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ORIGINAL ARTICLE

Factors and Considerations in No-Treatment Decisions in Patients With Key Hematological Malignancies: A Nationwide, Population-Based Study in the Netherlands

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ABSTRACT

Comprehensive insights are lacking into why patients with hematological malignancies (HMs) receive no cancer-directed treatment. We evaluated socio-demographic and cancer-related characteristics, decision-making rationales, and overall survival in patients with three common HMs—diffuse large B-cell lymphoma (DLBCL), symptomatic multiple myeloma (MM), and acute myeloid leukemia (AML)—who do not receive cancer-directed treatment, using the nationwide Netherlands Cancer Registry. A total of 26 945 patients diagnosed with DLBCL (47%), symptomatic MM (29%), or AML (25%) between 2014 and 2021 were included. About 16% of the patients did not receive cancer-directed treatment, ranging from 26% in AML to 15% in DLBCL and 10% in MM. The primary reason for not receiving cancer-directed treatment in all three HMs was related to physical condition. The second main reason was patient/family choice in DLBCL and MM, whereas in AML it was rapid disease progression. In female patients, patient/family choice was a more prevalent reason for not receiving cancer-directed treatment than in male patients. Patients with a lower socio-economic position more often did not receive cancer-directed treatment. Median OS varied by reason for not receiving cancer-directed treatment, with the shortest OS in patients experiencing rapid disease progression or death before treatment initiation (0.4 to 0.6 months).

1 | Introduction

In 2020, the global burden of cancer was marked by an estimated 19.3 million new cancer diagnoses and 10 million cancer-related

deaths [1]. Within this landscape, hematological malignancies (HMs)—representing 6.5% of global cancer incidence and 9% in the US and Europe—comprise a diverse range of cancers that originate from blood-forming tissues [2, 3]. HMs uniquely

Natasja J.H. Raijmakers and Avinash G Dinmohamed jointly supervised this work.

present potential for curative treatments, even in advanced, relapsed, or refractory settings, which distinguishes them from solid malignancies. The prognostic landscape of these malignancies varies markedly, with five-year relative survival rates ranging from 30% in acute myeloid leukemia (AML) to 90% in Hodgkin lymphoma [4, 5].

In recent years, significant improvements in outcomes have been observed, due to the availability of novel and effective treatments [6–8]. However, a considerable number of patients do not receive cancer-directed treatment, potentially affecting their prognosis and chance of cure. Real-world data show that 23% to 34% of AML patients do not receive cancer-directed treatment, with the proportion increasing with age [9–11]. In DLBCL, claims data showed that 15%–20% of patients did not receive cancer-directed treatment [12, 13]. Not initiating cancer-directed treatment may be attributed to both disease- and patient-related factors, such as highly aggressive diseases with poor outcome and comorbidities, hampering fitness [14]. Current literature offers limited insight into patients with HMs who receive no cancer-directed treatment, yet exposing factors and reasons underlying this decision may be valuable to better understand and improve decision-making processes.

The decision not to initiate cancer-directed treatment can be complex, influenced by both medical and personal factors. Emerging evidence highlights a preference for shared decision making (SDM) among patients with HMs and their caregivers, advocating for greater involvement in treatment decisions [15, 16]. SDM is an approach wherein clinicians and patients collaboratively use the best available evidence to align treatment options with individual values and preferences, facilitating informed treatment decisions. However, patients with HMs may experience difficulties in involvement in the decision-making process, including difficulty processing information, perceived poor communication and emotional support, possibly affecting treatment decisions [17].

Our nationwide, population-based study explores patients' characteristics, decision-making rationales, and survival outcomes to gain insight into the decision not to initiate cancer-directed treatment. Focusing on DLBCL, symptomatic MM, and AML—the three most common HMs that necessitate prompt treatment post-diagnosis—this research aims to enrich the discourse on SDM for patients with HMs not receiving cancer-directed treatment.

2 | Patients and Methods

2.1 | Study Population and Registry

Our study included patients (≥ 18 years) diagnosed with DLBCL, symptomatic MM, and AML between 1 January 2014 and 31 December 2021. We obtained data from the Netherlands Cancer Registry (NCR), a comprehensive, nationwide, population-based cancer registry maintained by the Netherlands Comprehensive Cancer Organisation (IKNL). As detailed in previous studies, patient identification was performed using the International Classification of Disease for Oncology morphology codes specific to DLBCL, MM, and

AML [18–20]. Symptomatic MM was classified according to the revised International Myeloma Working Group (IMWG) diagnostic criteria for (non smoldering) MM [21]. We excluded patients diagnosed post-mortem and patients of whom details on treatment or the reasons for not initiating cancer-directed treatment were lacking ($n = 7$).

The NCR was established in 1989 and records all newly diagnosed malignancies in the Netherlands. Case notifications to the NCR are mainly derived from the Nationwide Network of Histopathology and Cytopathology (PALGA), supplemented by inpatient and outpatient discharges from the National Hospital Discharge Registry. The latter source is essential for ascertaining malignancies like AML, where the diagnosis might be solely based on peripheral blood and/or bone marrow aspiration examinations. In other words, this notification source captures cases that do not necessarily require histopathological confirmation. Once a case is reported to the NCR, trained NCR registrars meticulously collect data, including patient demographics, disease-related characteristics, and details on primary treatment from retrospective medical records within a 12-month post-diagnosis window.

We included patients diagnosed from 2014 onwards because more detailed information on prognostic factors, reasons for not initiating cancer-directed treatment, and data on the exact therapeutic regimens were available in the NCR from that year onwards. To evaluate trends in cancer-directed treatment rates over time, an analysis was conducted across two distinct time periods: 2014–2017 and 2018–2021.

The observational, non-interventional nature of this study meant that it was not subject to approval by the Central Committee on Research involving Human Subjects (CCMO) in the Netherlands. However, the study was conducted with the approval of the NCR's Privacy Review Board, which ensures the ethical use of anonymized data for research purposes (K23.106).

2.2 | Study Measures

The non-initiation of cancer-directed treatment is documented in the NCR according to specific registration guidelines. These guidelines stipulate a predefined hierarchy for recording the primary reason for not initiating cancer-directed treatment (1) comorbidity, performance status, or presence of an additional malignancy; (2) rapid disease progression, short life expectancy, or death prior to treatment initiation; (3) patient or family preference; (4) limited cancer burden; (5) other reasons; (6) unknown reasons. If there were multiple reasons, the primary reason was recorded based on descending priority. If “other reasons” was selected, a descriptive free text was added to the NCR for further clarification. In scenarios where “limited cancer burden” was initially cited, it was reclassified under “other reasons” for the current study due to its infrequent occurrence in the malignancies investigated in this study. Patients receiving only supportive care measures, such as palliative radiotherapy, blood transfusions, or corticosteroids (i.e., prednisone, prednisolone, or dexamethasone), were considered not receiving cancer-directed treatment.

Socio-demographic and—clinical characteristics were also extracted from the NCR. These variables included sex, age at diagnosis, socio-economic position (SEP), history of a prior malignancy (excluding basal cell skin carcinomas, squamous cell skin carcinomas, and in situ carcinomas), World Health Organization (WHO) performance status, and the hospital where the diagnosis was made. SEP was derived using median household income as a proxy, with data provided by Statistics Netherlands based on six-digit postal codes in 2016. This information covers 99% of Dutch postal codes each representing an average of 17 households. The median household income data were grouped into nine levels and then categorized into three SEP levels; low (level 1–3), medium (level 4–6), and high (level 7–9).

For DLBCL and MM, additional prognostic variables were evaluated. An elevated lactate dehydrogenase (LDH) level was noted as an indicator in both malignancies. Specific to DLBCL, additional prognostic variables include the parameters relevant to computing International Prognostic Index (IPI) score, a clinicopathological tool developed to predict prognosis in patients with DLBCL [22]. Next to an elevated LDH, these parameters include age, Ann Arbor stage, presence of more than one extranodal location, and WHO performance status. Of note, the presence of rearrangements in *MYC*, *BCL2*, *BCL6*, or a combination of these rearrangements was not standardly ascertained in the NCR throughout the study period. For MM, prognostic evaluation incorporated the CRAB-criteria, encompassing hypercalcemia (> 2.75 mmol/L), renal dysfunction (creatinine > 173 mmol/L), anemia (hemoglobin > 1.24 mmol/L less than normal value or < 6.2 mmol/L), bone disease, and focal lesions. The International Staging System (ISS) was used as a prognostic staging system for MM, based on Serum $\beta 2$ microglobulin and serum albumin, because LDH was only standardly registered in the NCR for patients diagnosed as of 2016 [23]. Therefore the revised ISS could not be calculated for the overall cohort.

2.3 | Statistical Analyses

We used descriptive statistics to delineate socio-demographic and clinical characteristics, segregating patients into those who received initial cancer-directed treatment and those who did not. Age comparisons (based on a continuous scale) were conducted using the Mann–Whitney test. Associations between the receipt of cancer-directed treatment and other characteristics were analyzed using age-adjusted logistic regression to control for age confounding in each individual item, except for the IPI-score in DLBCL, as age is already a component of this score. The Kruskal–Wallis test was used to analyze age differences between different reasons for not receiving cancer-directed treatment, while categorical variables were analyzed using the Chi-squared test, including post hoc analysis. We used the Kaplan–Meier method to assess the overall survival (OS), with survival curves modelling the time from diagnosis to death or last follow-up (31 January 2023). Survival distributions were compared using the log-rank test. A p value of less than 0.05 was considered statistically significant. All analyses were conducted using STATA (version 17.0, StataCorp Texas).

3 | Results

3.1 | Patient Characteristics

Our cohort included 26945 patients diagnosed with DLBCL, symptomatic MM, and AML between 2014 and 2021 in the Netherlands, of whom 12592 (47%), 7708 (29%), and 6645 (25%) had DLBCL, symptomatic MM, and AML, respectively. In all the three HMs, the majority of patients were male; DLBCL 58%, MM 59%, and AML 58%. Socio-demographic and clinical characteristics of the patients with DLBCL, MM, and AML are presented in Table 1. We found that 16% of the total cohort did not receive cancer-directed treatment. Not receiving cancer-directed treatment was most common among patients with AML (26%), exceeding the proportions observed in patients with DLBCL (15%) and MM (10%). No substantial increase in cancer-directed treatment was observed over time, with the exception of AML, where the percentage increased from 72% in 2014–2017 to 75% in 2018–2021 ($p = 0.002$).

The median age was significantly higher in patients not receiving cancer-directed treatment in all the three HMs studied: DLBCL (80 vs. 68 years, $p < 0.001$), MM (80 vs. 69 years, $p < 0.001$), and AML (79 vs. 66 years, $p < 0.001$). Patients with DLBCL not receiving cancer-directed treatment were more often female, compared to those receiving cancer-directed treatment (49% vs. 41%, $p < 0.001$). No significant sex differences were observed in MM and AML treatment reception. More patients not receiving cancer-directed treatment had a low SEP (DLBCL 33% vs. 21%, $p < 0.001$, MM 30% vs. 20%, $p < 0.001$, AML 31% vs. 20%, $p < 0.001$) and a poor WHO performance status defined as score 3–4 (DLBCL 14% vs. 3%, $p < 0.001$, MM 9% vs. 3%, $p < 0.001$, AML 9% vs. 2%, $p < 0.001$), compared to patients receiving cancer-directed treatment. Patients not receiving cancer-directed treatment more often had a prior malignancy in MM (24% vs. 14%, $p < 0.036$) and AML (42% vs. 27%, $p < 0.001$) when compared to those receiving cancer-directed treatment. In DLBCL, a high IPI score was more common in patients not receiving cancer-directed treatment versus not receiving cancer-directed treatment (23% vs. 17%, $p < 0.001$) (Table 1). The ISS score in MM showed no significant differences between patients who received treatment or not, but in more than half of the patients not receiving treatment this score was missing. Clinical characteristics, including elevated LDH levels for patients with DLBCL and the CRAB criteria for patients with MM, are shown in Table S1.

3.2 | Reasons for Not Receiving Cancer-Directed Treatment

In 89% of patients who did not receive cancer-directed treatment, the reason for this decision was recorded. Overall, comorbidity, performance status, or having a second malignancy (as a collective category registered in the NCR) were the predominant reasons for not receiving cancer-directed treatment in patients with DLBCL (45%), MM (44%), and AML (43%). Patient or family choice was the second most common reason in DLBCL (29%) and MM (36%) but less common in AML (23%). For patients with AML, rapid disease progression, short life expectancy, or death before treatment initiation (as a

TABLE 1 | Socio-demographic and clinical characteristics of patients with DLBCL, MM, and AML, stratified by receiving or not receiving cancer-directed treatment (*n* = 26 945).

	DLBCL (<i>n</i> = 12 592)			MM (<i>n</i> = 7708)			AML (<i>n</i> = 6645)		
	Receiving treatment, <i>n</i> = 10 733	Not receiving treatment, <i>n</i> = 1859	<i>p</i> *	Receiving treatment, <i>n</i> = 6950	Not receiving treatment, <i>n</i> = 758	<i>p</i> *	Receiving treatment, <i>n</i> = 4905	Not receiving treatment, <i>n</i> = 1740	<i>p</i> *
Age, median [IQR]	68 [59–75]	80 [73–85]	< 0.001	69 [61–76]	80 [74–85]	< 0.001	66 [56–74]	79 [72–84]	< 0.001
Sex, % (<i>n</i>)			< 0.001			0.252			0.150
Male	59% (6307)	51% (939)		60% (4143)	54% (411)		58% (2856)	58% (1004)	
Female	41% (4426)	49% (920)		40% (2807)	46% (347)		42% (2049)	42% (736)	
SEP, % (<i>n</i>)			< 0.001			< 0.001			< 0.001
Low	21% (2245)	33% (606)		20% (1371)	30% (229)		20% (997)	31% (535)	
Medium	51% (5465)	47% (880)		52% (3629)	49% (374)		53% (2614)	51% (879)	
High	27% (2916)	19% (357)		28% (1913)	20% (153)		25% (1248)	18% (316)	
Missing	1% (107)	0.9% (16)		0.5% (37)	0.3% (2)		0.9% (46)	0.6% (10)	
Hospital of diagnosis, % (<i>n</i>)			< 0.001			0.993			< 0.001
Academic hospital	16% (1720)	18% (330)		10% (670)	6% (48)		43% (2129)	14% (239)	
Non-academic hospital	84% (9013)	82% (1529)		90% (6280)	94% (710)		57% (2776)	86% (1501)	
WHO score, % (<i>n</i>)			< 0.001			< 0.001			< 0.001
0–2	55% (5918)	26% (478)		48% (3317)	20% (153)		44% (2152)	18% (307)	
3–4	3% (358)	14% (265)		3% (200)	9% (70)		2% (102)	9% (152)	
Missing	42% (4457)	60% (1116)		49% (3433)	71% (535)		54% (2651)	74% (1281)	
Prior malignancy, % (<i>n</i>)			0.247			0.036			< 0.001
Yes	24% (2583)	31% (584)		14% (1001)	24% (183)		27% (1347)	42% (738)	
No	76% (8150)	69% (1275)		86% (5949)	76% (575)		73% (3558)	58% (1002)	

(Continues)

TABLE 1 | (Continued)

	DLBCL (<i>n</i> = 12 592)		<i>p</i> *	MM (<i>n</i> = 7708)		<i>p</i> *	AML (<i>n</i> = 6645)		<i>p</i> *
	Receiving treatment, <i>n</i> = 10 733	Not receiving treatment, <i>n</i> = 1859		Receiving treatment, <i>n</i> = 6950	Not receiving treatment, <i>n</i> = 758		Receiving treatment, <i>n</i> = 4905	Not receiving treatment, <i>n</i> = 1740	
Ann Arbor stage, % (<i>n</i>)			0.889						
I–II	33% (3489)	30% (553)							
III–IV	66% (7118)	58% (1082)							
Missing	1% (126)	12% (224)							
IPI-score, % (<i>n</i>)			< 0.001						
Low (0–1)	29% (3118)	20% (374)							
Low-intermediate (2)	26% (2842)	28% (522)							
High-intermediate (3)	28% (2998)	28% (529)							
High (4–5)	17% (1775)	23% (434)							
ISS (risk category), % (<i>n</i>)						0.241			
Stage 1				18% (1257)	8% (60)				
Stage 2				28% (1963)	15% (111)				
Stage 3				30% (2096)	24% (179)				
Missing				24% (1634)	54% (408)				

Abbreviations: AML, acute myeloid leukemia; DLBCL, diffuse large B-cell lymphoma; IPI, international prognostic index; IQR, interquartile range; MM, multiple myeloma; SEP, socio-economic position; WHO, performance status.

*All reported *p* were determined using age-adjusted univariate analysis, except for IPI-score.

collective category registered in the NCR) was the second most common reason (26%). Overall, sex differences were observed based on the reason for no cancer-directed treatment (DLBCL $p=0.002$, MM $p=0.001$, AML $p=0.009$). Comorbidity, performance status, or second malignancy as reason for no cancer-directed treatment was more common in male patients (DLBCL 53%, MM 60%, AML 60%) whereas patient or family choice as reason for no cancer-directed treatment was more common in female patients (DLBCL 57%, MM 56%, AML 51%) (Table 2).

3.3 | Survival

Overall survival analysis showed that 21% ($n=1,387$) of all AML patients died within 1 month of diagnosis, a higher proportion than in DLBCL (8%, $n=1,041$) and MM (5%, $n=390$) (Table 3). The median OS (95% CI) for patients who did not receive cancer-directed treatment was 1.5 (1.3–1.6) months for DLBCL, 2.0 (1.6–2.3) months for MM, and 1.1 (1.0–1.2) months for AML. Survival varied according to the reason for not receiving cancer-directed treatment. Patients whose reason was patient or family choice had a median OS ranging from 1.5 to 3.2 months. Those who did not receive cancer-directed treatment due to comorbidity, performance status, or a second malignancy had a median OS of 1.1 to 1.6 months. The shortest median OS, ranging from 0.4 to 0.6 months, was observed in patients who did not receive cancer-directed treatment due to rapid progression, short life expectancy, or death prior treatment initiation (Table 4). Patients with DLBCL and MM who had “other” as the reason for not receiving cancer-directed treatment had the longest median OS (2.7 and 15.7 months respectively), but given the small size of this category (3%–4%), these results must be interpreted with caution. Survival curves are shown in Figure 1.

4 | Discussion

This nationwide, Dutch, population-based study, including 26945 patients with the three most common HMs (DLBCL, symptomatic MM, and AML), provides important insights into treatment decisions and outcomes in this patient cohort. More specifically, this study fills a gap in the existing literature by comprehensively analyzing patient decision-making in HMs across different socio-demographic groups, a previously under-researched topic. Significantly, 16% of these patients did not receive cancer-directed treatment, with a higher proportion in AML (26%) compared to DLBCL (15%) and MM (10%), accompanied by a poor prognosis. The main reasons for not receiving cancer-directed treatment were related to the patients' physical condition and personal or family decision, the latter being more common in female patients than in male patients.

Our findings echo previous population-based studies which suggests that a substantial number of patients with solid tumors do not receive cancer-directed treatment [24, 25]. HMs often have a more unpredictable disease course than solid malignancies and factors associated with prognosis in solid tumor malignancies such as performance status, symptom burden and comorbidities are not as strongly correlated with prognosis in HM patients, making treatment decisions challenging [26, 27]. Nevertheless,

comorbidity, performance status, or second malignancy (as a collective category) were found to be the most common reasons for patients not receiving cancer-directed treatment. Hence, our study highlights the role of physical functioning in the decision making process of cancer-directed treatment in patients with DLBCL, MM, and AML. Moreover, survival was notably short in all three HMs not receiving cancer-directed treatment, which may indicate either an aggressive disease course or patients who were generally in poorer physical condition.

The pivotal role of patient and family choice in not initiating cancer-directed treatment is highlighted in our study, which is consistent with existing literature showing similar trends in solid malignancies. Previous studies in the Netherlands have shown that patient choice was a primary reason for not initiating treatment in patients with pancreatic cancer (27%), and advanced epithelial ovarian cancer (40%) [24, 25]. The fact that patient or family choice was the primary reason for a substantial proportion of our cohort suggests that these patients were involved in the decision-making process. This observation is relevant in the context of HMs, where SDM is also highly and increasingly valued by patients and their caregivers [15, 16, 28].

A striking aspect of our findings is the marked preference for not receiving cancer-directed treatment options among female patients across the HMs explored in our study. This sex-specific trend in approaching end-of-life care and decision making aligns with broader patterns observed in studies in oncology care, reporting that women typically exhibit a greater openness towards end-of-life discussions and palliative care than men. Conversely, men may focus more on concrete aspects such as medical facts and organizational details [29, 30]. This difference in approach facilitates more reflective end-of-life discussions for women, which may lead to less aggressive end-of-life care and reduced likelihood of undergoing chemotherapy near death [31]. Collectively, these insights highlight the indispensable role of SDM in oncology emphasizing the need to integrate patient preferences into decision-making processes, particularly in situations involving critical life-altering choices.

The lower proportion of AML patients who choose not to receive cancer-directed treatment compared to DLBCL and MM patients in our study (23% vs. 29% and 36% respectively) may be attributed to the aggressive nature of the disease, necessitating rapid treatment decisions. This urgency, as evidenced by literature suggesting a median time from diagnosis to initiation of treatment of 1–8 days [32], may limit the opportunity for in-depth deliberation, limiting patients' time to reflect, impacting the decision-making process. Nevertheless, in these cases, timely discussion with patients and family about advance care planning and early integration of palliative care is warranted, even when treatments are given with curative intents [33–35]. A body of research underscores the benefits of early palliative care integration for patients with HMs, yet palliative care involvement is notably underutilized compared to its application in patients with solid malignancies, where it is increasingly recognized and adopted to prevent inappropriate end-of-life care [26, 36–46].

Patients with a lower SEP were more likely to not receive cancer-directed treatment compared to patients with a higher SEP,

TABLE 2 | Socio-demographic characteristics of DLBCL, MM, and AML patients stratified by the reasons for not receiving cancer-directed treatment.

	Comorbidity/ performance status/second malignancy	Rapid progression /short life expectancy/ deceased	Patient or family choice	Other reason	Reason unknown	<i>p</i>
DLBCL (<i>n</i> = 1483), <i>n</i> (%)	660 (45%)	320 (22%)	433 (29%)	47 (3%)	23 (2%)	
Age, median [IQR]	80 [74–85]	77 [70–83]	81 [74–86]	77 [65–83]	80 [75–86]	<0.001
Sex, % (<i>n</i>)						0.002
Male	53% (348)	57% (182)	43% (188)	60% (28)	43% (10)	
Female	47% (312)	43% (138)	57% (245)	40% (19)	56% (13)	
SEP, % (<i>n</i>)						0.201
Low	33% (216)	30% (97)	36% (154)	45% (21)	26% (6)	
Medium	50% (329)	50% (160)	44% (189)	43% (20)	57% (13)	
High	16% (107)	20% (63)	20% (87)	11% (5)	17% (4)	
Missing	1% (8)	—	0.7% (3)	2% (1)	—	
MM (<i>n</i> = 708), <i>n</i> (%)	312 (44%)	102 (14%)	252 (36%)	30 (4%)	12 (2%)	
Age, median [IQR]	81 [75–85]	77 [71–83]	81 [76–85]	76 [70–84]	84 [81–86]	0.001
Sex, % (<i>n</i>)						0.001
Male	60% (186)	62% (63)	44% (110)	63% (19)	50% (6)	
Female	40% (126)	38% (39)	56% (142)	37% (11)	50% (6)	
SEP, % (<i>n</i>)						0.123
Low	28% (86)	42% (43)	30% (75)	20% (6)	50% (6)	
Medium	51% (159)	42% (43)	50% (125)	60% (18)	25% (3)	
High	21% (66)	16% (16)	20% (51)	20% (6)	25% (3)	
Missing	0.3% (1)	—	0.4% (1)	—	—	
AML (<i>n</i> = 1672), <i>n</i> (%)	711 (43%)	428 (26%)	385 (23%)	85 (5%)	63 (4%)	
Age, median [IQR]	79 [72–84]	79 [71–84]	79 [72–84]	77 [69–82]	81 [76–84]	0.019
Sex, % (<i>n</i>)						0.009
Male	60% (426)	60% (258)	49% (190)	56% (48)	57% (36)	
Female	40% (285)	40% (170)	51% (195)	44% (37)	43% (27)	
SEP, % (<i>n</i>)						0.075
Low	32% (225)	28% (119)	34% (129)	28% (24)	35% (22)	
Medium	53% (376)	50% (214)	46% (176)	56% (48)	51% (32)	
High	15% (107)	22% (92)	20% (78)	15% (13)	14% (9)	
Missing	0.4% (3)	0.7% (3)	0.5% (2)	—	—	

Note: Registrations for which NCR registrars did not actively search the reason for not receiving cancer-directed treatment were registered as missing, DLBCL ntotal missing included = 1859; MM ntotal missing included = 758; AML ntotal missing included = 1740.

Abbreviations: AML, acute myeloid leukemia; DLBCL, diffuse large B-cell lymphoma; MM, multiple myeloma.

TABLE 3 | Patient deceased within 1 month after diagnosis in DLBCL, MM, and AML.

Patient deceased within 1 month	DLBCL, <i>n</i> = 1041	MM, <i>n</i> = 390	AML, <i>n</i> = 1387
Received cancer-directed treatment	23% (<i>n</i> = 243)	32% (<i>n</i> = 123)	36% (<i>n</i> = 493)
Did not receive cancer-directed treatment	77% (<i>n</i> = 798)	68% (<i>n</i> = 267)	64% (<i>n</i> = 894)

TABLE 4 | Median overall survival of DLBCL, MM, and AML patients not receiving cancer-directed treatment, in months.

	DLBCL	(95% CI)	MM	(95% CI)	AML	(95% CI)
No cancer-directed treatment	1.5	(1.3–1.6)	2.0	(1.6–2.3)	1.1	(1.0–1.2)
Comorbidity, performance status, or second malignancy	1.1	(1.0–1.2)	1.6	(1.3–2.2)	1.1	(0.9–1.2)
Rapid progression, short life expectancy, or deceased	0.4	(0.3–0.5)	0.4	(0.3–0.7)	0.6	(0.5–0.7)
Patient or family choice	1.9	(1.6–2.3)	3.2	(2.6–4.5)	1.5	(1.3–1.9)
Other reason	2.7	(0.9–13.6)	15.7	(4.1–54)	1.5	(1.0–2.0)
Reason unknown	1.7	(1.0–5.7)	2.7	(0.6–13.1)	2.0	(1.4–2.7)

suggesting that SEP may influence treatment decisions. This socio-economic disparity, previously demonstrated in various cancer patient groups [47–50], raises concerns about equity in cancer care. A possible explanation is that a lower SEP is often associated with higher comorbidity rates, and patients with a low SEP may also face greater challenges in accessing medical care, including difficulties with travel and presenting with more advanced disease at diagnosis [51, 52]. These disparities may also be linked to the dynamics of doctor-patient communication. SEP can shape physicians' perceptions of patients' personalities and abilities, and how prognostic information is framed can influence decision-making [53–55]. Shared decision-making is particularly challenging when health literacy is limited, which is more common among patients from lower socioeconomic backgrounds [56]. Conversely, patients with a higher SEP are generally more likely to take an active role in the decision-making process compared to patients with a lower SEP [57]. When focusing on the specific reasons for non-initiation of cancer-directed treatment, our study found no significant difference in SEP across these reasons among patients with DLBCL, MM, or AML.

4.1 | Strengths and Limitations

The main strength of our study lies in the utilization of comprehensive, individualized data, available from a nationwide cancer registry. This approach allowed for an in-depth analysis of the characteristics of patients not receiving cancer-directed treatment, their decision-making rationale, and survival outcomes, providing awareness and valuable insights into decision-making in patients with DLBCL, MM, or AML, which, may in turn benefit decision-making processes in similar HMs.

However, our study is not without limitations. The coding system in the NCR captures only one primary reason category for not receiving cancer-directed treatment, potentially

underestimating multifactorial aspects of these decisions. Combining reasons into one category reduces interrelatedness but may provide a less detailed picture of underlying reasons for not receiving cancer-directed treatment. Furthermore, medical records often provide a physician-centric view, which may not fully capture the nuances of multidisciplinary team consultations and patient consultations.

When patients received only supportive care measures such as palliative radiotherapy, the reasons for not initiating cancer-directed treatment were often not actively pursued by the NCR registrars and hence recorded as missing, which may have introduced a selection bias. These patients may have been in a better condition because they were still receiving some form of treatment or, conversely, in a worse clinical condition with more symptoms, requiring intervention.

Another limitation relates to our approach for determining SEP. While median household income served as a proxy for SEP, categorizing into three broad SEP groups may lead to overlap and potentially dilute the granularity of socio-economic analysis. Also, information on patients' physical status is limited, and the number of missing data on the WHO performance score was substantial. Lastly, our study focused on reasons to forego cancer-directed treatment post-diagnosis, not including patients that did not receive further cancer-directed treatment after first-line treatment, and the reasons for this decision.

4.2 | Conclusions

Treatments for hematologic malignancies vary considerably, both in intensity and likelihood of cure, factors vital to treatment considerations. Our study highlights that patient's physical condition and the patient's or family's choice are crucial in the decision not to initiate cancer-directed treatment in patients with DLBCL, symptomatic MM, and AML. The observed

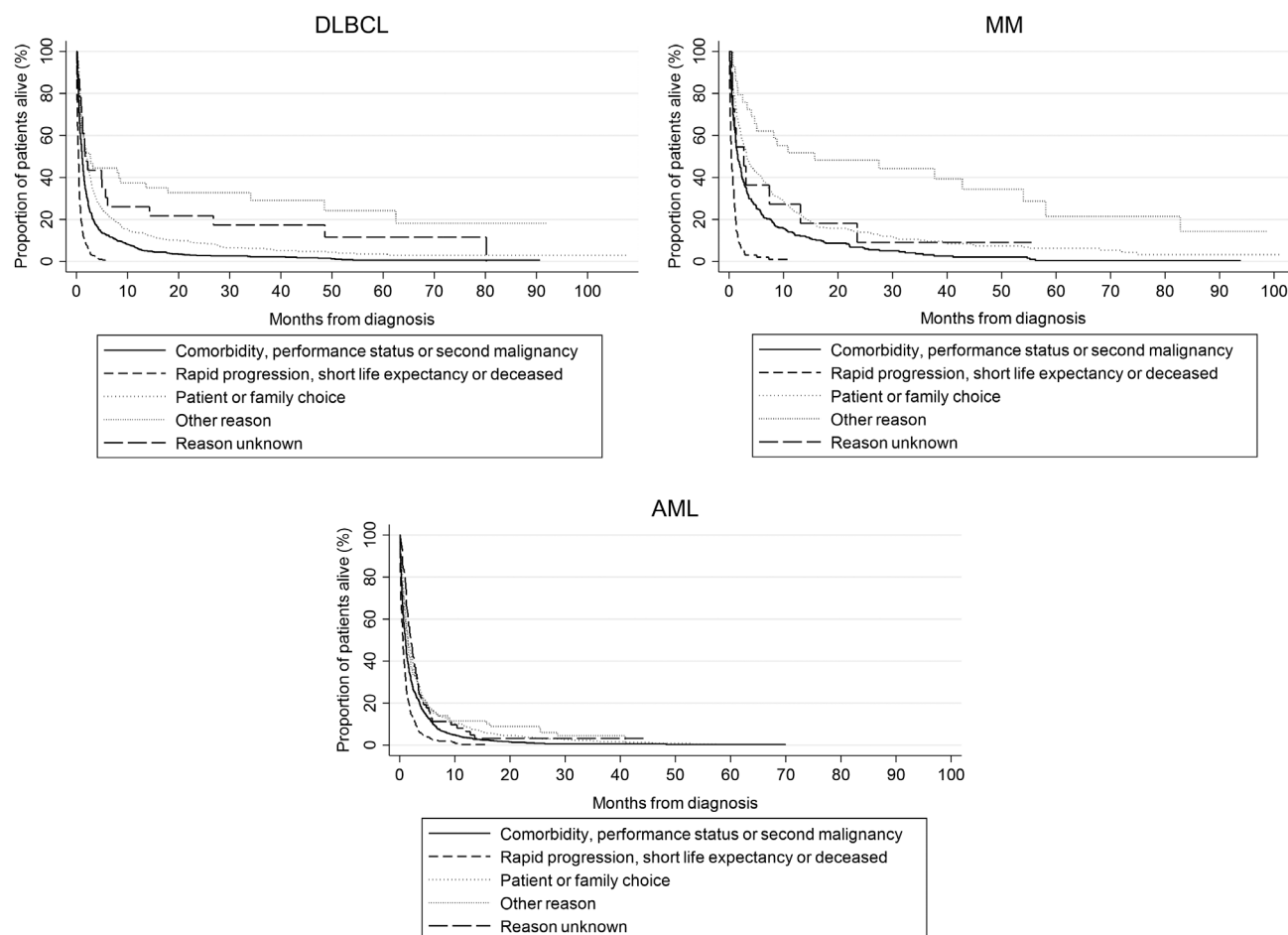


FIGURE 1 | Survival curves of DLBCL, MM, and AML patients presented per reason for not receiving cancer-directed treatment.

sex and SEP differences in treatment decisions highlight the need for personalized, patient-centered approach in hemato-oncology, and also indicate that improvement in resilience and empowerment of patients may improve cancer treatment decision-making. Improving our understanding of the cancer-directed treatment decisions, particularly among those opting out of cancer-directed treatment, is crucial for refining SDM processes and ensuring equitable, high-quality cancer care in hemato-oncology. This study provides scope for future research into ethnic and cultural influences and the level of information and involvement of patients in decision-making processes in HMs and how this affects their quality of life.

Author Contributions

N.J.H.R. and A.G.D. designed the study; R.A.H.S. and M.Z. analyzed the data; O.V. was responsible for the data collection; M.Z. and R.A.H.S. wrote the manuscript with contributions from all authors; who also interpreted the data, and read, commented, and approved the final version of the manuscript.

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Ethics Statement

Due to the observational and non-interventional nature of this study, approval from the Central Committee on Research Involving Human Subjects (CCMO) in the Netherlands was not required.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available via the Netherlands Comprehensive Cancer Organisation. These data are not publicly available, and restrictions apply to the availability of the data used for the current study. However, these data are available upon reasonable request with permission of the Netherlands Comprehensive Cancer Organisation.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.