LETTER TO THE EDITOR

Multiple myeloma in the young: insights on prognosis, clinical features and treatment outcome derived from nationwide German registry data and a nested multicenter sample

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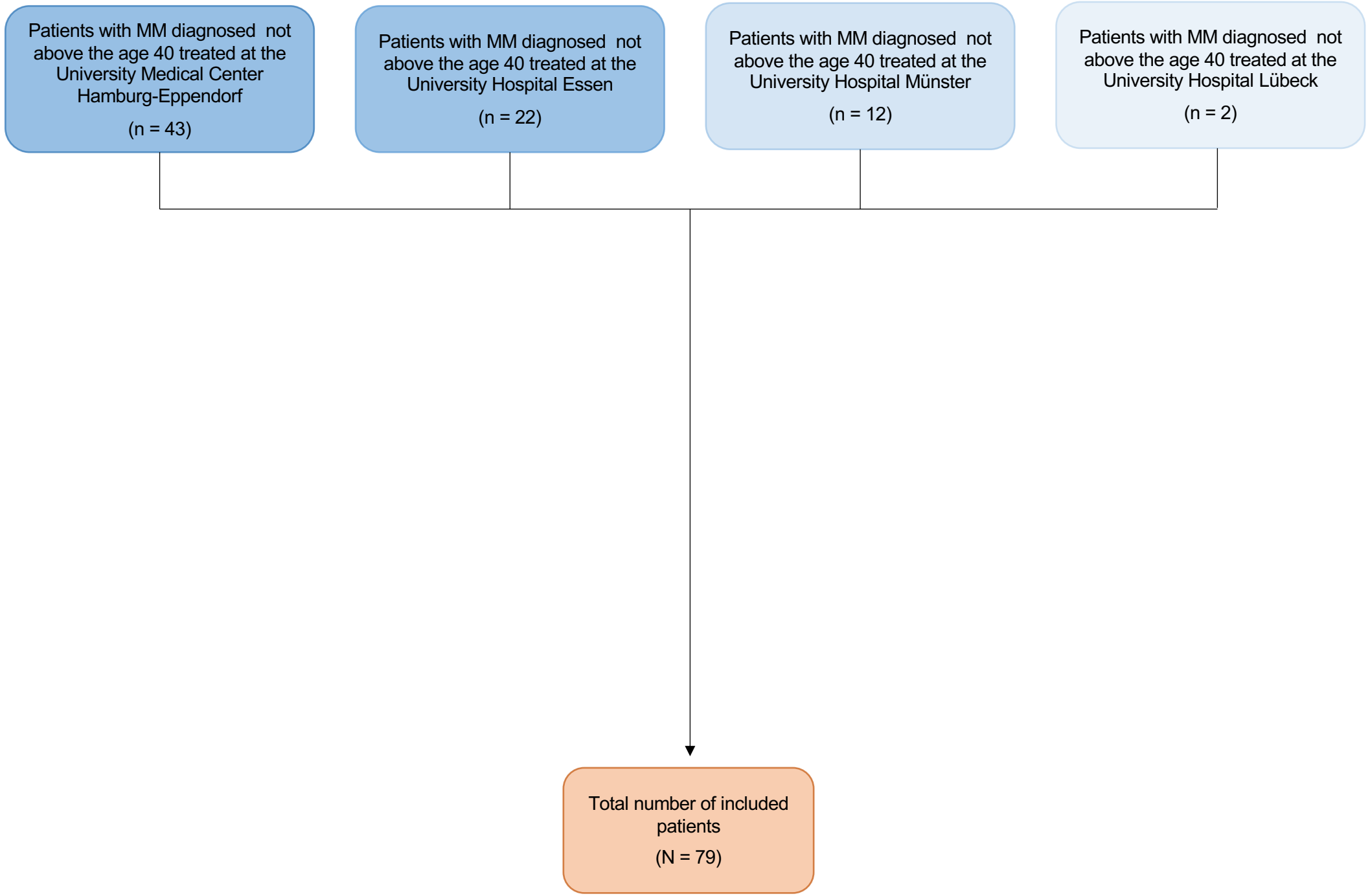
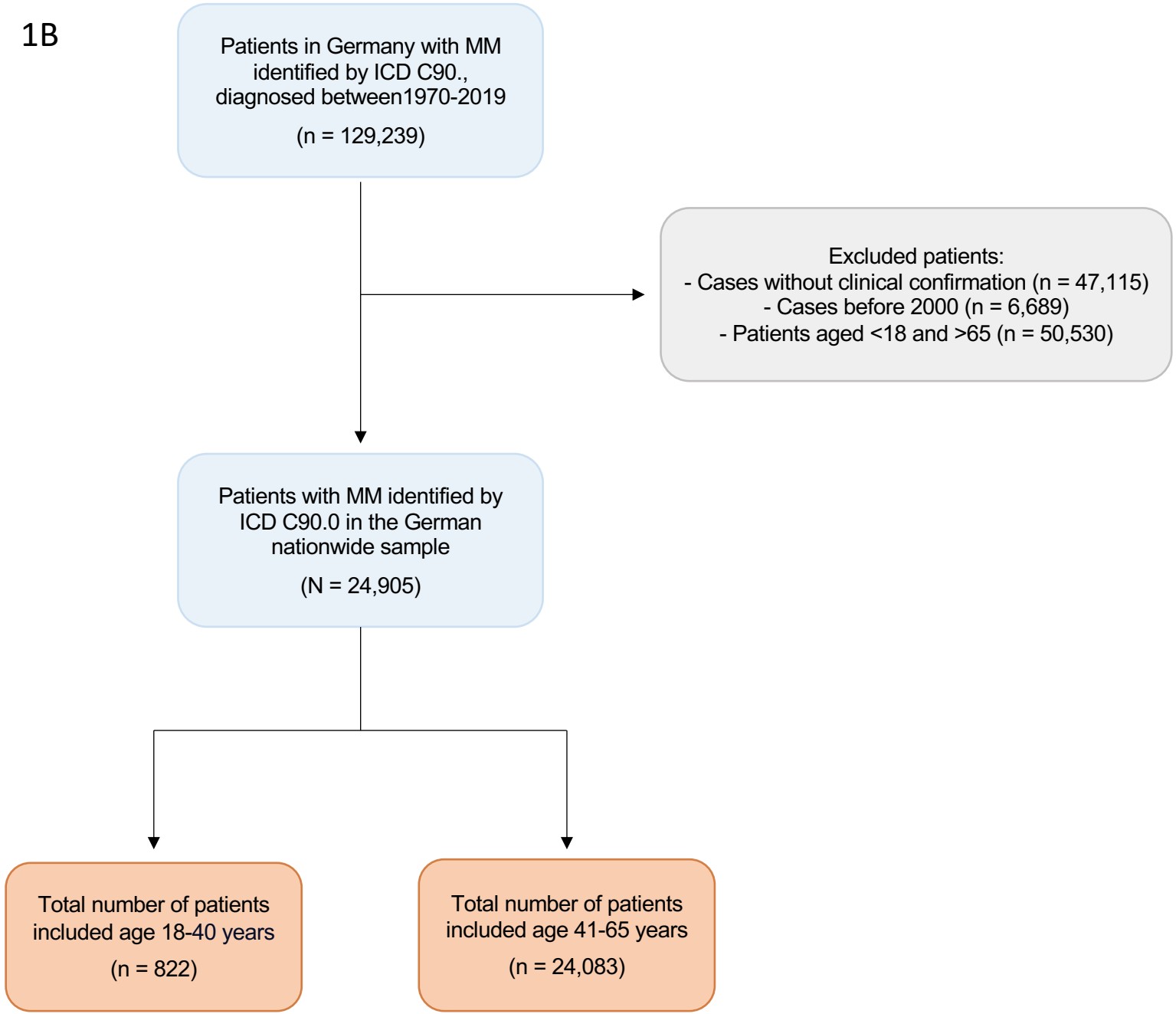
https://doi.org/10.3324/haematol.2024.285630

Supplementary Figure 1: Flowchart of the selected cohort from four German centers (1A) and the German nationwide sample (1B). In detail, we included 43, 22,12, and 2 myeloma patients treated between August 2000 and December 2023 at the University Medical Center Hamburg-Eppendorf, the University Hospital Essen, the University Hospital Münster, and the University Hospital Lübeck, respectively. The initial German nation-wide dataset consisted of 129,239 patients recorded between 1970 and 2019. The MM diagnosis was clinically confirmed for 82,124 patients. After applying the primary filter criteria, 24,905 patients remained in the German nationwide sample. Regarding the German nationwide sample of patients under the age of 18 or above 65 years, those with a follow-up duration of zero days (indicating death-certificate-only cases), and those without diagnostic confirmation were excluded.

1A


Patients with MM diagnosed not above the age 40 treated at the University Medical Center Hamburg-Eppendorf
(n = 43)
Patients with MM diagnosed not above the age 40 treated at the University Hospital Essen
(n = 22)
Patients with MM diagnosed not above the age 40 treated at the University Hospital Münster
(n = 12)
Patients with MM diagnosed not above the age 40 treated at the University Hospital Lübeck
(n = 2)
Total number of included patients
(N = 79)

1B


Patients in Germany with MM identified by ICD C90., diagnosed between1970-2019
(n = 129,239)
Excluded patients:
- Cases without clinical confirmation (n = 47,115)
- Cases before 2000 (n = 6,689)
- Patients aged <18 and >65 (n = 50,530)
Patients with MM identified by ICD C90.0 in the German nationwide sample
(N = 24,905)
Total number of patients included age 18-40 years
(n = 822)
Total number of patients included age 41-65 years
(n = 24,083)

Supplementary Table 1: Age distribution of the German nationwide sample and the selected center's cohort.

Age groups	**German nationwide sample, n (%)**	**Selected centers cohort, n (%)**
Total number of patients	822 (100)	79 (100)
18-25	35 (4.3)	1 (1.3)
26-30	52 (6.3)	8 (10.1)
31-35	187 (22.7)	22 (27.8)
36-40	548 (66.7)	48 (60.8)

Supplementary Table 2. Overview of previous data on survival outcome and clinical features of young multiple myeloma patients.

Author and Year	Study design and time scale	Total number of patients, n	Number of very young patients	Extramedullary disease[1]	High risk aberrations[1], in %	ISS I/II/III[1], in %	Treatment[1]	OS[1]	Referen-ces
Cheema et al., 2009	Retrospective, single center, U.S., 1990-2007	646	38	NA	NA	48%/NA/NA	Autologous SCT in 100%	Median FU 53 months, Median OS 81.4 months, no significant differences between both groups 5-year OS: 60%	(7)
Ludwig et al., 2008* and 2010	Retrospective, 17 institutions or study groups in North America, Europe, and Japan. 1982-2002	10,549	Patients ≤40 years, n= 312	NA	NA	41/29/31	NA	NA Median FU 4.09 years[2], 10-year OS: 43%[2]	(6)

Kapoor et al., 2011**	Retrospective, single center, U.S., 1999-2008	1,538	Patients ≤45 years, n= 100	NA	NA	50/21/29	Autologous HSCT in 85%. Allogeneic SCT in 15% patients.	Median FU 86 months, Median OS 93 months, significantly higher than in patients aged >45, 5-year OS: 69%	
Jurczyszyn et al., 2016	Retrospective case-control study, several institutions in poland, sweden, USA, Czech Republic, Denmark, 2000-2015	1,089	Patients ≤40 years, n= 173	NA	32%	47/33/20	Autologous SCT in 48%	Median FU 51 months, Median 5-year OS 83%, significantly higher than in patients aged 41-60 years	(5)
Yanamandra et al., 2018	Retrospective, single center, Indian, 2010-2015	415	Patients ≤40 years, n= 40	20 %	NA	Published data not plausible	Autologous SCT in 22.5%	3-year median OS: 80.2%[3]	(4)

Caulier et al., 2021	Retrospective, multicenter, French, 2000-2015	214	Patients ≤40 years, n= 214	NA	18%	52.4/27.5/20.1	Autologous HSCT in 93%. Allogeneic SCT in 24.9% patients.	Median FU 76 months, Median estimated OS 175 months, Median estimated 5-year OS: 84% Median 5 years relative survival: 83.5%	(2)
Martinez-Cordero et al., 2023***	Retrospective, multicenter, Latin American, 2010-2018	1316	103	23%	15.4%	29.7/33/37.4	Autologous SCT in 53.4%	Median FU 32 months, median OS for patients with autologous SCT: 78 months	(11)
Kamili et al. 2024	Retrospective, multicenter, German, 2000-2023	24,905	738	38%	40.6%	22.8/21.5/11.4	Autologous SCT in 96.2%	Median FU 55.2 months, 5-year absolute survival: 83%, 5-year relative survival: 83%	NA

[1] Relating to very young MM patients [2] Relating to patients aged < 50 years [3] No specific data on study population provided.

NA: Not applicable, SCT: Stem cell transplantation, FU: Follow-up

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