Persistent Infectious and Thrombotic Co-Mortality in Myeloproliferative Neoplasm–Associated Deaths: A National Multiple-Cause-of-Death Analysis, 2003–2024

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INTRODUCTION

- Thrombosis has long been recognized as the primary vascular threat and therapeutic focus in myeloproliferative neoplasms (MPNs).
- Disease progression, cumulative treatment-associated immunosuppression, and the widespread adoption of targeted pathway inhibitors (such as JAK inhibitors approved in 2011) have increasingly shifted the infectious risk profile in this population.
- Despite established guidelines prioritizing antithrombotic management, population-level trends comparing terminal infectious complications directly against thrombotic events remain poorly characterized.

AIM

Primary Aim: Quantify and compare nationwide 22-year trajectories (2003–2024) of terminal infection versus thrombosis co-mention among MPN decedents.

Secondary Aim: Evaluate longitudinal shifts across pre-targeted (2003–2011) vs. post-targeted (2012–2024) eras and assess subtype-specific trends (e.g., sepsis vs. PE).

METHOD

Data Source: CDC WONDER / NCHS Multiple Cause of Death records (2003–2024) identifying all MPN decedents (underlying or contributing ICD-10 codes).

Outcomes: Annual proportion of deaths co-mentioning **Infection** (sepsis, pneumonia, fungal) vs. **Thrombosis** (acute MI, stroke, PE, venous thrombosis).

Analysis: Multivariable and piecewise logistic regression (inflection knot at 2011) comparing pre- (2003–2011) vs. post-targeted (2012–2024) eras.

CONCLUSIONS

Disproportionate Infectious Burden: Terminal infection was documented **>2-fold more frequently** than thrombosis across all 22 years (~14–15% vs. ~6%).

Post-2011 Inflection: Following the introduction of targeted therapies, infection risk exhibited a significant upward inflection (OR 1.03/year post-2011, $p < 0.001$), led by rising sepsis.

Clinical Implication: While MPN paradigms prioritize antithrombotic prevention, infectious morbidity represents a far greater terminal mortality contributor—warranting aggressive infection surveillance, vaccination protocols, and vigilance during targeted therapy.

RESULTS

Overall Cohort (N = 56,296): Identified 22,866 MPN decedents in the pre-targeted era (2003–2011) and 33,430 in the modern era (2012–2024).

Infection vs. Thrombosis Burden: Terminal infection was documented more than twice as often as thrombosis in both eras (15.1% vs. 6.0% pre-2012; 13.7% vs. 6.3% modern era; ratio **2.52:1** and **2.17:1**).

Temporal Trajectories & Inflection:
Linear infection rates initially trended downward, but exhibited a significant upward inflection after 2011 (piecewise post-2011 OR **1.030** per year, 95% CI 1.014–1.047, $p < 0.001$).
Thrombosis rates also shifted from flat pre-2012 to a slight upward trajectory post-2011 (OR **1.025** per year, 95% CI 1.001–1.049, $p = 0.042$).

Subtype Shifts: Across eras, sepsis increased from 7.8% to **8.5%** and fungal infections doubled (0.23% to **0.45%**), while pneumonia decreased (8.5% to 6.6%). Among thrombotic causes, acute MI fell (3.1% to 2.5%) while pulmonary embolism rose (1.7% to **2.1%**).

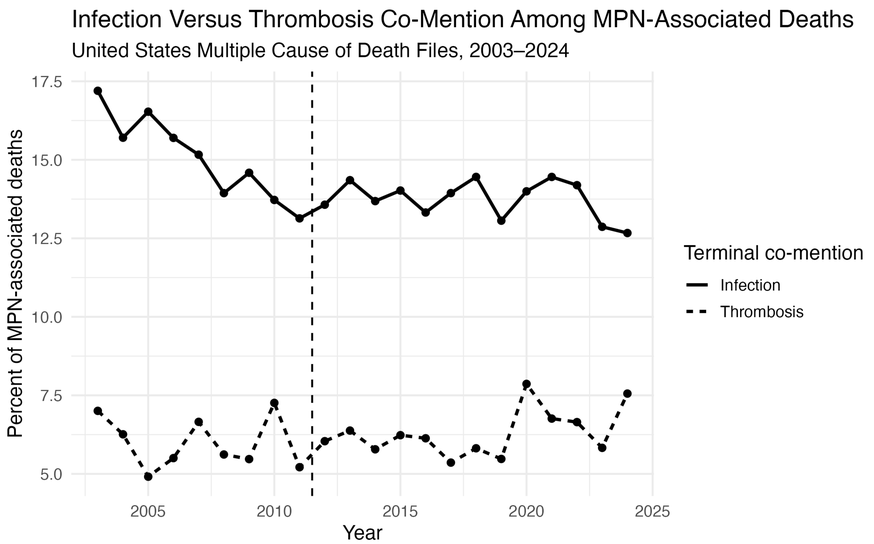

Figure 1. Longitudinal Trends in Terminal Infection Versus Thrombosis Co-Mention Among MPN-Associated Deaths (2003–2024). Annual proportions of decedents with myeloproliferative neoplasms (MPNs) co-mentioning infectious conditions (solid line) versus thrombotic events (dashed line) from the CDC WONDER/NCHS Multiple Cause of Death files. Dashed vertical line at 2011 denotes the introduction and FDA approval of targeted JAK inhibitor therapy (ruxolitinib). Terminal infection consistently exceeded thrombosis co-mention across the entire 22-year study period.

ACKNOWLEDGEMENTS

The authors appreciate the generous support of their affiliated institutions.

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