The Impact of the SARS-CoV-2 Pandemic (COVID-19) on the Incidence of Newly Diagnosed Multiple Myeloma Patients Using a Federated Network of Real-World Evidence in US and Germany

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INTRODUCTION

- COVID-19 had an impact on the access to healthcare [1], and delays in referrals resulting in late diagnoses, both in Europe and the US [2, 3].
- Early diagnosis of MM is a critical factor for prognosis [4].
- Annual incidence of MM expected to increase with aging demographics [5]. A significant deviation from this trend would indicate many patients going undiagnosed.

OBJECTIVES

- To assess the impact of COVID-19 on NDMM patients, we investigated the incidence and clinical characteristics (with a focus on the SLiM-CRAB diagnostic characteristics) of NDMM patients in the US and in Germany.

METHODS

- 44,162 NDMM patients were identified in TriNetX federated network across 55 healthcare organizations in the US between January 2018 and December 2021.
- 4,172 NDMM patients were identified in the German TherapyMonitor Multiple Myeloma (TM MM) curated registry database from >100 healthcare centers during the same time period.
- Each database was stratified into two cohorts before and after the start of the COVID-19 pandemic in March 2020 (Table 1).
- Pearson chi-squared bivariate comparison of a selection of clinical and diagnostic characteristics, with a focus on SLiM-CRAB multiple myeloma diagnostic criteria, was performed between the two cohorts for the US and German data.

Table 1. Measures of Association table showing outcome of cesarean deliveries.

	US (TriNetX)	Germany (TM MM)
Cohort 1 (diagnosis between 01/2018 – 02/2020)	25,513	2,252
Cohort 2 (diagnosis between 03/2020 – 12/2021)	18,651	1,920

RESULTS

- The annual NDMM incidence declined to 9,184 in 2020 compared to 11,263 and 11,286 in 2018 and 2019, respectively, across the TriNetX federated network (Figure 1). This decrease puts the 2020 incidence below the lower standard deviation for the time period.
- In the TM MM German registry, the 2020 annual incidence was reported as 1,054, comparable to the median for the time period (1,191). However, it starts a decline in NDMM annual incidence which continued into 2021, with 742 (Figure 2).
- Bivariate analysis of the US data revealed that NDMM patients in Cohort 2 have a significantly higher risk profile compared with patients in Cohort 1, higher incidence of renal failure (13.5% v. 15.43%), heart failure (10.3% v 11.26%), bone lesions (12.6% v. 13.05%) and anemia (26.8% v. 29.75%) (Table 2). The US data was limited by certain characteristics having low coverage (i.e., ECOG).
- The German data indicated an increased risk profile in Cohort 2, with higher reporting of renal impairment (12.3% v. 15.5%) and cardiac impairment (8.3% v. 10.9%). The higher risk profile was reflected in a significant increase of all SLiM-CRAB criteria, notably hypercalcemia (24.1 % v. 36.9%), bone marrow plasma cell infiltration (28.1% v. 36.8%) and free light chain involvement (27.3% v. 41.3%) (Table 3).

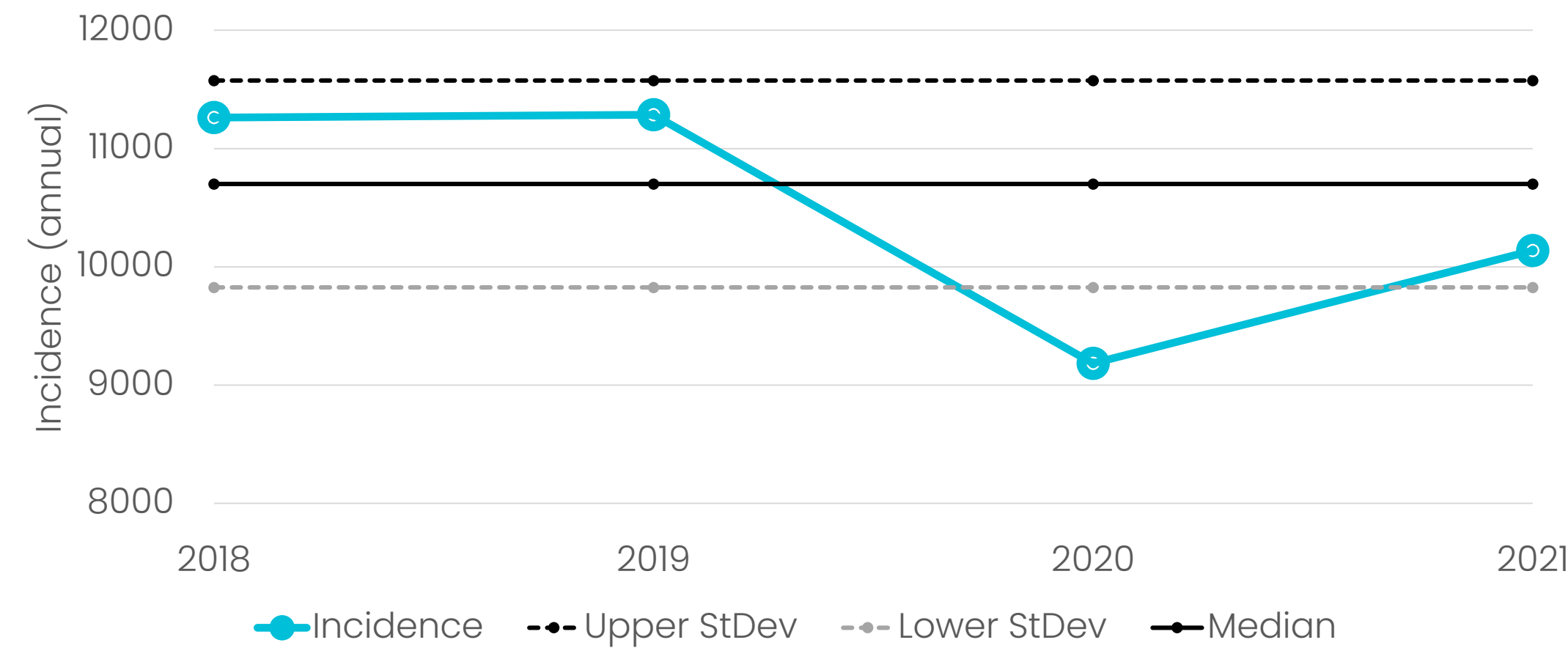**Figure 1**. Annual incidence of NDMM in the TriNetX Network (US).

Table 2. Select patient characteristics with Pearson chi-squared 2x2 analysis of NDMM patients identified in the TriNetX Network (US).

	Cohort 1 (Jan 2018 – Feb 2020)	Cohort 2 (Mar 2020 – Dec 2021)
Age <=70	62.1% (15,246)	59.86% (10,555)
ECOG <2	2.2% (542)	3.20% (565)
Renal failure	13.5% (3,311)	15.43% (2,720)
Cardiomyopathy	3.2% (796)	3.31% (583)
Heart failure	10.3% (2,527)	11.26% (1,985)
Heart complications	7.2% (1,769)	7.24% (1,277)
Cardiac impairment	15.1% (3,717)	15.91% (2,805)
Bone lesions	12.6% (3,085)	13.05% (2,301)
Anemia	26.8% (6,570)	29.75% (5,246)

⬆ Significant result above difference to complementary group
⬇ Significant result below difference to complementary group

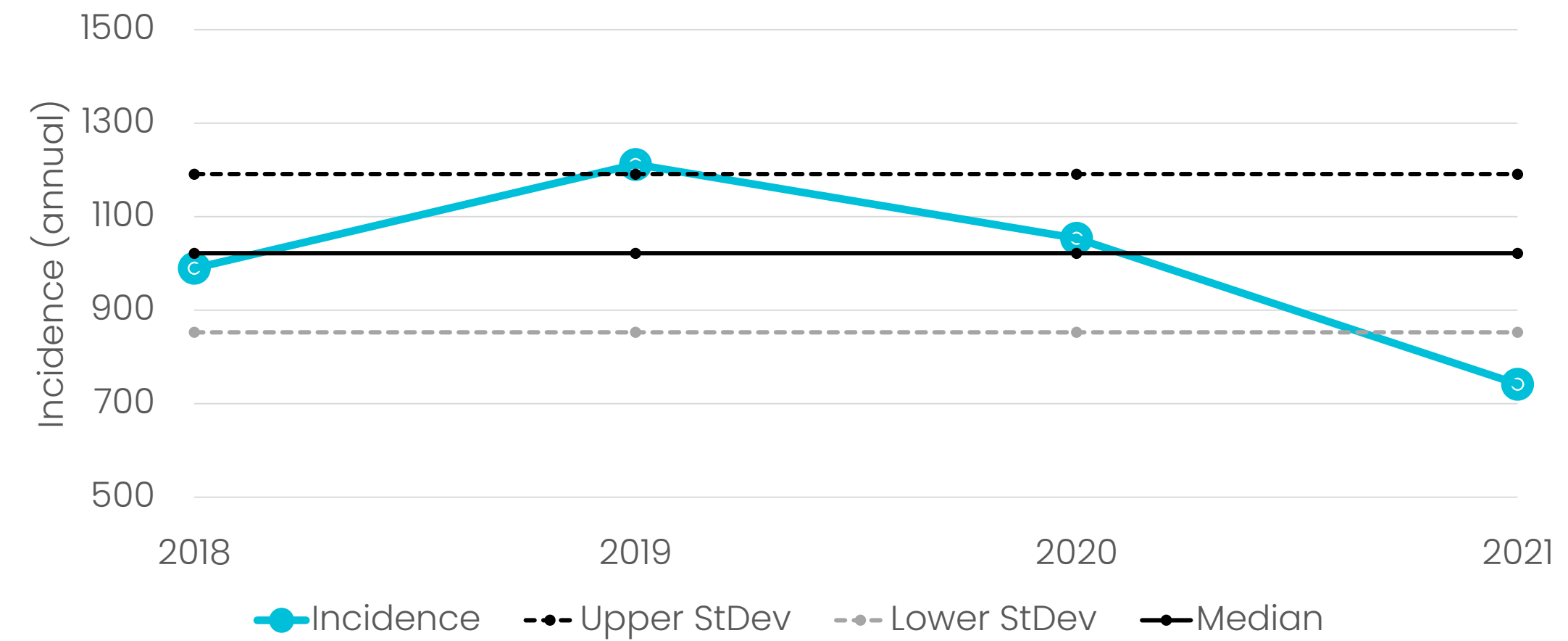**Figure 2**. Annual incidence of NDMM in the TherapyMonitor MM registry (Germany).

Table 2. Select patient characteristics of NDMM patients in the TM MM registry (Germany).

	Cohort 1 (Jan 2018 – Feb 2020)	Cohort 2 (Mar 2020 – Dec 2021)	Phi-Coefficient (φ)
Age ≤70	46.7%	36.3%	0,106
ECOG <2	60.6%	65.4%	0,050
Fit (assessed by physician)	46.3%	43.0%	0,034
International Staging System III	34.3%	39.1%	0,050
Symptoms present	74.5%	76.1%	-
Concomitant disease present	23.5%	27.1%	0,042
Cardiac impairment	8.3%	10.9%	0,045
Coronary heart disease	14.6%	16.2%	-
Cardiac arrhythmias	8.5%	12.3%	0,063
Renal impairment	12.3%	15.5%	0,046
Lung impairment	8.8%	12.2%	0,056
High cytogenetic risk (Del 17, t(4;14), t(14;16), Del 13)	6.9%	8.2%	-
Stem cell transplant eligible	21.1%	20.5%	-
Initiated in hospital	46.4%	50.4%	0,040
(C) - Hypercalcemia	24.1%	36.9%	0,139
(R) - Renal insufficiency	21.1%	23.7%	0,031
(A) - Anemia	66.5%	74.2%	0,084
(B) - Bone involvement	54.4%	58.1%	0,037
(S) - Bone marrow infiltration	28.1%	36.8%	0,092
(Li) - Free light chains	27.3%	41.3%	0,147
(M) - Focal lesions	20.9%	26.3%	0,063

CONCLUSION

- The results provide real-world evidence of a change in risk profile for patients with NDMM during COVID-19. This higher risk profile is observed in both the US and Germany.
- Contrary to previous trends, incidence of NDMM has decreased, indicating later diagnosis with more severe disease.
- This may negatively impact outcomes such as progression-free and five-year overall survival [6].

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