

Rising AML- and MDS-Associated Mortality Among Decedents With Multiple Myeloma in the United States, 2003–2024

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INTRODUCTION

- Therapeutic advances—including immunomodulatory drugs (IMiDs), proteasome inhibitors, anti-CD38 monoclonal antibodies, and autologous stem cell transplantation—have dramatically extended survival for patients with multiple myeloma (MM).
- Prolonged survival, cumulative exposure to DNA-damaging and alkylating therapies, and long-term maintenance strategies have expanded the cohort at risk for therapy-related myeloid neoplasms.
- Nationwide longitudinal trends in terminal acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) co-mortality among MM decedents remain incompletely characterized across modern therapeutic eras.

AIM

- Primary Aim:** Quantify national 22-year longitudinal trends (2003–2024) in AML/MDS co-mention among MM-associated decedents in the United States.
- Secondary Aim:** Evaluate trajectory inflection points across early (2003–2015) vs. contemporary (2016–2024) eras following the expanded adoption of continuous maintenance regimens and novel antibody therapies.

METHOD

Data Source: CDC WONDER / NCHS Multiple Cause of Death public-use files (2003–2024).

Cohort & Outcome Definitions: MM decedents identified via ICD-10 code C90.0 in underlying or contributing fields. Secondary myeloid neoplasms defined by co-mention of AML (C92.0) or MDS (D46.x).

Statistical Analysis: Binomial logistic regression modeling annual odds across 2003–2024 and piecewise regression with an inflection knot at 2015 comparing early vs. modern eras.

CONCLUSIONS

Secondary myeloid neoplasms (AML/MDS) represent an **escalating contributor to mortality** among patients dying with multiple myeloma in the United States.

The marked acceleration after 2015 highlights how improved longevity and cumulative therapeutic exposures have altered the survivorship landscape, emphasizing the need for proactive cytopenia monitoring, bone marrow surveillance, and long-term clonal hematopoiesis tracking in myeloma care

RESULTS

National Cohort Expansion: Annual MM-associated deaths rose from 12,671 (2003) to 14,730 (2024), while annual deaths co-mentioning AML/MDS nearly doubled from **112 to 220**.

Overall 22-Year Trajectory: The proportion of MM deaths with AML/MDS co-mention increased from **0.88% in 2003 to 1.49% in 2024** (Overall OR **1.020**/yr, 95% CI 1.014–1.026, $p = 1.89 \times 10^{-11}$).

Post-2015 Acceleration: Prevalence was stable through 2015 (0.88% in 2003 to 0.85% in 2015; OR 1.016/yr, $p = 0.022$).

Piecewise modeling demonstrated a significant upward inflection after 2015 (slope-change OR **1.027**, 95% CI 1.003–1.051, $p = 0.027$), with an era slope of OR **1.052**/yr (95% CI 1.031–1.074, $p < 0.001$) through 2024.

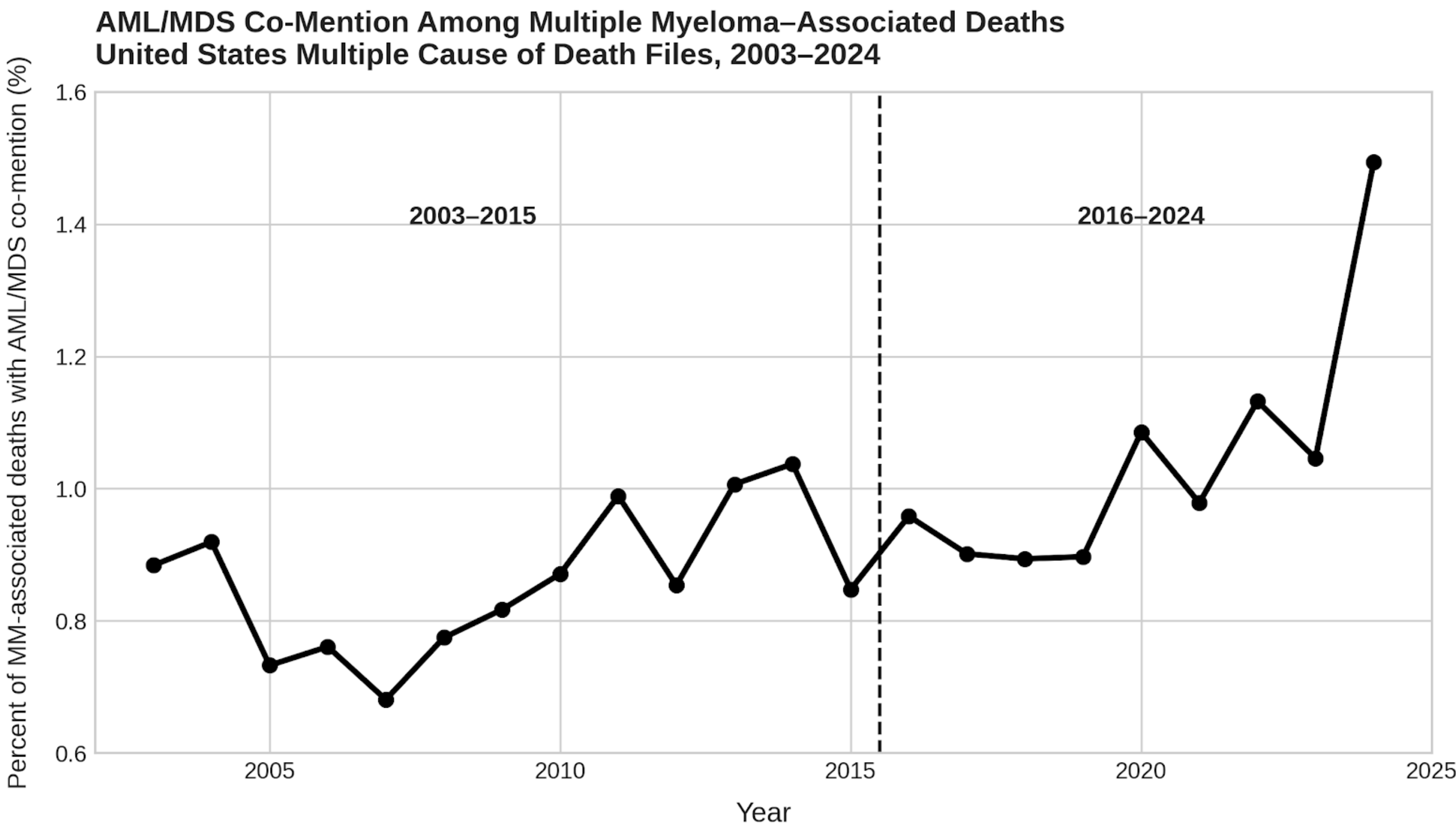
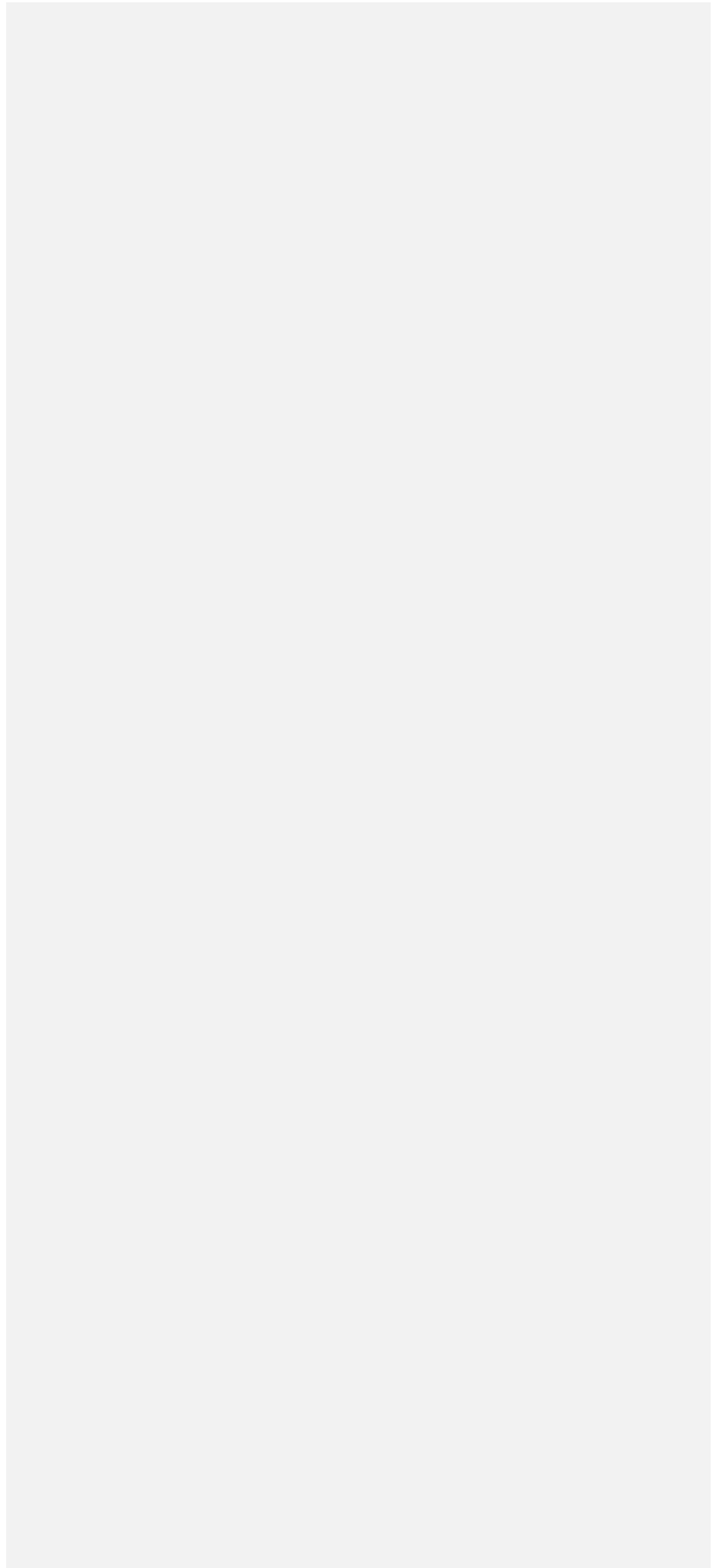


Figure 1. 22-Year National Trajectory of AML/MDS Co-Mention Among Multiple Myeloma Decedents (2003–2024). Annual proportions of nationwide MM-associated deaths co-mentioning acute myeloid leukemia (AML) or myelodysplastic syndromes (MDS) from NCHS Multiple Cause of Death records. Dashed vertical line at 2015 denotes the piecewise inflection knot. While AML/MDS co-mention remained stable (~0.85%) during 2003–2015, it increased sharply in the modern era, reaching 1.49% of all MM-associated deaths in 2024.

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