weight loss, sweats, bone pain — often dominate the patient experience.
- Risk stratification uses DIPSS or DIPSS-plus for baseline, MIPSS70+v2.0 for transplant-eligible patients, MYSEC-PM for post-PV/ET MF and GIPSS where clinical variables are uncertain.
- Allogeneic haematopoietic stem cell transplantation remains the only curative therapy and should be considered in eligible patients with higher-risk disease; specific eligibility criteria are discussed in Section 5.3.
- Nursing care can span observation, transfusion support, infection vigilance on JAK inhibitors, transplant pathway co-ordination and advance-care planning for those who progress.
- Pregnancy in myelofibrosis is rare and carries high risk for both mother and baby; women of childbearing age who are considering pregnancy should be referred to a specialist haematology and obstetric input for pre-conception guidance and ongoing multidisciplinary management.

Contents:

A. Pathophysiology
B. Clinical Features
C. Risk Stratification Scores
D. Treatment Options
   a. Observation and supportive care
   b. JAK inhibitors
   c. Allogeneic stem cell transplantation
   d. Anaemia-directed therapy
   e. Splenectomy and radiotherapy
   f. Emerging agents
E. Nursing Implications and Key Take-Home Messages
F. References

Note: 'Myelofibrosis' encompasses primary myelofibrosis (PMF) — both pre-fibrotic and overt — and secondary (post-PV / post-ET) myelofibrosis. Most management principles apply across these entities, although prognostic models differ. This module addresses all three forms collectively unless specified.

Learning Objective

By the end of this module, you will be able to describe the clinical features, prognostic scoring and treatment options for primary myelofibrosis, including the nursing management of disease-related symptoms and treatment side effects.

Pre-fibrotic primary myelofibrosis (pre-PMF) — ICC 2022 Diagnostic Criteria

Major criteria

1. Bone marrow biopsy showing megakaryocytic proliferation and atypia,* bone marrow fibrosis grade <2, increased age-adjusted BM cellularity, granulocytic proliferation, and (often) decreased erythropoiesis
2. JAK2, CALR, or MPL mutation† or presence of another clonal marker‡ or absence of reactive bone marrow reticulin fibrosis§
3. Diagnostic criteria for BCR::ABL1-positive CML, PV, ET, myelodysplastic syndromes, or other myeloid neoplasms are not met

Minor criteria

Anemia not attributed to comorbid condition

Leukocytosis ≥11 × 10^9/L

Palpable splenomegaly

LDH level above reference range

Overt primary myelofibrosis (overt PMF) — ICC 2022 Diagnostic Criteria

Major criteria

1. Bone marrow biopsy showing megakaryocytic proliferation and atypia,* accompanied by reticulin and/or collagen fibrosis grades 2 or 3
2. JAK2, CALR, or MPL mutation† or presence of another clonal marker‡ or absence of reactive myelofibrosis§
3. Diagnostic criteria for ET, PV, BCR::ABL1-positive CML, myelodysplastic syndrome, or other myeloid neoplasms‖ are not met

Minor criteria

Anemia not attributed to comorbid condition

Leukocytosis ≥11 × 10^9/L

Palpable splenomegaly

LDH level above reference range

Leukoerythroblastosis

Diagnosis: All 3 major criteria and at least 1 minor criterion confirmed in 2 consecutive determinations

* Morphology of megakaryocytes in pre-PMF and overt PMF usually demonstrates a higher degree of megakaryocytic atypia than in any other MPN subtype; distinctive features of megakaryocytes include small to giant megakaryocytes with a prevalence of severe maturation defects (cloud-like, hypolobulated, and hyperchromatic nuclei) and presence of abnormal large dense clusters (mostly >6 megakaryocytes lying strictly adjacent).

† It is recommended to use highly sensitive assays for JAK2 V617F (sensitivity level <1%) and CALR and MPL (sensitivity level 1% to 3%); in negative cases, consider searching for noncanonical JAK2 and MPL mutations.

‡ Assessed by cytogenetics or sensitive NGS techniques; detection of mutations associated with myeloid neoplasms (eg, ASXL1, EZH2, IDH1, IDH2, SF3B1, SRSF2, and TET2 mutations) supports the clonal nature of the disease.

§ Minimal reticulin fibrosis (grade 1) secondary to infection, autoimmune disorder or other chronic inflammatory conditions, hairy cell leukemia or another lymphoid neoplasm, metastatic malignancy, or toxic (chronic) myelopathies.

‖ Monocytosis can be present at diagnosis or develop during the course of PMF; in these cases, a history of MPN excludes CMML, whereas a higher variant allelic frequency for MPN-associated driver mutations is supporting the diagnosis of PMF with monocytosis rather than CMML.

Adapted from: Arber DA, Orazi A, Hasserjian RP, et al. (2022) 'International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical, and genomic data', Blood, 140(11), pp. 1200–1228. © 2022 The Author(s). Published by American Society of Hematology. Open access.

Figure 6. ICC 2022 diagnostic criteria for pre-fibrotic and overt primary myelofibrosis (PMF).
Source: Arber DA, Orazi A, Hasserjian RP, et al, 2022.

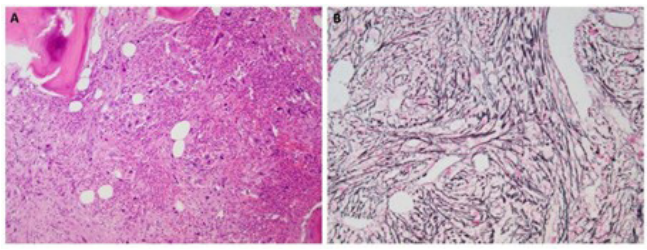


Figure 7. Bone marrow biopsy in primary myelofibrosis. (A) Haematoxylin and eosin stain showing megakaryocytic hyperplasia with large hyperlobulated and hyperchromatic forms (×100). (B) Reticulin stain demonstrating marked fibrosis (grade 3 of 3).

Source: Shao, R., Ryder, C., Wang, L. et al. (2025) A review of the pathological and molecular diagnosis of primary myelofibrosis. Cancers (Basel). © 2025 The Authors. CC BY 4.0.

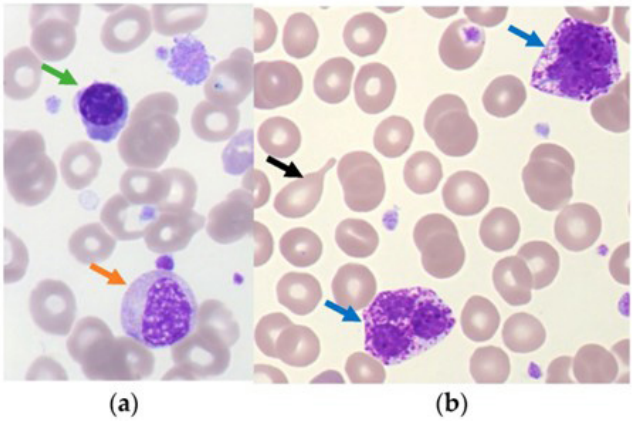


Figure 8. Peripheral blood smear in myelofibrosis showing leukoerythroblastosis: teardrop-shaped erythrocytes (dacrocytes), nucleated red cells, and immature granulocytic cells (×50).

Source : Combaluzier, B. et al. (2023) Cytological diagnosis of classic myeloproliferative neoplasms. Cells, 12(6), 946. © 2023 The Authors. CC BY 3.0.

5.1 Pathophysiology

Myelofibrosis arises from clonal proliferation of an abnormal haematopoietic stem cell carrying one of the three driver mutations (JAK2 V617F, CALR or MPL) in approximately 90% of patients. The remainder are 'triple-negative', often with a more aggressive course and a higher rate of leukaemic transformation (McLornan et al., 2024a; Tefferi, 2023).

Constitutive activation of JAK–STAT signalling drives megakaryocytic hyperplasia and clonal expansion, with secondary release of pro-inflammatory and pro-fibrotic cytokines — transforming growth factor beta (TGF-β), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), tumour necrosis factor alpha (TNF-α), and interleukins 6 and 8 (IL-6, IL-8) (Rampal et al., 2014).

These cytokines provoke a stromal response: marrow stromal cells deposit reticulin and collagen, leading to progressive marrow failure, leukoerythroblastosis (immature granulocytic and erythroid forms in the peripheral blood, with teardrop erythrocytes), and extramedullary haematopoiesis — most prominently in the spleen, but also in the liver, retroperitoneum, paravertebral regions, lung and skin (McLornan et al., 2024a; Tefferi, 2023). The same cytokine milieu drives the hallmark constitutional symptoms — fatigue, weight loss, drenching sweats, pruritus, bone pain.

High-molecular-risk (HMR) co-mutations — ASXL1, EZH2, IDH1/2, SRSF2 and U2AF1 Q157 — shorten survival, increase the risk of leukaemic transformation and influence treatment decisions, including the timing of allogeneic transplantation (Tefferi et al., 2018). TP53 and RAS-pathway mutations are associated with particularly adverse disease features and outcomes.

5.2 Clinical Features

Clinical presentation is heterogeneous. Some patients are asymptomatic at diagnosis with abnormal blood counts on routine testing; others present with symptomatic splenomegaly, fatigue, weight loss, drenching sweats, bone pain, pruritus, anaemia or thrombosis (McLornan et al., 2024a; Tefferi, 2023). Pre-fibrotic PMF can mimic ET clinically and is often characterised by isolated thrombocytosis with subtle marrow morphology — its recognition is important because survival and risk of fibrotic and leukaemic transformation are inferior to those of true ET.

Splenomegaly is present in around 80% of patients with overt PMF; it can cause early satiety, abdominal discomfort, and (rarely) splenic infarction. Anaemia is the dominant cytopenia, with around 25–40% of patients transfusion-dependent at presentation; thrombocytopenia and leukopenia develop with advancing disease and confer poorer prognosis (McLornan et al., 2024a; Tefferi, 2023; Gerds et al., 2024).

Symptom burden in MF is among the highest in MPNs. The MPN-SAF Total Symptom Score (MPN10) regularly demonstrates substantial impairment of quality of life,

with fatigue, early satiety, abdominal discomfort and itching the dominant complaints (McLornan et al., 2024a; Emanuel et al., 2012). Symptom burden does not always track with conventional disease severity scores and should be monitored independently.

Nursing Assessment of Symptom Burden

Primary myelofibrosis is associated with one of the highest symptom burdens among the classical myeloproliferative neoplasms. Nurses should perform structured symptom assessments at baseline and throughout follow-up using validated patient-reported outcome measures where available. Symptom assessment should complement laboratory findings and imaging, as disease burden is often underestimated when relying solely on clinical parameters.

Routine nursing assessment should include:

- Fatigue
- Night sweats
- Fever
- Weight loss
- Pruritus
- Bone pain
- Abdominal discomfort
- Early satiety
- Reduced exercise tolerance
- Sleep disturbance
- Emotional wellbeing
- Overall quality of life

Patient-reported symptom burden using the MPN-SAF Total Symptom Score (MPN-SAF TSS), where available.

5.3 Risk Stratification Scores

Risk stratification in MF has matured over the last decade from simple clinical scores to integrated clinical–cytogenetic–molecular models. Choice of score depends on the disease type (PMF vs. post-PV/ET MF) and on whether transplant decision-making is in view (Passamonti et al., 2017; Tefferi et al., 2018).

In UK practice (McLornan et al., 2024a), DIPSS or DIPSS-plus is acceptable as a baseline score, but MIPSS70+v2.0 should be used in transplant-eligible patients.

The European LeukemiaNet (ELN) and European Society for Blood and Marrow Transplantation (EBMT) jointly recommend that all patients with intermediate-2 or high-risk disease aged ≤70 years be considered potential transplant candidates; intermediate-1 patients <65 years with refractory transfusion-dependent anaemia, peripheral blasts >2%, adverse cytogenetics, triple-negative or ASXL1-mutated status should also be considered (McLornan et al., 2024a; Kröger et al., 2024; Tefferi et al., 2018).

Score	Population	Inputs	Use
International Prognostic Scoring System (IPSS)	PMF at diagnosis	Age >65, constitutional symptoms, haemoglobin (Hb) <10 g/dL, white blood cell (WBC) count >25 × 10^9/L, blasts ≥1%	Historic baseline; superseded for treatment decisions
Dynamic IPSS (DIPSS) / DIPSS-plus	PMF, dynamic (any time-point)	Same as IPSS; plus platelets <100, transfusion need, unfavourable karyotype (DIPSS-plus)	Widely used; available without molecular data
Mutation-enhanced IPSS for transplant-age patients (MIPSS70) / MIPSS70+ version 2.0	PMF, transplant-age	Clinical + cytogenetic + HMR mutations + driver type	Preferred for transplant decision-making
Genetics-only IPSS (GIPSS)	PMF, genetics-only	Karyotype + driver type + HMR mutations	Useful when clinical variables are uncertain
Myelofibrosis Secondary to PV/ET Prognostic Model (MYSEC-PM)	Post-PV / post-ET MF	Age, Hb, platelets, blasts, constitutional symptoms, CALR status	Disease-specific prognostic model for post-PV/post-ET MF
Myelofibrosis Transplant Scoring System (MTSS) / Response to Ruxolitinib at 6 months (RR6)	Transplant outcome / on-treatment risk	Pre-transplant or on-ruxolitinib variables	Adjuncts for transplant timing and JAK inhibitor response monitoring

Table 8. Prognostic scoring systems available for primary and secondary myelofibrosis, summarising the target population, the input variables and the typical use case for each model in current clinical practice.
Sources: Gagelmann et al., 2019; Kröger et al., 2024; McLornan et al., 2024a; Passamonti et al., 2017; Tefferi, 2023; Tefferi et al., 2018.

Nursing Assessment

Anaemia should be assessed from both a laboratory and patient-centred perspective. Haemoglobin values should always be interpreted alongside the patient's symptoms, functional status and overall quality of life, as the clinical impact of anaemia varies considerably between individuals.

During each outpatient visit, nurses should assess:

- fatigue and its impact on activities of daily living
- dyspnoea on exertion or at rest
- dizziness or light-headedness
- palpitations
- reduced physical activity
- cognitive difficulties or reduced concentration
- falls risk, particularly in older adults
- need for supportive interventions, including transfusion support

Nursing assessment should also evaluate how anaemia affects the patient's independence, employment, emotional wellbeing and ability to participate in daily activities.

5.4 Treatment Options

Allogeneic transplantation remains the only curative option but is feasible only in a minority. JAK inhibitors form the backbone of disease control for the majority of patients, with supportive care and disease-modifying agents (interferon in some early-phase cases) as adjuncts (Gotlib, 2025; McLornan et al., 2024b).

Observation and supportive care

Asymptomatic, low-risk patients can be observed with attention to symptom burden, blood counts, cardiovascular risk and screening for transformation.

JAK inhibitors

Four JAK inhibitors are now licensed across different indications within MF, each with distinct positioning. The choice between them is increasingly driven by platelet count and the dominant clinical problem. Availability varies by country — for example, pacritinib is not currently licensed in the UK/EU

Ruxolitinib remains the most widely used agent. The COMFORT-I and -II studies demonstrated meaningful spleen volume reduction (≥35% at 24 weeks) and symptom improvement, with a survival benefit in pooled analyses (Harrison et al., 2012; Verstovsek et al., 2012). Anaemia and thrombocytopenia are the main early toxicities; rebound flares (rapid recurrence of symptoms and splenomegaly, sometimes a SIRS-like picture) can follow abrupt discontinuation, so tapering is recommended.

Fedratinib is licensed for newly diagnosed and post-ruxolitinib patients, with JAKARTA and JAKARTA-2 supporting its activity. Wernicke-encephalopathy concern from early studies translates clinically into pre-treatment thiamine measurement, supplementation if low, and clinical vigilance (McLornan et al., 2024b; Pardanani et

Agent	Indication / dosing	Strengths	Watch-outs
Ruxolitinib	Intermediate-2 / high-risk MF; symptomatic splenomegaly. Dose by platelets (5–25 mg BD)	Robust spleen and symptom responses (COMFORT-I/II); widely used first-line option	Anaemia, thrombocytopenia, herpes zoster, NMSC; rebound on abrupt withdrawal
Fedratinib	First- or second-line; 400 mg OD if platelets ≥50 × 10^9/L	Effective post-ruxolitinib (JAKARTA-2)	GI toxicity (anti-emetic prophylaxis); thiamine monitoring (Wernicke risk)
Pacritinib	Platelets <50 × 10^9/L; 200 mg BD	Active in severe thrombocytopenia (PERSIST-2, PACIFICA)	GI toxicity; QT prolongation; cardiac monitoring
Momelotinib	MF with anaemia (transfusion-dependent or symptomatic); 200 mg OD	Spleen + symptom + anaemia benefit (MOMENTUM, SIMPLIFY)	Peripheral neuropathy; HBV reactivation risk; infection vigilance

Table 9. Comparison of the four licensed JAK inhibitors used in the management of myelofibrosis: licensed indication and dosing, principal strengths from the pivotal trial programmes and clinical watch-outs to flag during monitoring.
Sources: Harrison et al., 2012; Mascarenhas et al., 2018; McLornan et al., 2024b; Mesa et al., 2017; Pardanani et al., 2015; Verstovsek et al., 2012; Verstovsek et al., 2023.

al., 2015). Gastrointestinal toxicity (nausea, vomiting, diarrhoea) is common with fedratinib, particularly during the first weeks; prophylactic antiemetics and dose modification should be considered proactively.

Pacritinib is specifically positioned for patients with platelets <50 × 10^9/L, where ruxolitinib and fedratinib may be limited by haematological toxicity. The PERSIST-2 study showed both spleen and symptom benefit in this previously under-served group (Mascarenhas et al., 2018).

Momelotinib has a distinctive activity profile combining spleen and symptom benefit with improvement in anaemia, attributed to suppression of ACVR1/hepcidin signalling. MOMENTUM (against danazol) and the SIMPLIFY-1/-2 programmes underpin its current label for symptomatic anaemic MF (Mesa et al., 2017; Verstovsek et al., 2023).

Nursing checklist before starting a JAK inhibitor

- Verify viral status: hepatitis B virus (HBV) / hepatitis C virus (HCV) / human immunodeficiency virus (HIV) — especially before momelotinib. HBV reactivation is a recognised risk associated with JAK inhibitor therapy. Screen for latent or active tuberculosis (TB) before starting a JAK inhibitor, given the recognised risk of TB reactivation. Also assess herpes zoster history/vaccination eligibility and avoid live vaccines during significant immunosuppression; if stopping or tapering a JAK inhibitor, follow the prescriber's plan rather than acting independently, since abrupt ruxolitinib withdrawal can cause symptom rebound and, rarely, a severe withdrawal syndrome.

- Vaccinate where possible: VZV (recombinant zoster vaccine) prior to ruxolitinib; pneumococcal and seasonal influenza; severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) per local schedules.

- Counsel about symptom rebound following missed or stopped doses and ensure that patients know whom to contact for advice.

- Document baseline: MPN10 score, spleen size, FBC, urea and electrolytes (U&E), LFTs, lipids, BP, weight, thiamine (fedratinib).

- Arrange early clinical and laboratory review according to the selected JAK inhibitor and local protocol; dose adjustments may be required based on response and cytopenias.

Nursing Monitoring

Nurses should assess:

- medication adherence
- symptom response
- infections
- bruising or bleeding
- gastrointestinal toxicity
- weight changes
- quality of life
- patient expectations
- Patients should also be educated regarding:
- infection prevention
- prompt reporting of fever
- avoiding abrupt discontinuation unless medically advised
- importance of regular blood monitoring

Allogeneic haematopoietic stem cell transplantation (allo-HSCT)

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) is the only curative therapy for MF. It carries substantial early morbidity and non-relapse mortality (NRM) of 15–30% at one year (Gagelmann et al., 2019; Kröger et al., 2024), balanced against a long-term survival benefit in higher-risk patients. Candidates are selected based on age (typically ≤70 years), performance status, other health problems, donor availability and the patient's own wishes. The Myelofibrosis Transplant Scoring System (MTSS) uses age >57, Karnofsky performance status <90%, thrombocytopenia, leukocytosis >25 × 10^9/L, human leukocyte antigen (HLA)-mismatched unrelated donor, ASXL1 mutation and non-CALR/MPL driver to estimate post-transplant outcomes (Gagelmann et al., 2019; Kröger et al., 2024).

JAK inhibitor therapy is now routinely used in the run-up to transplant, both to shrink the spleen (ideally to <5 cm palpable below the costal margin) and improve the patient's general condition.

Tapering should begin 7–10 days before conditioning, with the final dose given the day before conditioning starts, in accordance with current BSH guidance (McLornan et al., 2024b). Pre-transplant work-up should include oesophagogastroduodenoscopy (OGD) to exclude varices, liver imaging where indicated, iron-overload assessment, and donor sourcing through the British Society of Blood and Marrow Transplantation pathway (McLornan et al., 2024b).

For patients being evaluated for allogeneic haematopoietic stem cell transplantation, nurses play an essential role in patient education, psychosocial preparation, coordination of pre-transplant investigations and ongoing communication with transplant services.

Anaemia-directed therapy

Beyond JAK inhibitor selection, supportive options for anaemia include erythropoiesis-stimulating agents (ESAs, where serum EPO is <500 IU/L), danazol, and (in select cases) lenalidomide or thalidomide-based regimens. Luspatercept has shown efficacy in transfusion-dependent MF and is now an option in many jurisdictions, often combined with ongoing JAK inhibitor therapy (Gerds et al., 2024; McLornan et al., 2024b).

Splenectomy and splenic radiotherapy

Splenectomy is reserved for symptomatic massive splenomegaly refractory to medical therapy and for transfusion-dependent disease unresponsive to other measures, in carefully selected patients. It carries high peri-operative morbidity and mortality. Splenic radiotherapy provides shorter-lived symptomatic relief and is reserved for patients unfit for surgery or as a bridge (McLornan et al., 2024b).

Emerging agents

Several novel agents are in late-stage trial development, including BET inhibitors (pelabresib), BCL-XL/BCL-2 inhibitors (navitoclax), MDM2 inhibitors and imetelstat (a telomerase inhibitor licensed in lower-risk MDS, in development for MF). Combination strategies — JAK inhibitor + add-on agent — aim for deeper, more durable responses and potentially disease modification (Gotlib, 2025). Mutant-calreticulin-targeted therapies — INCA033989, a first-in-class monoclonal antibody selectively targeting mutant CALR, is in clinical development for CALR-mutated ET and MF and has received FDA Breakthrough Therapy Designation, representing a novel genotype-directed therapeutic approach in MPN.

Nursing Implications for Primary Myelofibrosis

Nursing care for MF spans a wide spectrum: the well, low-risk patient on observation; the JAK inhibitor patient navigating cytopenias and infection risk; the transfusion-dependent patient managing iron overload and chronic fatigue; and the transplant candidate or recipient. Common threads include:

- Symptom assessment with MPN10 at baseline and at clinically appropriate intervals; take patient-reported symptom burden into account alongside blood counts when guiding management.
- Infection vigilance — particularly herpes zoster, opportunistic infections on JAK inhibitors, and post-transplant immunosuppression-related infections.
- Transfusion support and iron-overload monitoring (ferritin trends); chelation when appropriate, especially pre-transplant.
- Nutritional support — early satiety, weight loss and pre-transplant deconditioning all benefit from dietitian input.
- Weight loss and reduced nutritional intake are common in patients with symptomatic splenomegaly. Nurses should routinely assess nutritional status and consider early referral to a dietitian where clinically indicated.
- Psychosocial care and end-of-life conversations — for patients who progress, advance care planning and timely involvement of palliative care are important components of multidisciplinary care, with nurses playing a key role.
- Haematology nurses play a central role throughout the disease trajectory of primary myelofibrosis. As symptom burden, treatment goals and supportive care needs frequently change over time, comprehensive nursing assessment should integrate physical symptoms, psychosocial wellbeing, treatment tolerance and quality of life. Early recognition of clinical deterioration and timely communication with the multidisciplinary team are essential to optimise patient outcomes. Given the progressive nature of primary myelofibrosis, nurses should also assess changes in functional status, nutritional intake, transfusion requirements and patient-reported outcomes during every follow-up consultation. A structured, holistic assessment facilitates timely intervention and supports person-centred care.

Key Nursing Take-Home Messages	
1	MF (primary or secondary) is associated with a substantial clinical and symptom burden; cytokine-driven symptoms often dominate the patient experience.
2	Modern risk stratification uses DIPSS, MIPSS70+v2.0, MYSEC-PM and GIPSS — apply the right model for the right population.
3	JAK inhibitor selection is increasingly individualized according to factors including symptom burden, prior therapy, platelet count, anaemia and treatment availability.
4	Allogeneic transplantation remains the only curative option; nursing input is an important component of care throughout the transplant pathway.
5	Symptom burden is a key patient-reported outcome; nurses play a central role in systematic symptom assessment, monitoring and timely escalation.
6	Quality of life represents an important clinical outcome alongside laboratory response.
7	Nurses play a key role in coordinating supportive care and multidisciplinary management.
8	Nutritional assessment should form part of routine nursing follow-up.
9	Patient education should evolve throughout the disease trajectory and reflect changing treatment goals.
Patient Education	
1	Explain that myelofibrosis varies widely — some people remain stable for many years while others need active treatment sooner; the team will tailor care to the patient's individual risk score and symptoms.
2	Acknowledge that fatigue, night sweats and weight loss can have a substantial impact on daily life, and explain that pacing, gentle exercise and good sleep habits may help alongside medical treatment.
3	Discuss allogeneic transplantation openly and early in those who may be eligible: it remains the only potentially curative therapy but carries significant risks that need to be carefully weighed against the potential benefits.
4	Encourage patients to track their symptoms using the MPN-SAF (MPN10) and bring the score to clinic; as trends over time can provide valuable information for the clinical team.
5	Advise patients to contact the team promptly for any new fevers, drenching sweats, weight loss, rapidly increasing abdominal fullness, or unexplained bruising or bleeding — these can signal disease progression or transformation.

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Quick Facts:

- MPN type, age, comorbidities, pregnancy plans and platelet count all shape the use of cytoreductive therapy.
- Hydroxycarbamide and pegylated interferon are established cytoreductive treatment options in PV and ET, with treatment choice individualised according to factors including age, pregnancy plans, comorbidities and patient preference.
- Pegylated interferons are considered disease-modifying options and are increasingly used in younger patients; their use in pregnancy or pregnancy planning should follow formulation-specific and national guidance.
- Four JAK inhibitors are available for the treatment of myelofibrosis in different jurisdictions — ruxolitinib, fedratinib, pacritinib and momelotinib.
- Pre-emptive infection screening, vaccination, skin and metabolic monitoring, and careful tapering of JAK inhibitors at withdrawal are essential competencies.
- Haematology nurses play a key role in ensuring the safe delivery of systemic treatment by combining clinical assessment, patient education, toxicity monitoring and multidisciplinary coordination. Treatment goals should be regularly reviewed with patients, recognising that priorities may change throughout the disease trajectory. Nurses also facilitate shared decision-making by supporting patients in understanding the benefits, limitations and potential adverse effects of individual treatment options.

Module VI: Treatment Strategies Across MPN

Contents:

A. Cytoreductive Therapies
B. Interferon Therapy
C. JAK Inhibitors
D. Side Effect Management
E. Nursing Competencies and Key Take-Home Messages
F. References

Learning Objective

By the end of this module, you will be able to compare the main cytoreductive and targeted therapies used across the MPN spectrum, including their mechanisms, indications, monitoring requirements and associated patient education needs.

6.1 Cytoreductive Therapies

Cytoreduction reduces clonal cell proliferation to lower the risk of thrombosis and control disease-related blood counts and symptoms. The key non-targeted cytoreductive agents are hydroxycarbamide (also called hydroxyurea), anagrelide and busulfan, each with a distinct role, side-effect profile and monitoring requirement (McMullin et al., 2019; Tefferi and Barbui, 2023, 2024).

Hydroxycarbamide is a ribonucleotide reductase inhibitor that reduces all three myeloid lineages and is first-line cytoreduction in high-risk PV and ET. Common adverse effects include macrocytosis (an expected pharmacological marker), cytopenias, mucositis, pigmentation changes, leg and oral ulcers, and cutaneous malignancy — particularly squamous cell carcinoma in fair-skinned patients with cumulative sun exposure. Hydroxycarbamide is contraindicated during pregnancy and requires specialist review before planned conception. Patients who are pregnant or planning pregnancy should be referred to a specialist haematologist, with obstetric input sought to guide treatment decisions.

Nursing Monitoring

Prior to treatment initiation and during follow-up, nurses should assess:

- medication adherence
- skin changes
- oral ulcers
- gastrointestinal symptoms
- signs of infection
- bleeding
- patient understanding of treatment
- concerns regarding long-term therapy

Patient Education

Patients should understand:

- purpose of therapy
- importance of adherence
- skin protection
- routine blood monitoring
- when to contact the haematology team

Anagrelide is a phosphodiesterase III inhibitor used as platelet-selective cytoreduction in ET, particularly when hydroxycarbamide is poorly tolerated. The PT-1 trial favoured hydroxycarbamide for arterial-thrombosis prevention; anagrelide was associated with a lower rate of venous thrombosis but higher rates of myelofibrosis transformation, bleeding and minor adverse effects (Harrison et al., 2005). Baseline cardiac assessment, including ECG, blood pressure and assessment of cardiac symptoms, is appropriate before treatment initiation.

Busulfan is typically reserved for selected older patients or when other agents are unsuitable. It has greater leukaemogenic potential and requires careful dose titration; it should be used selectively rather than as a routine choice (McMullin et al., 2019).

Agent	Indications across MPN	Notable side effects	Pregnancy
Hydroxycarbamide	First-line for high-risk PV and ET	Cytopenias, mucositis, leg/oral ulcers, NMSC	Contraindicated
Anagrelide	ET (selective platelet lowering)	Headache, palpitations, fluid retention, cardiomyopathy	Contraindicated
Busulfan	Selected older patients with PV/ET when other options are unsuitable	Late leukaemogenic risk	Contraindicated

Table 10. Non-targeted cytoreductive agents in MPN: hydroxycarbamide, anagrelide and busulfan — their indications across PV and ET, notable side-effect profile and pregnancy status. Sources: Birgegård et al., 2018; Björkholm et al., 2011; Harrison et al., 2005; McMullin et al., 2019; Tefferi and Barbui, 2023; Tefferi and Barbui, 2024.

6.2 Interferon Therapy

Interferon-alfa has been used in MPN for over three decades and is the only widely used agent with documented capacity to reduce JAK2 V617F allele burden in some patients — a putative marker of disease modification. (Kiladjian et al., 2016) Pegylated formulations (pegylated interferon alfa-2a; ropeginterferon alfa-2b) are now standard, offering improved tolerability and weekly or fortnightly dosing (Kiladjian et al., 2016).

Ropeginterferon alfa-2b is licensed in PV without symptomatic splenomegaly. PROUD-PV and CONTINUATION-PV demonstrated non-inferiority to hydroxycarbamide at 12 months and superiority at 36 months for combined haematological response and molecular response (Gisslinger et al., 2020).

In ET, several phase-2 and phase-3 studies of ropeginterferon and pegylated interferon alfa-2a support efficacy, including in younger patients. Treatment choice in patients planning pregnancy should follow formulation-specific and national guidance (Kiladjian et al., 2016; Yacoub et al., 2019).

Tolerability is a key limiting factor. Flu-like symptoms are common during dose titration; fatigue, mood disturbance (depression, anxiety), raised transaminases and autoimmune phenomena (thyroid disease, autoimmune cytopenias, vasculitis) need active monitoring. Patients with a history of significant depression or autoimmune disease need careful counselling before starting.

Starting interferon — practical points

- Titrate slowly (e.g. ropeginterferon 100 µg every 2 weeks → up by 50 µg every 2 weeks as tolerated, to a maximum of 500 µg). Peginterferon alfa-2a is an alternative, starting at 45 µg weekly and titrating according to response and tolerability.
- Pre-dose paracetamol can blunt flu-like symptoms in the first weeks.
- Teach subcutaneous self-injection (often into the abdominal wall); rotate sites.
- Schedule baseline and periodic TFTs, LFTs, FBC, mood screen and a self-completed side-effect diary.
- Counsel about contraception and pregnancy planning. Where cytoreductive therapy is required during pregnancy, treatment should be selected in consultation with the specialist haematology and obstetric team and according to formulation-specific and national guidance.

Nursing Considerations

Prior to initiation of interferon therapy, nurses should assess the patient's psychological history, pre-existing autoimmune disease and expectations regarding treatment. During follow-up, particular attention should be paid to fatigue, flu-like symptoms, mood changes, injection-site reactions and treatment adherence.

- Interferon can also occasionally worsen pruritus, at least initially, so patients started on interferon for itch should be counselled that symptoms may transiently increase before improving.

6.3 JAK Inhibitors

JAK inhibitors block the constitutively active JAK–STAT signalling that drives MPN, providing potent symptom and spleen control in MF and disease-control benefit in PV. Four JAK inhibitors are currently used across different MPN indications and jurisdictions:

- Ruxolitinib — JAK1/2 inhibitor; licensed for MF (intermediate and high-risk) and for PV after hydroxycarbamide failure or intolerance. Provides robust spleen and symptom responses in MF and strong haematocrit control plus pruritus relief in PV (Vannucchi et al., 2015; Verstovsek et al., 2012).
- Fedratinib — selective JAK2 inhibitor; licensed for MF in JAK-inhibitor naïve and post-ruxolitinib settings. Pre-treatment thiamine assessment is recommended due to early reports of Wernicke encephalopathy (Pardanani et al., 2015).
- Pacritinib — JAK2/IRAK1/FLT3 inhibitor; licensed for MF with thrombocytopenia (platelets <50 × 10^9/L) where ruxolitinib and fedratinib are limited (Mascarenhas et al., 2018).
- Momelotinib — JAK1/2 + ACVR1 inhibitor with hepcidin-suppressing activity; licensed for MF with anaemia. The MOMENTUM and SIMPLIFY trials demonstrated concurrent improvement in spleen, symptoms and anaemia (Mesa et al., 2017; Verstovsek et al., 2023).

Dose selection and platelet thresholds should follow the current product information and national guidance.

Agent	MPN setting	Platelet threshold	Distinctive feature
Ruxolitinib	MF (Int-2/high), PV (post-HU)	≥50 × 10^9/L for full dose	Extensive symptom and spleen response data; survival benefit reported in pooled COMFORT analyses.
Fedratinib	MF first/second line	≥50 × 10^9/L	Active post-ruxolitinib; thiamine monitoring
Pacritinib	MF (severe thrombocytopenia)	Any (often <50 × 10^9/L)	Useful where other JAKi limited by cytopenias
Momelotinib	MF with anaemia	≥25 × 10^9/L commonly	Anaemia benefit via hepcidin suppression

Table 11. Positioning of JAK inhibitors in MF and PV: principal MPN setting, the practical platelet-count threshold for use and the distinctive feature that guides selection. Sources: Harrison et al., 2012; Mascarenhas et al., 2018; Mesa et al., 2017; Pardanani et al., 2015; Vannucchi et al., 2015; Verstovsek et al., 2012; Verstovsek et al., 2023.

Nursing Monitoring

During JAK inhibitor treatment, routinely assess:

- treatment response
- infections
- bruising
- bleeding
- weight
- gastrointestinal toxicity
- quality of life
- medication adherence

Patient Education

Patients should receive education regarding:

- infection prevention
- prompt reporting of fever
- avoiding abrupt treatment discontinuation
- regular laboratory monitoring

6.4 Side Effect Management

Managing MPN therapy well depends on anticipating and preventing toxicity. Key issues include:

- Cytopenias — anaemia and thrombocytopenia are the most common reasons for JAK inhibitor dose reduction. (Verstovsek et al., 2012; Harrison et al., 2012)
- Infection — JAK inhibitors increase risk of herpes zoster (recombinant zoster vaccine recommended), urinary and respiratory infections (Verstovsek et al., 2012; Harrison et al., 2012)
- Skin — hydroxycarbamide-associated skin malignancy and ulceration require sun protection counselling and at least annual skin review; JAK inhibitors can also increase non-melanoma skin cancer risk. (Björkholm et al., 2011; McMullin et al., 2019)
- Patients receiving long-term hydroxycarbamide or JAK inhibitor therapy should undergo regular skin assessment in accordance with individual risk and local guidance.
- Cardiometabolic — ruxolitinib is associated with weight gain, hypertension and lipid changes (Vannucchi et al., 2015)
- Neuropsychiatric — interferons can precipitate or worsen depression; pacritinib is rarely associated with QT prolongation; fedratinib has the Wernicke flag (thiamine). (Kiladjian et al., 2016; Pardanani et al., 2015; Mascarenhas et al., 2018)
- Withdrawal phenomena — abrupt cessation of ruxolitinib (and other JAKi) can cause a rebound flare with rapid recurrence of splenomegaly and symptoms, occasionally a SIRS-like clinical picture (Verstovsek et al., 2012; Harrison et al., 2012; McLornan et al., 2024b)

Nursing Implications for MPN Treatment Strategies

- Independent assessment of MPN symptom burden using MPN10 and communication of findings to inform multidisciplinary treatment planning.
- Safe administration and titration of subcutaneous interferons and oral JAK inhibitors, including teaching self-administration where appropriate.
- Counselling on adherence, missed-dose protocols and emergency contact pathways.
- Recognition and triage of treatment-related emergencies — neutropenic sepsis, shingles, severe haemorrhage, suspected withdrawal flare.
- Arranging vaccinations (shingles, pneumococcal, flu, COVID-19) and pre-treatment screening (HBV, HCV, HIV, TB, thiamine).
- Recording patient-reported outcomes and bringing them to MDT discussions.
- Shared decision-making should form an integral component of treatment planning. Nurses support this process by exploring patient values, preferences and expectations, ensuring that treatment decisions align with individual goals and quality-of-life priorities.
- Successful treatment extends beyond achieving haematological response. Nurses should evaluate symptom burden, functional status, quality of life and patient treatment goals throughout the disease trajectory, recognising that these outcomes are equally important to patients.

Key Nursing Take-Home Messages	
1	Match the agent to the patient: cytoreduction class is shaped by MPN type, age, comorbidities, pregnancy plans and platelet count.
2	Hydroxycarbamide and interferon are established cytoreductive options; treatment choice should be individualised according to age, comorbidities, pregnancy plans and formulation-specific guidance.
3	JAK inhibitors transformed MF care in the 2010s; newer agents have expanded treatment options for patients with thrombocytopenia or anaemia.
4	Pre-emptive infection, skin and metabolic monitoring is essential component of nursing care.
5	Abrupt discontinuation of JAK inhibitors can cause symptom rebound; treatment interruption or discontinuation should be discussed with the clinical team.
6	Treatment success should be evaluated from both clinical and patient perspectives.
7	Nurses play a central role in monitoring treatment toxicity.
8	Patient education should be reinforced throughout treatment.
9	Early recognition of adverse events improves patient safety.
10	Shared decision-making enhances treatment adherence and patient satisfaction.
11	Holistic nursing assessment should accompany every treatment review.
Patient Education	
1	Make sure patients know the name of every medication they are taking, what it is for, and the most common side effects to watch for; a written medication card is helpful.
2	Stress the importance of not stopping a JAK inhibitor abruptly — withdrawal can cause rapid recurrence of symptoms and rebound flare. Always contact the team first.
3	Encourage patients to bring an up-to-date list of all medications, including over-the-counter remedies, herbal supplements and vitamins, to every clinic visit.
4	Highlight that vaccinations (shingles, pneumococcal, influenza, COVID-19) are particularly important on JAK inhibitors; ideally given before starting where possible.
5	Reassure that most side effects are dose-related and manageable with adjustment — patients should report them rather than stopping the medication on their own.

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Quick Facts:

- Thrombosis is a major cause of morbidity and mortality in MPN; both arterial and venous events occur, with splanchnic and cerebral venous sinus thromboses over-represented in younger JAK2-mutated patients.
- Bleeding can complicate very high platelet counts through acquired von Willebrand syndrome should be considered in patients with very high platelet counts, and antiplatelet therapy may require review while cytoreduction is initiated.
- Anaemia in myelofibrosis is multifactorial; momelotinib, luspatercept, ESAs and danazol now sit alongside transfusion in its management.
- Transformation to AML ('blast phase') is a serious complication — uncommon in PV and ET, more frequent in MF, and signalled by rapidly changing counts, new B-symptoms and rising blasts.
- MPN-specific emergencies — thrombosis, haemorrhage, sepsis on JAK inhibitors, withdrawal flares — should be rehearsed and escalation routes clearly defined for nursing teams.
- Haematology nurses play a pivotal role in the early recognition and management of disease- and treatment-related complications. Through systematic assessment, patient education and prompt escalation of concerns, nurses contribute significantly to preventing complications from progressing to life-threatening events. Each patient encounter should include an assessment of new symptoms, treatment-related toxicities and patient understanding of when urgent medical review is required.

Module VII: Management of Complications in MPN

Contents:

A. Thrombosis and Bleeding
B. Anaemia and Cytopenias
C. Transformation to Acute Leukaemia
D. Emergency Nursing Considerations
E. Key Nursing Take-Home Messages
F. References

Learning Objective

By the end of this module, you will be able to recognise key complications of MPN — including thrombosis, haemorrhage, infection and disease transformation — and apply structured nursing assessment and escalation principles in clinical practice.

7.1 Thrombosis and Bleeding

Thrombosis is a dominant cause of morbidity and mortality in PV and ET, and an important early-disease event in MF. Annual thrombosis rates range from <1% in very low-risk ET to 4% or more in high-risk PV. (Barbui et al., 2015; Tefferi and Barbui, 2023) The mechanisms are multifactorial: increased blood viscosity (especially in PV), elevated and activated platelets, JAK2 V617F-driven endothelial activation, high white cell counts, and standard cardiovascular risk factors (De Stefano et al., 2018; Tefferi and Barbui, 2023).

Both arterial and venous events occur. In PV and ET, arterial events (stroke, myocardial infarction (MI), peripheral arterial disease (PAD)) are more common than venous events. Atypical sites — including splanchnic veins (Budd–Chiari syndrome, portal and mesenteric vein thrombosis) and cerebral venous sinuses — are over-represented compared with the general population, particularly in younger women and in patients with high JAK2 V617F allele burden (De Stefano et al., 2018).

Acute management of arterial or venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), follows standard pathways: prompt anticoagulation, imaging confirmation and search for reversible factors. Important MPN-specific points include rapid haematocrit control in PV (target <45%), controlling white cells and platelets in ET, and a low threshold for cytoreduction following any vascular event. Long-term anticoagulation is generally indicated after VTE, with the duration and choice of drug tailored to the individual — direct oral anticoagulants (DOACs) are increasingly used for venous events, with vitamin K antagonists (VKAs, e.g. warfarin) still preferred for splanchnic-vein thrombosis in many guidelines (Barbui et al., 2021; De Stefano et al., 2018).

Major haemorrhage occurs in approximately 4% of patients at presentation and persists as a lifelong concern, particularly in:

- Patients with very high platelet counts (>1500 × 10⁹/L), where acquired von Willebrand syndrome can develop and antiplatelet therapy may require review while the platelet count is being controlled.
- Patients on dual anti-platelet therapy or anticoagulation, particularly with co-existing thrombocytopenia or hepatic dysfunction.
- Post-operative or trauma settings, where peri-procedure planning is essential.
- Patients on JAK inhibitors with profound thrombocytopenia.

Recognising thrombosis and bleeding emergencies

- FAST assessment for stroke; chest pain pathway for MI — do not assume MPN is a benign explanation for new symptoms.
- Sudden severe abdominal pain in an MPN patient should prompt consideration of splanchnic vein thrombosis (Budd–Chiari, portal, mesenteric).
- Headache, focal neurology or new visual disturbance can reflect cerebral venous sinus thrombosis — consider imaging.
- Bleeding: sudden bruising, mucosal bleeding, melaena or unexplained anaemia in a patient with very high platelets — think acquired vWF deficiency.
- Always document the platelet count, anti-platelet/anticoagulant exposure and JAK inhibitor adherence on admission.

Nursing Assessment

Nurses should routinely assess patients for early signs and symptoms of arterial and venous thrombosis, recognising that prompt identification may reduce morbidity and mortality. Assess:

- unilateral limb swelling
- chest pain
- dyspnoea
- neurological symptoms
- visual disturbances
- severe headache
- abdominal pain suggestive of splanchnic thrombosis

Patient Education

Patients should understand:

- warning signs of thrombosis
- when to seek emergency medical attention
- importance of adherence to antithrombotic therapy

7.2 Anaemia and Cytopenias

Anaemia is prominent in MF — approximately 25–40% of patients are transfusion-dependent at diagnosis, and many more become so over time. Causes are mixed: poor red cell production from marrow fibrosis, iron deficiency from chronic bleeding or phlebotomy, JAK inhibitor-induced anaemia (particularly ruxolitinib), pooling in the spleen, autoimmune haemolysis (rare) and nutritional

deficiencies (Tefferi, 2023; Verstovsek et al., 2023).

Initial work-up of anaemia in an MPN patient should include reticulocyte count, blood film, iron studies, B12, folate, thyroid function, renal function, liver function, haptoglobin, LDH, direct antiglobulin test (if haemolysis suspected) and serum erythropoietin. The MF-specific options for anaemia include erythropoiesis-stimulating agents (most active when EPO <500 IU/L), danazol, momelotinib (an option where symptomatic anaemia is a dominant clinical problem), luspatercept and, in selected cases, lenalidomide- or thalidomide-based regimens (Gerds et al., 2024; Verstovsek et al., 2023).

Thrombocytopenia in MF is associated with poorer prognosis and historically constrained the use of ruxolitinib and fedratinib. Pacritinib has expanded the treatment options for patients with platelets <50 × 10^9/L, while still requiring vigilance for bleeding and infection. Leukopenia is less common at presentation but develops during disease progression and predicts transformation; infection risk rises sharply (McLornan et al., 2024b).

Cytopenia	Potential causes	Nursing assessment and actions
Anaemia	Marrow fibrosis, JAK inhibitor toxicity, iron deficiency, splenic pooling, transformation	Confirm cause; arrange transfusion thresholds; iron and EPO levels; consider luspatercept/ momelotinib. Escalate for review of anaemia-directed treatment options where appropriate.
Thrombocytopenia	Disease progression, splenic sequestration, JAKi dose, alcohol, drug interactions	Review medications; assess bleeding risk; escalate for specialist review of JAK inhibitor choice and dosing, including consideration of pacritinib or dose adjustment where appropriate.
Leukopenia	Disease progression, JAKi toxicity, transformation	Infection education, prompt review of fever, dose review

Table 12. Common cytopenias encountered in MPN — anaemia, thrombocytopenia and leukopenia — with their typical drivers and the initial nursing actions that should be triggered.
Sources: Gerds et al., 2024; McLornan et al., 2024b; Mascarenhas et al., 2018; Tefferi, 2023; Verstovsek et al., 2023.

Nursing Considerations for Bleeding Complications:

Nurses should assess both major and minor bleeding symptoms and evaluate their impact on daily activities. Particular attention should be paid to patients receiving antiplatelet or anticoagulant therapy and those with extreme thrombocytosis or acquired von Willebrand syndrome.

Assess:

- epistaxis
- bruising
- gingival bleeding
- gastrointestinal bleeding
- prolonged bleeding
- heavy menstrual bleeding

Nursing Considerations for Infection:

Patients should be educated to report:

- fever
- chills
- productive cough
- urinary symptoms
- skin infection
- persistent sore throat

Nurses should reinforce:

- hand hygiene
- vaccination recommendations
- infection prevention strategies
- prompt reporting of symptoms

7.3 Transformation to Acute Leukaemia

Transformation to acute myeloid leukaemia (AML; 'blast phase') is a serious complication of MPN. Cumulative 20-year incidence is approximately 4% in PV, less than 4% in ET, and substantially higher in MF (10–20% over 10 years). (Tefferi et al., 2018; Tefferi et al., 2018b; Tefferi and Barbui, 2023) Risk factors include older age, advanced disease, leukocytosis, blasts in the blood (≥10% defines accelerated phase, ≥20% defines blast phase), unfavourable karyotype, and high-molecular-risk mutations — particularly TP53, RAS-pathway mutations, ASXL1 and IDH1/2 (McLornan et al., 2024b; Tefferi et al., 2018; Tefferi et al., 2018b).

Clinical features that should prompt urgent investigation include rapid changes in blood counts (rising white cell count with circulating blasts, falling platelets or haemoglobin), new B-symptoms, rapidly progressive splenomegaly and bone pain. The transformation prognosis is poor — median survival is measured in months — but younger, fitter patients can be treated with intensive induction chemotherapy (7+3 or hypomethylating agent + venetoclax regimens) bridging to allogeneic transplantation. Hypomethylating agents alone, with or without venetoclax, are an option for patients unfit for intensive therapy (DiNardo et al., 2020; Tefferi et al., 2018b).

Watch for transformation

- Rapidly changing FBC with circulating blasts: send urgent film and notify the MPN team the same day.
- New or escalating B-symptoms (drenching sweats, weight loss, fevers) without infection should be treated as a transformation flag.
- Increasing transfusion need or rising LDH may signal blast-phase or accelerated disease.
- Patients should be told what to report and given a direct contact route between scheduled visits.
- Once transformation is suspected, urgent haematology assessment, including consideration of bone marrow examination, is required to confirm the diagnosis and inform treatment.

Nursing Assessment

Nurses should recognise clinical changes that may suggest disease progression and promptly communicate concerns to the treating haematologist.

Assess:

- rapidly worsening fatigue
- increasing transfusion requirements
- recurrent infections
- unexplained bruising
- weight loss
- declining performance status

Nursing Implications for Complication Management

Nursing staff should be able to recognise and escalate these MPN-specific emergencies:

- Acute thrombosis (arterial or venous, including splanchnic and cerebral venous sinus events) — urgent escalation and assessment according to local thrombosis pathways.
- Acute haemorrhage — rapid assessment of the platelet count, von Willebrand status and current anti-platelet/anticoagulant therapy.
- Sepsis in patients receiving JAK inhibitors — recognise that infections may present subtly and escalate urgently according to local sepsis pathways.
- Suspected JAK inhibitor withdrawal flare — recognise recurrence of constitutional symptoms, splenic enlargement or a SIRS-like presentation after discontinuation and escalate urgently for clinical review.
- Tumour-lysis or differentiation-syndrome-like presentations during rapid cytoreduction or in transformation.
- Pulmonary hypertension or pulmonary fibrosis-like presentations — uncommon but described in MPN; require cardiology and respiratory input.

Module VII: Management of Complications in MPN

Key Nursing Take-Home Messages	
1	Thrombosis is a major cause of morbidity and mortality in MPN; risk reduction should be addressed at every nursing encounter (CV risk factors, adherence, symptom review).
2	Acquired von Willebrand syndrome can complicate very high platelet counts; bleeding presentations require thoughtful assessment.
3	Anaemia management has evolved, with several treatment options available alongside transfusion support depending on the clinical context and local guidance.
4	Transformation to AML is uncommon but serious; nurses may be among the first to recognise signals such as rapidly changing blood counts or symptoms.
5	MPN emergencies share principles with other haematological emergencies but have MPN-specific twists that nursing teams should rehearse.
6	Early recognition of complications improves patient outcomes.
7	Structured nursing assessment should accompany every outpatient review.
8	Patient education regarding emergency symptoms is essential.
9	Multidisciplinary collaboration enhances patient safety.
10	Psychosocial support should be integrated into complication management.
Patient Education	
1	Teach patients the Face, Arms, Speech, Time (FAST) test for stroke and the warning signs of a heart attack — these symptoms require an immediate emergency services call.
2	Warn patients to seek same-day urgent assessment for sudden severe abdominal pain, unexplained leg swelling, breathlessness, or coughing up blood — these may be signs of clot at typical or atypical sites.
3	Explain the signs of anaemia (increasing shortness of breath, dizziness, palpitations, profound tiredness) and when to contact the team for review and possible transfusion.
4	On JAK inhibitors, advise patients that a temperature above 38°C, new shivering, cough or burning when passing urine should trigger an urgent call to the haematology team — infection presentations can be subtle but evolve quickly.
5	Ask patients to report new bone pain, drenching night sweats, unexplained weight loss, or rapidly enlarging abdomen — these can be early signs of disease transformation that need prompt assessment.

Red Flag Symptoms Requiring Immediate Medical Review

- sudden neurological symptoms
- chest pain
- acute dyspnoea
- unilateral limb swelling
- significant bleeding
- fever ≥38°C (according to local policy)
- rapidly enlarging spleen
- severe abdominal pain
- sudden deterioration in performance status

Many serious complications are preceded by subtle changes in symptoms rather than dramatic laboratory abnormalities. Careful nursing assessment and patient education therefore remain essential components of safe long-term MPN management.

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Module VIII: Living with MPN — Providing Support for Patients and Caregivers

Quick Facts:

- MPN imposes a substantial quality-of-life burden — fatigue, brain fog, anxiety, mood and role disruption — that is often invisible on routine blood tests.
- The MPN-SAF Total Symptom Score (MPN10) is a validated 10-item patient-reported outcome that should be used at baseline and at clinically appropriate intervals to track the patient experience over time.
- Fatigue is multifactorial; addressing reversible causes (anaemia, sleep, mood, thyroid) and adding non-pharmacological strategies (graded exercise, mindfulness, peer support) may help improve fatigue and quality of life.
- Pregnancy in MPN is higher-risk and requires pre-conception planning; a specialist obstetric haematologist should lead all treatment decisions during pregnancy.
- Shared decision-making — weighing thrombosis prevention against bleeding risk, disease control against drug toxicity, and the curative potential of transplant against early mortality — is fundamental to MPN care.
- Living with an MPN extends far beyond disease control. Haematology nurses play a key role in empowering patients to self-manage their condition, maintain quality of life and navigate the physical, emotional and social challenges associated with living with a chronic haematological malignancy. Long-term nursing follow-up should focus on patient education, symptom management, psychosocial wellbeing and promoting independence.

Module VIII: Living with MPN — Providing Support for Patients and Caregivers

Contents:

A. Quality of Life
B. Fatigue and Symptom Burden
C. Fertility and Pregnancy
D. Shared Decision-Making
E. Key Nursing Take-Home Messages
F. References

Learning Objective

By the end of this module, you will be able to apply a holistic approach to supporting patients and caregivers living with MPN, addressing survivorship, psychological wellbeing, fertility, end-of-life care and access to patient support organisations.

8.1 Quality of Life

Several large international studies — including the MPN Landmark survey programme — have shown that quality of life (QoL) in MPN is impaired. Patients commonly report fatigue, concentration difficulty ('brain fog'), reduced exercise tolerance, sleep disturbance, anxiety, depression and an erosion of professional, social and intimate roles (Geyer et al., 2014; Mesa et al., 2016). Symptom burden does not correlate strongly with conventional disease severity; patients with low-risk PV or ET can have substantial QoL impairment, and even minor blood-count abnormalities can carry a heavy psychological load because of the cancer label.

Structured symptom and QoL measurement should be incorporated into routine MPN care, including at diagnosis and at clinically appropriate intervals during follow up. The MPN-SAF Total Symptom Score (also known as MPN10) is a validated 10-item patient-reported outcome with each item scored 0–10, providing both a total score (0–100) and a profile of dominant symptoms (Emanuel et al., 2012). The European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire Core 30 (EORTC QLQ-C30) and the Patient-Reported Outcomes Measurement Information System 29-item profile (PROMIS-29) are alternative generic tools; the EuroQoL EQ-5D (a five-dimension health-state instrument) is widely used for health-economic purposes.

8.2 Fatigue and Symptom Burden

Fatigue is one the most prevalent and disabling symptoms across MPN. Fatigue has multiple causes — cytokines, anaemia, poor sleep and psychological distress — and assessment should reflect this. The fatigue item of MPN10 is a useful screening question; the Brief Fatigue Inventory (BFI) or the Functional Assessment of Chronic Illness Therapy-Fatigue scale (FACIT-Fatigue) can be used for deeper assessment (Emanuel et al., 2012; Geyer et al., 2014).

Management should include assessment and appropriate treatment of potentially reversible or contributing factors, such as anaemia, hypothyroidism, sleep disturbance and depression. Iron deficiency should be assessed in the clinical context, particularly in patients with PV undergoing venesection. Disease-directed treatment may also improve fatigue when symptoms are driven by poorly controlled MPN.

Non-drug approaches — including graded exercise, sleep hygiene, mindfulness, peer support — may also help improve fatigue and quality of life (Eckert et al., 2019).

Symptom domain (MPN10 item)	Common drivers	Useful nursing actions
Fatigue	Cytokines, anaemia, sleep, depression	Treat/identify reversible causes; graded exercise; discuss persistent symptoms with the treating team
Early satiety / abdominal discomfort	Splenomegaly	Assess symptom progression; small frequent meals; escalate worsening symptoms to the treating team
Inactivity / impaired concentration	Cytokines, mood, sleep	Mood screening; cognitive strategies; signpost work-place support
Night sweats	Cytokines	Assess severity and impact; exclude other causes and discuss disease-directed treatment with the treating team
Itching / pruritus	Histamine and cytokine driven	Skin care, antihistamines, SSRIs, narrow-band UVB, JAKi
Bone pain	Cytokines, marrow expansion	Analgesic ladder; JAKi; physiotherapy
Fever (without infection)	Cytokines	Exclude infection first; treat as B-symptom of MPN with disease therapy
Weight loss	Disease activity, splenomegaly	Dietitian referral; review for transformation

Table 13. Selected clinical symptom domains assessed by the MPN-SAF Total Symptom Score (MPN10), with common underlying drivers and corresponding nursing actions. Sources: Eckert et al., 2019; Emanuel et al., 2012; Geyer et al., 2014; Mesa et al., 2016.

Practical use of MPN10 in clinic

- Hand patients the form on arrival; takes 2 minutes to complete.
- Score items 0 (absent) to 10 (worst imaginable); add for total (0–100).
- Use the trend over visits, not single values, as the most informative signal.
- Highlight symptoms that are moderate to severe, worsening over time or particularly distressing to the patient in your consultation summary.
- Changes in MPN10 over time can help assess symptom response alongside clinical and disease-specific parameters.

Nursing Considerations

Fatigue remains one of the most frequently reported and distressing symptoms experienced by patients with MPNs. Nurses should assess fatigue systematically and evaluate its impact on daily activities, employment, sleep, emotional wellbeing and participation in social activities.

Patients should receive advice regarding:

- energy conservation
- physical activity
- sleep hygiene
- nutrition
- pacing of daily activities

Physical Activity

Nurses should encourage patients to remain physically active according to their individual abilities and clinical condition. Regular physical activity may improve fatigue, physical functioning and overall quality of life. Exercise recommendations should be individualised and adapted to symptom burden and treatment status.

Psychosocial Wellbeing

Nurses should routinely assess emotional wellbeing throughout the disease trajectory. Anxiety, uncertainty regarding prognosis and fear of disease progression may persist despite stable disease. Psychological assessment should include coping strategies, resilience, caregiver burden and the need for referral to specialist supportive care services.

8.3 Fertility and Pregnancy

MPN affects men and women across the reproductive age range, and several MPN drugs have implications for fertility and pregnancy. Clear, early conversations are essential; nurses are often the trusted point of contact for this sensitive topic.

Family-planning discussions should include all patients of reproductive potential, as disease-directed therapies may have implications for fertility and conception.

- Pregnancy in MPN is associated with increased maternal and fetal risks, including thrombosis, early pregnancy loss, fetal growth restriction, placental insufficiency and preterm delivery. These risks require careful monitoring and planning by the specialist multidisciplinary team.
- Some cytoreductive treatments used in MPN are contraindicated in pregnancy or may affect fertility. Patients should not make any changes to their medication without specialist guidance.
- If a patient is planning a pregnancy, or becomes pregnant unexpectedly, they should be referred promptly to a specialist multidisciplinary team with expertise in MPN and high -risk pregnancy. All treatment decisions — including any changes before, during or after pregnancy — must be made by a specialist team.
- Nurses play an important role in encouraging patients to raise pregnancy plans early, before conception where possible, to allow time for appropriate specialist review and planning.
- Pre-conception planning should involve a joint discussion between haematology, obstetrics and (where relevant) a fertility specialist. The nurse's role is to facilitate this referral and to support the patient in engaging with specialist care.

8.4 Shared Decision-Making

MPN management almost always involves trade-offs — between thrombosis prevention and bleeding risk, between disease control and cumulative drug toxicity, between the curative potential of transplant and its early risks. Shared decision-making is therefore essential (McLornan et al., 2024b).

Good shared decision-making in MPN means:

- Eliciting what matters most to the patient — this varies greatly between, for example, a 30-year-old planning a family and a 75-year-old who prioritises symptom control.
- Explaining realistic risks and benefits in plain language; using decision aids where available.
- Being honest about uncertainty, including the limits of available evidence and prognostic models.
- Documenting the discussion and revisiting decisions as circumstances change.
- Ensuring family or chosen supporters are included where the patient wishes.

Particular decision points include whether and when to initiate cytoreductive therapy, choice of disease-directed treatment, changes in therapy when response wanes or toxicity develops, and the timing and consideration of allogeneic transplantation.

End-of-life conversations should not be saved for a single moment — timely advance care planning, palliative care input and open discussion about prognosis can support patients and families throughout advanced disease.

Successful long-term management of MPNs requires more than disease control. Nurses should continuously evaluate quality of life, patient goals, psychosocial wellbeing and self-management skills, recognising that these outcomes are central to person-centred care

Key Nursing Take-Home Messages	
1	MPN imposes a substantial QoL burden that is often invisible on routine blood tests.
2	Use MPN10 as a structured patient-reported outcome at baseline and at clinically appropriate intervals — it makes the invisible visible.
3	Fatigue is multifactorial; assess potentially reversible causes and combine appropriate disease- and symptom-directed treatment with non-pharmacological strategies.
4	Pregnancy in MPN requires pre-conception planning and shared specialist care.
5	Shared decision-making is fundamental to MPN care, helping patients and clinicians navigate complex treatment trade-offs together.
6	Living well with an MPN requires ongoing partnership between patients and the multidisciplinary team.
7	Quality of life should be assessed routinely alongside disease response.
8	Patient education is a continuous process.
9	Nurses play a central role in empowering self-management.
10	Holistic nursing care extends beyond medical treatment.
Patient Education	
1	Acknowledge that fatigue, brain fog and concentration difficulties are genuine symptoms of MPN, and discuss strategies such as pacing, appropriate physical activity and good sleep habits that may help patients manage their impact.
2	Encourage patients to become active partners in their own care and share decisions with the team: there is rarely one 'right' answer in MPN, and choices should reflect what matters most to them (work, family, fertility, treatment burden, life goals).
3	Signpost patients to appropriate national or international MPN patient organisations and peer-support resources; connecting with others living with MPN may reduce isolation and support coping.
4	Encourage patients and partners of reproductive age to discuss fertility and pregnancy plans early, so that treatment can be reviewed by the specialist team before conception where possible.
5	Encourage patients, where they wish, to bring a partner, family member or trusted friend to important consultations, especially when complex decisions about treatment or transplant are being discussed.
6	Patients should understand: • their treatment plan • symptom monitoring • medication adherence • when to contact the haematology team • importance of follow-up • lifestyle recommendations • vaccination advice • travel advice
The Haematology Nurse's Role Across the MPN Journey	
From diagnosis through treatment and long-term follow-up, the haematology nurse contributes to: • Comprehensive assessment • Patient education • Self-management support • Symptom management • Treatment monitoring • Psychosocial support • Shared decision-making • Multidisciplinary coordination • Survivorship care • Caregiver support • Promotion of quality of life	

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Appendix

List of Abbreviations

Abbreviations are spelled out in full at first use within each module. The consolidated list below is provided as a quick reference for readers.

allo-HSCT — allogeneic haematopoietic stem cell transplantation

AML — acute myeloid leukaemia

ASXL1 — additional sex combs like 1 (gene)

BD — twice daily (bis die)

BFI — Brief Fatigue Inventory

BP — blood pressure

BSH — British Society for Haematology

CALR — calreticulin

CML — chronic myeloid leukaemia

COMFORT-I/II — Controlled Myelofibrosis Study with Oral JAK Inhibitor Treatment I and II

CRP — C-reactive protein

CT — computed tomography

CV — cardiovascular

CYTO-PV — Cytoreductive Therapy in Polycythaemia Vera (trial)

DIPSS — Dynamic International Prognostic Scoring System

DOAC — direct oral anticoagulant

DVT — deep vein thrombosis

EBMT — European Society for Blood and Marrow Transplantation

ECG — electrocardiogram

ECLAP — European Collaboration on Low-dose Aspirin in Polycythaemia (trial)

EDTA — ethylenediaminetetraacetic acid

ELN — European LeukemiaNet

EORTC QLQ-C30 — European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire, Core 30 items

EPO — erythropoietin

EQ-5D — EuroQoL five-dimension health-state instrument

ESA — erythropoiesis-stimulating agent

ET — essential thrombocythaemia

EZH2 — enhancer of zeste homolog 2 (gene)

FACIT-Fatigue — Functional Assessment of Chronic Illness Therapy — Fatigue scale

FAST — Face, Arms, Speech, Time (stroke recognition tool)

FBC — full blood count

FGF — fibroblast growth factor

FGR — fetal growth restriction

FISH — fluorescence in situ hybridisation

G-CSF — granulocyte colony-stimulating factor

GIPSS — Genetics-only International Prognostic Scoring System (PMF)

Hb — haemoglobin

HBV — hepatitis B virus

HCV — hepatitis C virus

Hct — haematocrit

HIV — human immunodeficiency virus

HLA — human leukocyte antigen

HMR — high molecular risk

HNHCP — Haematology Nurses & Healthcare Professionals Group

HSCT — haematopoietic stem cell transplantation

HU — hydroxyurea (also called hydroxycarbamide)

ICC — International Consensus Classification

IDH1/2 — isocitrate dehydrogenase 1 / 2 (genes)

IL — interleukin (e.g. IL-6, IL-8)

IFN — interferon

IPSET — International Prognostic Score for Essential Thrombocythaemia

IPSS — International Prognostic Scoring System (PMF)

IWG-MRT — International Working Group for Myeloproliferative Neoplasms Research and Treatment

JAK — Janus kinase

JAK2 — Janus kinase 2

JAKARTA — JAK-inhibitor in Myelofibrosis (fedratinib trial)

JAKi — Janus kinase inhibitor

JAK–STAT — Janus kinase – signal transducer and activator of transcription

LCM — left costal margin

LDH — lactate dehydrogenase

LFT — liver function test

LMWH — low-molecular-weight heparin

MDS — myelodysplastic syndrome

MF — myelofibrosis

MI — myocardial infarction

MIPSS-ET — Mutation-Enhanced IPSS for Essential Thrombocythaemia

MIPSS-PV — Mutation-Enhanced IPSS for Polycythaemia Vera

MIPSS70 / MIPSS70+v2.0 — Mutation-Enhanced IPSS for transplant-age PMF / version 2.0

MOMENTUM — momelotinib versus danazol in MF (phase 3 trial)

MPL — myeloproliferative leukaemia virus oncogene

MPN — myeloproliferative neoplasm

MPN-RC 112 — MPN Research Consortium trial 112 (pegylated interferon)

MPN-SAF — MPN Symptom Assessment Form

MPN10 — MPN-SAF Total Symptom Score (10 items)

MRI — magnetic resonance imaging

MTSS — Myelofibrosis Transplant Scoring System

MYSEC-PM — Myelofibrosis Secondary to PV/ET Prognostic Model

NCCN — National Comprehensive Cancer Network

NGS — next-generation sequencing

NMSC — non-melanoma skin cancer

NRM — non-relapse mortality

OD — once daily (omni die)

OGD — oesophagogastroduodenoscopy

PAD — peripheral arterial disease

PE — pulmonary embolism

PERSIST-2 — pacritinib in thrombocytopenic MF (phase 3 trial)

PDGF — platelet-derived growth factor

PJP — Pneumocystis jirovecii pneumonia

PMF — primary myelofibrosis

PROMIS-29 — Patient-Reported Outcomes Measurement Information System (29-item profile)

PROUD-PV / CONTINUATION-PV — ropeginterferon trials in polycythaemia vera

PT-1 — Primary Thrombocythaemia 1 (HU vs anagrelide trial)

PV — polycythaemia vera

QoL — quality of life

RCM — red cell mass

RESPONSE / RESPONSE-2 — ruxolitinib in polycythaemia vera (trials)

RR6 — Response to Ruxolitinib at 6 months (score)

SARS-CoV-2 — severe acute respiratory syndrome coronavirus 2

SF3B1 — splicing factor 3b subunit 1 (gene)

SIMPLIFY-1 / -2 — momelotinib versus ruxolitinib / best available therapy (trials)

SIRS — systemic inflammatory response syndrome

SRSF2 — serine/arginine-rich splicing factor 2 (gene)

SSRI — selective serotonin reuptake inhibitor

STAT — signal transducer and activator of transcription

SVR35 — spleen volume reduction of ≥35% from baseline

TB — tuberculosis

TFT — thyroid function test

TGF-β — transforming growth factor beta

TNF-α — tumour necrosis factor alpha

TPO — thrombopoietin

TSS — total symptom score

U2AF1 — U2 small nuclear RNA auxiliary factor 1 (gene)

U&E — urea and electrolytes

UVB — ultraviolet B

VEGF — vascular endothelial growth factor

VKA — vitamin K antagonist (e.g. warfarin)

VTE — venous thromboembolism

vWF — von Willebrand factor

vWS — acquired von Willebrand syndrome

VZV — varicella-zoster virus

WBC — white blood cell

WHO — World Health Organization

Glossary

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) — Transplantation of donor-derived stem cells; currently the only curative treatment for myelofibrosis in selected patients.

Aquagenic pruritus — Itch precipitated by contact with water, commonly associated with polycythaemia vera; often responds poorly to antihistamines.

Blast phase — Transformation of an MPN into acute myeloid leukaemia, defined by ≥20% peripheral or bone marrow blasts.

CALR — Calreticulin gene; mutations (chiefly type-1 52-bp deletion and type-2 5-bp insertion in exon 9) are driver mutations in ET and PMF.

CYTO-PV — Trial that established a haematocrit target of <45% for cardiovascular event reduction in PV.

DIPSS / DIPSS-plus — Dynamic International Prognostic Scoring System (and karyotype-enhanced version) for myelofibrosis.

Driver mutation — JAK2, CALR or MPL mutation that contributes to constituve activation of JAK_STAT signalling in classical MPNs.

ET — Essential thrombocythaemia — an MPN characterised by sustained thrombocytosis.

GIPSS — Genetics-only International Prognostic Scoring System for PMF, based on karyotype, driver type and HMR mutations.

HMR mutations — 'High molecular risk' mutations — ASXL1, EZH2, IDH1/2, SRSF2, U2AF1 (Q157) — associated with adverse prognosis in MF.

IPSET / Revised IPSET-Thrombosis — International Prognostic Score for ET (survival) and the revised thrombosis-risk score used to direct first-line treatment.

JAK2 V617F — G-to-T point mutation in exon 14 of JAK2 producing a valine-to-phenylalanine substitution at codon 617; the commonest driver mutation across MPN.

JAK–STAT pathway — Janus kinase–signal transducer and activator of transcription pathway; constitutively activated in MPN.

Leukoerythroblastic film — Peripheral blood film showing immature granulocytic and erythroid cells; characteristic of myelofibrosis.

MIPSS70 / MIPSS70+v2.0 — Mutation- and karyotype-enhanced international prognostic scoring systems for transplant-age PMF.

MPL — Myeloproliferative leukaemia virus oncogene; mutations (notably W515L/K) drive a minority of ET and PMF cases.

MPN-SAF (MPN10) — Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score; 10-item patient-reported outcome scored 0–100.

MYSEC-PM — Myelofibrosis Secondary to PV/ET prognostic model used for risk stratification in post-PV/ET myelofibrosis.

Pre-fibrotic PMF — Early phase of PMF that may clinically resemble ET but has distinct bone marrow features and prognosis.

PMF — Primary myelofibrosis.

Polycythaemia vera (PV) — JAK2-mutated MPN with sustained erythrocytosis; can transform to post-PV myelofibrosis.

Post-PV / post-ET myelofibrosis — Secondary myelofibrosis evolving from antecedent PV or ET; diagnosed using IWG-MRT criteria.

Reticulin / collagen fibrosis (MF-0 to MF-3) — European consensus grading system for marrow fibrosis.

Ropeginterferon alfa-2b — Long-acting monopegylated interferon used in the treatment of polycythaemia vera.

SVR35 — Spleen volume reduction of ≥35% from baseline; a commonly used efficacy endpoint in MF clinical trials, often assessed at week 24.

Triple-negative — MPN without detectable JAK2, CALR or MPL mutations; in PMF associated with poorer prognosis.

Selected online resources and guidelines

- Haematology Nurses & Healthcare Professionals Group (HNHCP) — hemcare.org
- British Society for Haematology guidelines on PV, ET and MF — b-s-h.org.uk/guidelines
- European LeukemiaNet — leukemia-net.org/physicians/recommendations
- NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms — nccn.org
- Pan-London MPN Guidelines — rmpartners.nhs.uk
- Greater Manchester Cancer Network MPN Guidelines — gmcancer.org.uk
- MPN Advocates Network (MPN AN) – international patient advocacy and support network
- MPN Schweiz – Swiss patient support and self-help organisation for people living with MPN and their families
- MPN Voice (UK patient charity) — mpnvoice.org.uk
- MPN Alliance Australia — mpnallianceaustralia.org.au/understanding-mpn/mpn-guidelines
- MPN Research Foundation — mpnresearchfoundation.org

Additional national MPN patient organisations and support groups can be found through the MPN Advocates Network.

Consolidated bibliography (Harvard style)

Per-section Harvard references appear at the end of each module. The list below consolidates the principal sources used across the programme.

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