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REVEAL-MM: Retrospective Evaluation of Variables in Early Assessment and Landmark trends in Multiple Myeloma – a US Claims-Based Case-Control Study

Faith E Davies, MD, MBBCh, MRCP, FRCPath[1], Beth Faiman, PhD, MSN, FAAN, FAPO[2], Hayley Beer, RN, BN[3,4], Anne Quinn Young, MPH[5], Katie Joyner[6], Kate Morgan[6], Stephen Huo, PhD[7], J Blake Bartlett, PhD[8], Yi Han, PhD[9], Georgia Attfield, MPharm, NMP[9], Daniel Egbase PhD[9], Joseph Mikhael, MD, MEd, FRCPC, FACP[10,11]

[1]Center for Blood Cancers, NYU Langone Health, New York; [2]Cleveland Clinic, Ohio, United States; [3]Peter MacCallum Cancer Centre, Melbourne, Australia; [4]Myeloma Australia, Victoria, Australia; [5]Multiple Myeloma Research Foundation, Connecticut, United States; [6]Myeloma Patients Europe, Brussels, Belgium; [7]Janssen Research & Development, Titusville, New Jersey., [8]Janssen Global Services, LLC, Raritan, New Jersey, United States; [9]VML Health, London, United Kingdom; [10]Translational Genomics Research Institute, City of Hope Cancer Center, Arizona, USA; [11]International Myeloma Foundation, California, USA

Key Takeaway

Distinct healthcare encounter patterns emerge up to a year before an initial MM diagnosis, suggesting opportunities to identify patients earlier in the disease course.

Conclusions

- Pre-diagnostic signals such as anemia, other cytopenias, and musculoskeletal pain were consistently more common among patients who were later diagnosed with MM.
- Unexpected associations with GERD and cardiovascular disorders also emerged, warranting further investigation as potential early indicators or markers of diagnostic complexity.
- Higher frequencies of vaccination-related codes in the control cohort highlight the need to consider care-setting differences, coding practices, and other confounding factors when interpreting claims-based data.
- Future work will focus on validating results and applying risk models to identify combinations of encounter descriptors that may predict MM diagnosis.

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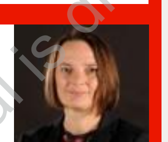

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Disclosures
FD has served on advisory boards and provided consultancy to GlaxoSmithKline, Sanofi, Bristol Myers Squibb, Regeneron, Johnson & Johnson, and Takeda. BF has served in a consulting or advisory role for Johnson & Johnson. HB has served in a consulting or advisory role for Johnson & Johnson. AQY has served in a consulting or advisory role for Johnson & Johnson. KJ has served in a consulting or advisory role for Johnson & Johnson. KM has served in a consulting or advisory role for Johnson & Johnson. SH and BB are employees of Johnson & Johnson and hold stock and/or stock options in the company. YH has provided consultancy for Johnson & Johnson. GA and DE are employees of VML Health and supported the development of this poster. JM has provided consultancy for Sanofi, Bristol Myers Squibb, Johnson & Johnson, and Menarini.

Introduction

Multiple myeloma (MM) remains challenging to diagnose in a timely manner due to its broad spectrum of non-specific symptoms,[1] often resulting in diagnostic delays or mis-referrals to non-hematology specialists, including primary care physicians, nephrologists, orthopedic surgeons, or rheumatologists.[2]

Compared to other cancers, MM has one of the highest proportions of patients requiring more than three consultations before specialist referral.[3] Such delays are not benign; they are associated with secondary complications, higher disease stage at diagnosis, reduced disease-free survival, and poorer quality of life.[4,5]

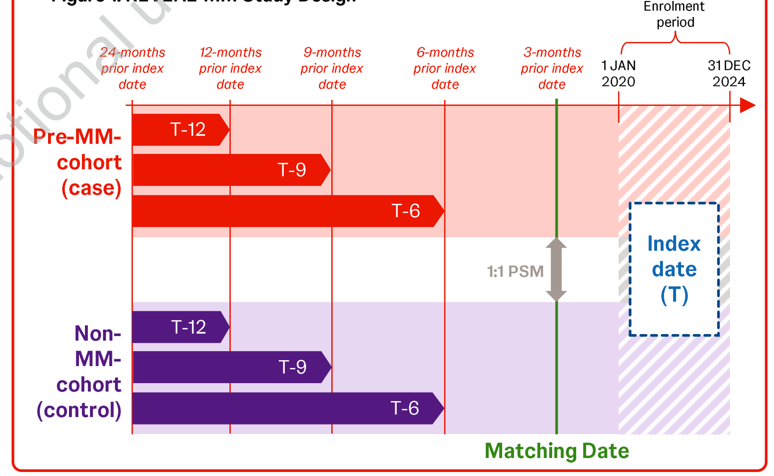
Claims databases offer an opportunity to identify recurring encounter patterns that may serve as early warning signals.

Methodology

REVEAL-MM is a retrospective case–control study using de-identified Optum Clinformatics Data Mart (CDM) claims to compare healthcare utilization (diagnostic, procedure, prescription, and physician visit codes) between patients later diagnosed with MM (pre-MM cohort) and matched controls in the two years before MM diagnosis.

- The pre-MM cohort included adults aged ≥50 years with a confirmed MM diagnosis between Jan 1, 2020, and Jan 31, 2024, defined by at least two MM-coded claims (ICD-10 C90.x or ICD-9 203.x) ≥30 days apart. Patients needed ≥24 months of prior continuous data coverage prior to their first MM diagnosis (the index date) and were excluded if they had any malignant cancer diagnosis or monoclonal gammopathy of undetermined significance (MGUS) during the study period.
- The control cohort comprised adults aged ≥50 years without an MM diagnosis during the study period, matched 1:1 via propensity score matching (PSM) on age, gender, race, region, insurance type, Charlson Comorbidity Index (CCI), and National Cancer Institute Comorbidity Index (NCI) scores assessed three months prior to the index date. Covariate balance was achieved with standardized mean differences below 0.1.
- Medical history was captured from 24 months prior to the index date, with encounter descriptors calculated at 12, 9, and 6 months before diagnosis (**Figure 1**). Codes have not been copied across verbatim but instead presented in expanded text form to improve clarity and interpretability. Diagnostic, procedural, and prescription codes were grouped into clinically meaningful categories, and physician visits were categorized by specialty. Between-group comparisons used Wilcoxon tests and chi-square tests, applying Bonferroni adjustment for multiple comparisons. Analyses at T-6, T-9, and T-12 pre-index were conducted, but only codes or code groups statistically significant at the earliest timepoint assessed (T-12 pre-index) are displayed.

Figure 1: REVEAL-MM Study Design



Results

The pre-MM cohort (n=4,733) and control cohort (n=4,733) were balanced, with a mean age of 74.1 years, 50% male, 51% White, and 45% residing in the US South Census Region. Medicare was the primary insurer for 86% of patients. Mean NCI scores were 0.71 (pre-MM) vs. 0.67 (control), and CCI scores 2.29 vs. 2.18, respectively (**Table 1**).

Table 1: Baseline characteristics of the study population

		Overall	Pre-MM cohort	Non-MM cohort
n		9466	4733	4733
		Mean (SD)	Mean (SD)	Mean (SD)
Age		73.96 (8.25)	74.10 (8.14)	73.81 (8.36)
CCI		2.24 (2.33)	2.29 (2.29)	2.18 (2.36)
NCI*		0.69 (0.73)	0.71 (0.72)	0.67 (0.73)
		Count (%)	Count (%)	Count (%)
Gender	Female	4,717 (50%)	2,360 (50%)	2,357 (50%)
	Male	4,744 (50%)	2,370 (50%)	2,374 (50%)
	Undisclosed	5 (<0.1%)	3 (<0.1%)	2 (<0.1%)
Race	White	4,847 (51%)	2,419 (51%)	2,428 (51%)
	Asian	205 (2.2%)	104 (2.2%)	101 (2.1%)
	Black	1,579 (17%)	786 (17%)	793 (17%)
	Undisclosed	298 (3.1%)	149 (3.1%)	149 (3.1%)
	Other	2,537 (27%)	1,275 (27%)	1,262 (27%)
Region	Midwest	1,858 (20%)	938 (20%)	920 (19%)
	Northeast	1,360 (14%)	673 (14%)	687 (15%)
	South	4,278 (45%)	2,149 (45%)	2,129 (45%)
	West	1,956 (21%)	966 (20%)	990 (21%)
	Other	14 (0.1%)	7 (0.1%)	7 (0.1%)
Insurance Type	COM	1,290 (14%)	624 (13%)	666 (14%)
	MCR	8,176 (86%)	4,109 (87%)	4,067 (86%)

* Statistically significant after Bonferroni multiplicity adjustment
** All SMD values for age, CCI, NCI, gender, race, region and insurance type were within -0.1, 0.1 and therefore were regarded as good match

Diagnostic codes

Distinct differences in diagnostic coding emerged as early as 12 months prior to MM diagnosis (**Table 2**). Anemia-related codes, including iron deficiency anemia, anemia of chronic disease, and unspecified anemia, were significantly more prevalent in the pre-MM cohort (29%) compared to controls (18%, p<0.001). Cytopenias, including pancytopenia and neutropenia, also appeared more frequently in pre-MM patients from the 12-month mark onward (p<0.001).

Musculoskeletal complaints, particularly low back pain and osteoarthritis, were more common among pre-MM patients, reflecting the disease's hallmark symptoms. Interestingly, several diagnostic codes not directly related to MM criteria, such as gastroesophageal reflux disease (GERD) with esophagitis (1.7% vs. 0.6%, p<0.001) and cardiovascular disorders (chronic atrial fibrillation and unspecified cardiac murmurs) were also more prevalent in the pre-MM cohort (5.4% vs. 2.9%, p<0.001).

Table 2: Comparative distribution of diagnostic codes

Variable	Claim code or code group description	Overall No. of claims (% of cohort)	Pre- MM cohort No. of claims (% of cohort)	Non-MM cohort No. of claims (% of cohort)	T-6M: p<0.001	T-9M: p<0.001	T-12M: p<0.001
DX_Group1	Anemias	2,243 (24%)	1,387 (29%)	856 (18%)	✓	✓	✓
DX_D61818	Other pancytopenia	112 (1.2%)	93 (2.0%)	19 (0.4%)	✓	✓	✓
DX_Group2	Neutropenia	235 (2.5%)	182 (3.8%)	53 (1.1%)	✓	✓	✓
DX_Group3	Musculoskeletal pain	2,396 (25%)	1,326 (28%)	1,070 (23%)	✓	✓	✓
DX_K210	Gerd with esophagitis	112 (1.2%)	82 (1.7%)	30 (0.6%)	✓	✓	✓
DX_Group4	Cardiovascular disorders	394 (4.2%)	257 (5.4%)	137 (2.9%)	✓	✓	✓

Only codes or code groups reaching statistical significance as early as the T12 pre-index pool are shown. Red data denote the greater value between cohorts. ✓ indicates statistical significance (p < 0.05) between both cohorts across the T6, T9, or T12 pre-index timepoints. Anemias group codes: Iron-deficiency anemia due to chronic blood loss, Iron-deficiency anemia, unspecified, Nutritional anemia, unspecified, Anemia in other chronic disease classified elsewhere, Anemia, unspecified; Neutropenia group codes: Neutropenia, unspecified, Low/↓ white blood cell count, unspecified; Musculoskeletal pain group codes: Osteoarthritis, unspecified site, Low back pain, Low back pain, unspecified; Cardiovascular disorders group codes: Chronic atrial fibrillation, Cardiac murmur, unspecified.

Prescription codes

Differences in prescription codes were also observed (**Table 3**). The non-MM cohort had significantly higher frequencies of antiviral (nirmatrelvir/ritonavir) prescription claims and COVID-19–related vaccine claims prior to the index date.

Table 3: Comparative distribution of prescription codes

Variable	Claim code or code group description	Overall No. of claims (SD)	Pre- MM cohort No. of claims (SD)	Non-MM cohort No. of claims (SD)	T-6M: p<0.001	T-9M: p<0.001	T-12M: p<0.001
GNM_00798	Nirmatrelvir/ Ritonavir	0.03 (0.18)	0.02 (0.15)	0.04 (0.20)	✓	✓	✓
GNM_Group1	COVID Vaccine	0.18 (0.43)	0.13 (0.38)	0.22 (0.46)	✓	✓	✓

Only codes or code groups reaching statistical significance as early as the T12 pre-index pool are shown. Red data denote the greater value between cohorts. ✓ indicates statistical significance (p < 0.05) between both cohorts across the T6, T9, or T12 pre-index timepoints. COVID Vaccine: COVID vaccine 23–24 (12+ yrs) Andu Preservative-free (PF), COVID vaccine 23–24 (12+ yrs) Raxt PF, COVID-19 vaccine, TRIS Pfizer PF, COVID-19 mRNA vaccine (Moderna), PF

Healthcare provider (HCP) visit codes

Patterns of healthcare utilization varied notably between cohorts (**Table 4**). The pre-MM cohort demonstrated increased visit frequency with cardiology, hematology/oncology, and pathology specialists. In contrast, the non-MM cohort had more frequent visits with other non-physician providers and registered nurse practitioners.

Table 4: Comparative distribution of HCP visit codes

Variable	Claim code description	Overall Mean No. of claims (SD)	Pre- MM cohort Mean No. of claims (SD)	Non-MM cohort Mean No. of claims (SD)	T-6M: p<0.001	T-9M: p<0.001	T-12M: p<0.001
HCP_00009	Cardiology	3.32 (8.14)	3.66 (8.70)	2.99 (7.53)	✓	✓	✓
HCP_00030	Hematology & oncology	0.62 (4.41)	0.97 (5.74)	0.28 (2.39)	✓	✓	✓
HCP_00055	Other non-physician provider	0.95 (3.87)	0.75 (3.32)	1.14 (4.34)	✓	✓	✓
HCP_00058	Pathology	0.22 (1.11)	0.28 (1.31)	0.17 (0.85)	✓	✓	✓
HCP_00077	Registered nurse - practitioner	1.41 (5.19)	1.17 (4.59)	1.64 (5.72)	✓	✓	✓

Only codes or code groups reaching statistical significance as early as the T12 pre-index pool are shown. Red data denote the greater value between cohorts. ✓ indicates statistical significance (p < 0.05) across the T6, T9, or T12 pre-index timepoints. HCP - Healthcare professional; SD - standard deviation

Procedure codes

The pre-MM cohort was significantly more likely to have procedure codes consistent with a MM workup (anemia, plasma cell disorder workup, metabolic panel, among others). Unexpectedly, higher frequencies of EGD biopsy and intermediate ophthalmology examinations for established patients were also observed (**Table 5**). Higher rates of vaccination administration codes were identified in the control cohort.

Table 5: Comparative distribution of procedure codes

Variable	Claim code or code group description	Overall Mean No. of claims (SD)	Pre- MM cohort Mean No. of claims (SD)	Non-MM cohort Mean No. of claims (SD)	T-6M: p<0.001	T-9M: p<0.001	T-12M: p<0.001
PROC_1126F	Amount of pain assessed- none present	0.15 (0.81)	0.13 (0.69)	0.18 (0.92)	✓	✓	✓
PROC_Group1	Anemia workup	1.20 (3.61)	1.54 (4.22)	0.86 (2.83)	✓	✓	✓
PROC_83883	Nephelometry assay - not specified	0.03 (0.35)	0.05 (0.48)	0.01 (0.13)	✓	✓	✓
PROC_Group2	Bone Marrow and Cytogenetics	0.84 (3.02)	1.07 (3.96)	0.61 (1.57)	✓	✓	✓
PROC_Group3	COVID-19 Related Diagnostics	0.62 (3.44)	0.73 (3.36)	0.50 (3.52)	✓	✓	✓
PROC_43239	EGD biopsy single/multiple	0.12 (0.52)	0.14 (0.58)	0.09 (0.46)	✓	✓	✓
PROC_Group4	Established Patient Office Visits/Routine or follow-up outpatient care	9.26 (8.67)	9.90 (8.93)	8.62 (8.35)	✓	✓	✓
PROC_Group5	Identification, quantification, and typing of M-proteins and immunoglobulins	0.39 (2.04)	0.58 (2.68)	0.19 (1.02)	✓	✓	✓
PROC_88342	Immunochem/cytochem first antibody	0.12 (0.59)	0.16 (0.72)	0.08 (0.43)	✓	✓	✓
PROC_92012	Interim ophthalmic exam, established pt	0.21 (0.97)	0.25 (1.13)	0.17 (0.77)	✓	✓	✓
PROC_83550	Iron-binding test	0.32 (1.22)	0.41 (1.35)	0.24 (1.06)	✓	✓	✓
PROC_1159F	Medication list documented in record	0.47 (1.64)	0.37 (1.42)	0.57 (1.83)	✓	✓	✓
PROC_Group6	Metabolic panel	2.83 (4.84)	3.19 (6.03)	2.47 (3.19)	✓	✓	✓
PROC_Group7	Nursing Facility or Long-Term Care Visits	0.55 (4.53)	0.32 (3.41)	0.77 (5.42)	✓	✓	✓
PROC_Group8	Observation or Inpatient Transitional Care	0.09 (0.48)	0.12 (0.52)	0.06 (0.42)	✓	✓	✓
PROC_Group9	Peripheral Blood Analysis	3.71 (7.19)	4.21 (8.02)	3.22 (6.22)	✓	✓	✓
PROC_Group10	Routine monitoring	1.36 (3.83)	1.15 (3.48)	1.57 (4.14)	✓	✓	✓
PROC_88313	Special stains – group 2	0.07 (0.54)	0.11 (0.72)	0.03 (0.28)	✓	✓	✓
PROC_Group12	Vaccination administration	0.51 (1.06)	0.59 (1.22)	0.42 (0.86)	✓	✓	✓

Only codes or code groups reaching statistical significance as early as the T12 pre-index pool are shown. Red data denote the greater value between cohorts. ✓ indicates statistical significance (p < 0.05) across the T6, T9, or T12 pre-index timepoints. Identification, quantification, and typing of M-proteins and immunoglobulins: IgA/IgD/IgG/IgM assay - each, Quantitative immunoassay, NOS, non-antibody, Serum immunofixation electrophoresis, Immunofixation electrophoresis - urine/CSF, Serum protein electrophoresis, Protein electrophoresis - urine/CSF, Serum protein assay; Anemia workup: Ferritin assay, Iron assay, Transferrin assay, Erythropoietin assay, Quant haptoglobin assay, Serum folate assay, Automated retic count; Bone marrow and cytogenetics: Bone marrow biopsy & aspiration, Flow cytometry, 1 marker, Flow cytometry add-on, Flow cytometry read, ≥16 markers, Bone marrow tissue culture, Bone marrow pathology interpretation, Pathologist tissue exam, Decalcify tissue; Peripheral blood analysis: Blood smear + diff WBC count, CBC + automated WBC diff, Blood smear interpretation, Prothrombin time, RBC sed rate - manual, Partial thromboplastin time; Metabolic panel: Comprehensive metabolic panel, LD/LDH enzyme; COVID-19 related diagnostics: SARS-CoV-2 antibody test, SARS-CoV-2 diagnostic test, Specimen collection - SARS-CoV-2, COVID NAAT amplification, Specimen collection - any source, Nucleic acid detection, SARS-CoV-2 test - any type; Established patient office visits/routine or follow-up outpatient care: Office/OP visit - est may req MD/QHP, Office visit - est low 20-min, Office visit - est mod, 30-min; Nursing facility or long-term care visits: Initial NF care - moderate MDM 35-min, Subsequent NF care - low MDM 20-min, Subsequent NF care - moderate MDM 30-min; Routine monitoring: Systolic BP <130 mmHg, Diastolic BP <80 mmHg, Medication review by prescriber/record; Vaccination administration: Pneumococcal vaccine given & documented, High-dose inactivated flu vaccine, no preservative - IM,PCV13 pneumococcal conjugate vaccine – IM, PCV20 pneumococcal conjugate vaccine - IM, Quadrivalent split IIV flu vaccine 0.5 mL IM, PPSV23 pneumococcal vaccine (age ≥ 2) - SQ/IM, Influenza vaccine administration

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Multiple Myeloma

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