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Full Length Article

Understanding European patterns of deprescribing antithrombotic medication during end-of-life care in patients with cancer

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ABSTRACT

Background: Even though antithrombotic therapy (ATT) probably has little or even negative effect on the well-being of patients with cancer near the end of life, it is often continued until death, possibly leading to excess bleeding complications, increased disease burden, reduced quality of life and higher healthcare costs.
Aim: To explore and describe European practice patterns and perspectives of healthcare professionals from different disciplines and specialties on ATT in the end-of-life care (EOLC) of patients with cancer.
Methods: We performed a two-week international cross-sectional survey study using flash-mob research methodology. Eligible were healthcare professionals from different institutions across Europe, who prescribed ATT and/or dealt with EOLC of patients with cancer. The survey comprised three parts, including a series of choice sets (hypothetical scenarios involving a set of characteristics changing in level [e.g., high vs. low thrombotic risk]) on ATT management in EOLC. The discrete choice experiment analysis was conducted using multinomial logistic regression.
Results: Out of 467 pre-registrants, 208 participated in the survey from 4 to 18 July 2023. The majority (53 %) considered a patient with cancer as in EOLC when life expectancy is below 3 months. Respondents reported seeing or treating 20 patients with cancer on ATT in EOLC per year (IQR 10–50). The median estimated frequency of considering ATT deprescription per healthcare professional was 10 times per year (IQR 4–10), while the frequency of actual deprescription was 5 times per year (IQR 2–10). Twenty percent of respondents had never deprescribed ATT in the context of EOLC. Across the eight choice sets, five respondents (2.7 %) found deprescribing inappropriate in any scenario. Deprescribing was more often considered in patients with poor ECOG-

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performance status, high bleeding risk and low-molecular-weight heparin use as opposed to oral ATT. Haemato-oncology and cardiovascular medicine specialists were more inclined to deprescribe antiplatelet therapy than other specialties.

Conclusion: Our study describes medical decision-making regarding ATT in EOLC of patients with cancer. Healthcare professionals' perspectives and practice patterns vary, and some preferences appear associated with the therapists' professional focus and region of practice.

Introduction

Patients with cancer are at an increased risk of venous and arterial thrombosis, particularly during the advanced palliative phase when cancer progresses and mobility is reduced or absent [1,2]. To prevent formation or propagation of thrombi, patients are managed with antithrombotic therapy (ATT), comprising anticoagulant and anti-platelet therapy. Almost half of the patients with cancer on palliative care are on ATT [3–5]. Moreover, this percentage is likely to increase due to improvements in early cancer detection and novel anticancer therapies, leading to longer life expectancy, each of which resulting in an added risk of cardiovascular complications [6–8]. Even though the risk of thrombosis is high and likely underestimated in terminally ill patients on palliative care, bleeding remains a prevalent issue in advanced cancer, even without the use of thromboprophylaxis or ATT [9]. Despite evidence that ATT probably has little or even negative effect on the well-being of patients in this clinical setting, it is often continued until death, often leading to bleeding complications, increased disease burden, reduced quality of life, and higher healthcare costs [5,9–12]. Prescribing inertia, the perceived benefit of ATT aimed to prevent symptomatic vascular events, the uncertainty about how to predict life expectancy (e.g., months, weeks) and fragmentation of the healthcare system might be barriers for ATT deprescribing [11,13,14].

There are no clear guidelines as to when ATT should be deprescribed in patients with cancer receiving end-of-life care, partly because of a lack of evidence. Therefore, the choice whether to deprescribe ATT for these patients is made on a case-by-case basis and depends largely on the individual clinician's judgement. Understanding current patterns of management of ATT within the context of end-of-life care as well as the motivations and preferences behind these patterns is crucial for improving clinical practice and shared-decision making regarding ATT.

The aim of this study was to explore and describe current European practice patterns regarding the use of ATT in the end-of-life care of patients with cancer among healthcare professionals. Furthermore, we aimed to evaluate and understand the processes and factors that drive decisions concerning the discontinuation of ATT in patients with cancer receiving end-of-life care.

Methods

Study design

The study was conducted as a two-week, international, cross-sectional survey using flash-mob research (FMR) methodology [15]. This FMR study is part of the multinational "Towards Cancer Patient Empowerment for Optimal Use of Antithrombotic Therapy at the End of Life" (SERENITY) project and funded by Horizon Europe Research Innovations (grant agreement ID: 101057292) [16]. The research aim and design of the current study were conceived at the University Medical Center in Mainz (UMCM), Germany, and the Leiden University Medical Center (LUMC), the Netherlands. The UMCM acted as coordinating centre for the duration of the study. The responsible ethics committees of Germany and participating countries waived the requirement for ethics approval due to the non-interventional nature of the study and the absence of personal data collection or processing.

Study procedures and participants

The FMR steering committee invited members of the SERENITY consortium from eight European countries (Denmark, France, Germany, Italy, The Netherlands, Poland, Spain and the United Kingdom) with specialties in different clinical areas to act as ambassadors for the study. These ambassadors, alongside the steering committee members of UMCM and LUMC, advertised the study through traditional professional networks and their social media channels. Information about the study was distributed via personal communication, relevant scientific organisations and congresses, social media as well as the UMCM website and SERENITY website (https://serenity-research.eu/).

Healthcare professionals from various institutions across Europe who prescribe ATT or deal with end-of-life care of patients with cancer were eligible for study participation. In view of the advertisement of the study through international networks and social media, interested healthcare professionals from other countries and regions were not excluded from participation.

Between 27 February 2023, and 2 July 2023, an online pre-registration survey for study participation was accessible at Formdesk (https://en.formdesk.com/). Prior to commencement of this survey, all healthcare professionals provided implicit electronic consent for the use of their data for the current study.

On 4 July 2023, all healthcare professionals who had pre-registered simultaneously received an invitation e-mail containing a unique link to the flash-mob survey on the Castor electronic data capture platform (https://www.castoredc.com/). The flash-mob survey was originally planned to be available over one week, which we extended to two weeks to increase the sample size. Automatic reminders were sent after 4 and 11 days if the survey had not yet been completed.

Data collection and processing

Apart from the pre-registrants' e-mail address for forwarding information about the launch of the study and assigning a unique link to the electronic case report forms of the flash-mob survey, no personal data were stored or processed.

The pre-registration survey included six questions on demographics, professional information and the estimated number of patients seen or treated on a yearly basis with active cancer, focusing on those considered to be in end-of-life care and on ATT.

The flash-mob survey consisted of three parts, with the third part being optional for participants: i) general questions about end-of-life care for patients with cancer and (de)prescribing in the last three months of a patient's life; ii) series of discrete choice sets, i.e., hypothetical scenarios defined by different ATT types and a set of factors changing in level (e.g., high vs. low thrombotic risk) throughout the choice sets; and iii) actual case decisions made in up to three consecutive cases involving patients with active cancer who were considered to receive end-of-life care. For the latter part, only fully anonymous patient data were collected via multiple-choice questions including sex, age group, primary tumour, tumour stage, the time point in the course of the disease when the conversation about discontinuation of ATT took place, and the type and indication of ATT. The survey questionnaire can be found as part of the Supplementary Material, Annexes S1 to S3.

For the discrete choice experiment (DCE; survey part ii), 10 candidate factors/levels informed by literature review and discussion with

experts, were presented to members of the SERENITY working group to capture the most salient factors and associated levels [17]. The working group included researchers and clinicians from 14 hospitals located in 8 European countries with specialisation in oncology, cardiology, geriatrics, haemostasis, haematology, family medicine, palliative care, health economy, epidemiology, health communication and psychology. The final subset of factors/levels for inclusion in the scenarios was decided through discussion.

Statistical analysis

Descriptive analysis was performed with IBM SPSS Statistics (version 29.0.0.0) [18]. Categorical variables are presented as counts with corresponding percentages, while continuous variables are reported as medians with corresponding interquartile ranges (IQR) in the case skewed data.

The responses to the DCE were analysed using R (version 4.3.2) including the mlogit package (version 1.1–1) [19]. A multinomial logistic regression model was fitted to the observed probabilities of choosing a certain scenario within a choice set, allowing to estimate the relative contribution of each factor to the utility of deprescribing ATT while accounting for random errors. In the first step, we included only the predictors defining the choice sets and scenarios – low/high thrombotic risk, low/high bleeding risk, low/high Eastern Cooperative Oncology Group performance status (ECOG-PS) score, and ATT type (direct oral anticoagulant [DOAC], vitamin K antagonist [VKA], low-molecular-weight heparin [LMWH], or antiplatelet agent) [20].

In the second step, we added participant characteristics from the pre-registration survey like professional experience (in years and number of patients with cancer receiving ATT treated), professional focus (cardiovascular medicine, haemato-oncology, primary and elderly care, or other), sex (male or female) and region of practice (Northern/Western Europe, Eastern Europe, Southern Europe, or other countries) to examine whether different subgroups demonstrate different preferences. For details on the categories of professional focus and region of practice, see Table 1 and Supplementary Material Annex S4, respectively [21]. Additionally, we tested the significance of each factor using likelihood ratio tests comparing the full model to a reduced model without the respective factor on a 5 % alpha level.

Results

Pre-registrant and participant characteristics

A total of 468 healthcare professionals from 27 countries pre-registered for the flash-mob survey; one withdrew due to ineligibility. Of the remaining 467 healthcare professionals, 208 (58 %) actually participated in the survey. Of these respondents from 21 countries, 145 (70 %) completed the survey in full and 63 (30 %) partially during the study period. The characteristics of the healthcare professionals who pre-registered for participation in the flash-mob survey and of those who actually participated in the flash-mob survey are described in Table 1.

General questions

The majority of respondents (53 %) considered a patient with cancer as being in end-of-life care when life expectancy is below 3 months (Table 2); 13 % of them considered patients to be in end-of-life care if life expectancy is less than one year, 27 % if <6 months and 7.2 % if <2 weeks. Responses were heterogeneous both between specialties and within each specialty. Twenty-five percent of the respondents (51/205) indicated that they always prescribe ATT upon diagnosing a thrombotic event even at the end-of-life stage (Table S1). Regarding deprescription, 20 % (41/203) had never deprescribed ATT in the context of end-of-life care. Of those who did, most respondents (61 %) reported that they deprescribe ATT 'sometimes' (Table 3). One internist reported always

Table 1
Characteristics of the pre-registrants and flash-mob survey participants.

	Pre-registration	Flash-mob
Number of participants (n)	467	208
Women	277 (59)	121 (58)
Age category		
- 25–34 years	95 (20)	42 (20)
- 35–44 years	152 (33)	65 (31)
- 45–54 years	142 (30)	66 (32)
- 55–64 years	65 (14)	28 (13)
- ≥65 years	13 (2.8)	7 (3.4)
Country		
- Denmark	6 (1.3)	1 (0.5)
- France	51 (11)	17 (8.2)
- Germany	11 (2.4)	4 (1.9)
- Italy	27 (5.8)	14 (6.7)
- The Netherlands	96 (21)	51 (25)
- Poland	89 (19)	20 (9.6)
- Spain	114 (24)	58 (28)
- United Kingdom	23 (4.9)	13 (6.3)
- Other country	50 (11)[a]	30 (14)[b]
Profession		
Primary and elderly care		
- General practitioner	38 (8.1)[c]	20 (9.6)[c]
- Palliative care specialist	41 (8.8)	14 (6.7)
- Nursing home physician	5 (1.1)	0 (0.0)
- Geriatrician	3 (0.6)	3 (1.4)
Haemato-oncology		
- Oncologist	66 (14)	23 (11)
- Haematologist	33 (7.1)	19 (9.1)
- Internist	101 (22)[d]	54 (26)[e]
Cardiovascular medicine		
- Cardiologist	61 (13)	23 (11)
- Vascular medicine specialist	58 (12)	27 (13)
- Vascular surgeon	6 (1.3)	0 (0.0)
Other specialties		
- Pulmonologist	30 (6.4)[f]	19 (9.1)[g]
- Neurologist	2 (0.4)	2 (1.0)
- Physician assistant, nurse practitioner or nurse	12 (2.6)	1 (0.5)
- Other profession	11 (2.4)[h]	3 (1.4)[i]
Professional experience		
- <5 years	81 (17)	35 (17)
- 5–10 years	106 (23)	51 (25)
- 11–15 years	91 (19)	35 (17)
- 16–20 years	66 (14)	25 (12)
- ≥21 years	123 (26)	62 (30)
Estimated number of patients seen/treated each year with active cancer, who are considered to be in end-of-life care and are on antithrombotic medication (median, IQR).	30 [10–70]	20 [10–50]

Data are presented as numbers (n, % in brackets), unless otherwise stated.
In the regression models, general practitioners, palliative care specialists, nursing home physicians, and geriatricians were grouped under the professional focus 'primary and elderly care'; vascular medicine specialists, vascular surgeons, and cardiologists were grouped under 'cardiovascular medicine'; oncologists, haematologists, and internists were grouped under 'haemato-oncology'; and the remaining professionals were grouped under 'other specialties'.
Abbreviations: IQR, interquartile range.
[a] Argentina (n = 1); Australia (n = 1); Austria (n = 1); Belgium (n = 2); Canada (n = 5), Chile (n = 1), Greece (n = 3); Ireland (n = 2); Israel (n = 1); Lithuania (n = 1); North Macedonia (n = 1); Peru (n = 1); Portugal (n = 19); Slovenia (n = 2); South Africa (n = 1); Sweden (n = 1); Switzerland (n = 3); Turkey (n = 1); United States (n = 3).
[b] Argentina (n = 1); Austria (n = 1); Belgium (n = 1); Canada (n = 5), Chile (n = 1), Greece (n = 2); North Macedonia (n = 1); Portugal (n = 9); Slovenia (n = 2); Sweden (n = 1); Switzerland (n = 3); Turkey (n = 1); United States (n = 2).
[c] Including one general practitioner in training.
[d] Including six internal medicine residents.
[e] Including three internal medicine residents.
[f] Including three pulmonology residents.
[g] Including one pulmonology resident.
[h] Clinical pathologist (n = 1); emergency doctor (1); medical student (n = 1); oncology specialist registrar (n = 1); paediatrician (n = 1); pharmacist (n = 1); radiotherapist (n = 2); oncological surgeon (n = 1); neurosurgeon (n = 1); unknown (n = 1).
[i] Clinical pathologist (n = 1); paediatrician (n = 1); radiotherapist (n = 1).

Table 2
Healthcare professionals' perspectives on end-of-life care for patients with cancer.

When do you consider a patient with cancer to be in end-of-life care? If the life-expectancy is:				
Respondents by profession (n = 208)	<1 year (n = 26)	<6 months (n = 57)	<3 months (n = 110)	<2 weeks (n = 15)
Primary and elderly care	12 (46)	12 (21)	10 (9.1)	3 (20)
- General practitioner	6 (23)	6 (11)	8 (7.3)	0 (0.0)
- Palliative care specialist	5 (19)	4 (7.0)	2 (1.8)	3 (20)
- Geriatrician	1 (3.8)	2 (3.5)	0 (0.0)	0 (0.0)
Haemato-oncology	9 (35)	20 (35)	59 (54)	8 (53)
- Oncologist	1 (3.8)	3 (5.3)	18 (16)	1 (6.7)
- Haematologist	4 (15)	3 (5.3)	11 (10)	1 (6.7)
- Internist	4 (15)	14 (25)	30 (27)	6 (40)
Cardiovascular medicine	3 (12)	18 (32)	26 (24)	3 (20)
- Cardiologist	2 (7.7)	10 (18)	11 (10)	0 (0.0)
- Vascular medicine specialist	1 (3.8)	8 (14)	15 (14)	3 (20)
Other specialties	2 (7.7)	7 (12)	15 (14)	1 (6.7)
- Pulmonologist	1 (3.8)	5 (8.8)	12 (11)	1 (6.7)
- Neurologist	0 (0.0)	1 (1.8)	1 (0.9)	0 (0.0)
- Physician assistant, nurse practitioner or nurse	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)
- Other profession	1 (3.8)	1 (1.8)	1 (0.9)	0 (0.0)

Data are presented as numbers (n, % in brackets).

Table 3
Deprescribing antithrombotic therapy in patients with cancer considered in end-of-life care.

When a patient with cancer is considered in end-of-life care, I deprescribe antithrombotic therapy:				
Respondents by profession (n = 203)	Never (n = 41)	Sometimes (n = 123)	Often (n = 38)	Always (n = 1)
Primary and elderly care	6 (15)	20 (16)	10 (26)	0 (0.0)
- General practitioner	5 (12)	8 (6.5)	6 (16)	0 (0.0)
- Palliative care specialist	1 (2.4)	9 (7.3)	4 (11)	0 (0.0)
- Geriatrician	0 (0.0)	3 (2.4)	0 (0.0)	0 (0.0)
Haemato-oncology	18 (44)	44 (36)	22 (58)	1 (100)
- Oncologist	4 (9.8)	13 (11)	6 (16)	0 (0.0)
- Haematologist	4 (9.8)	12 (9.8)	3 (7.9)	0 (0.0)
- Internist	10 (24)	29 (24)	13 (34)	1 (100)
Cardiovascular medicine	12 (29)	32 (26)	5 (13)	0 (0.0)
- Cardiologist	8 (20)	13 (11)	1 (2.6)	0 (0.0)
- Vascular medicine specialist	4 (9.8)	19 (15)	4 (11)	0 (0.0)
Other specialties	5 (12)	17 (14)	1 (2.6)	0 (0.0)
- Pulmonologist	4 (9.8)	13 (11)	1 (2.6)	0 (0.0)
- Neurologist	1 (2.4)	1 (0.8)	0 (0.0)	0 (0.0)
- Physician assistant, nurse practitioner or nurse[a]	–	–	–	–
- Other profession	0 (0.0)	3 (2.4)	0 (0.0)	0 (0.0)

Data are presented as numbers (n, % in brackets).
[a] No responses were provided by physician assistants, nurse practitioners or nurses for this particular question.

deprescribing ATT at this stage, while the remaining healthcare professionals (19 %) from different specialties reported deprescribing ATT often.

The median number of patients with cancer in end-of-life care and receiving ATT, seen or treated by the respondents, was 20 (IQR 10–50). Among these patients, the median estimated frequency per healthcare professional of considering ATT deprescription was 10 times per year (IQR 4–10), while the median frequency of actual deprescription was 5 times per year (IQR 2–10) (Table S2). When considering whether to prescribe or deprescribe ATTs, most healthcare providers reported seeking advice from colleagues at least sometimes in both settings (Table 4). The factors determining the decision to either prescribe or deprescribe ATT were similar for both cases (Table 5). The main determinants were the bleeding risk, thrombotic risk, the indication for ATT, the patient's performance status and the patient's preference. Of note, the ATT type, ATT indication and thrombotic risk were slightly more frequently reported as determinants for ATT prescription than for ATT deprescription.

Discrete choice experiment

A total of 191 respondents participated in the DCE, 183 (96 %) of whom answered all choice sets. The practice regions of the DCE respondents are shown in Table S3, and the healthcare professionals' responses to the series of choice sets are presented in Table 6.

The main driver for deprescribing ATT, and DOACs and VKAs in particular, was high bleeding risk. Also, an ECOG-PS score of 3 or higher (indicating a notable lack of self-care ability and being bedridden or confined to a chair for over 50 % of waking hours) made healthcare professionals consider deprescription of ATT. High thrombotic risk, on the other hand, was often an obstacle to deprescribing ATT, except for the case of patients with high bleeding risk and poor ECOG-PS (score $\geq$ 3) in whom 88 % of respondents deemed deprescribing LMWH most appropriate [20]. Compared to the other types of ATT, the respondents rarely favoured deprescription of antiplatelet agents in any situation, while the preference for deprescribing DOACs, VKAs or LMWH depended on the specific circumstances. Across the eight choice sets, five respondents (2.7 %) felt that deprescribing was inappropriate in anyone of the scenarios.

Results of the multinomial logistic regression analysis are presented in Fig. 1. The model's predicted probabilities matched well with the observed proportions for the majority of choice sets. All factors (ECOG-PS, thrombotic risk, and bleeding risk) were individually associated with the tendency towards deprescribing ATT, each yielding p-values below 0.0001 in the likelihood ratio test. For high bleeding risk, this association was positive and significant across all ATT types, with oral or parenteral anticoagulants having the strongest impact. A poor ECOG-PS score also promoted deprescription in all ATT types; however, this trend was significant only in LMWH. Conversely, high thrombotic risk led to a general tendency of maintaining ATT, but this was significant in the case of DOACs or VKAs only.

When incorporating participant-related variables from the preregistration survey into the model, McFadden's R^2 increased from 0.078 to 0.097. While the results of the model coincided with the results from the simpler model with respect to the factors defining the choice sets, the enlarged model revealed some preferences associated to the healthcare professionals' characteristics (Table 7). Healthcare professionals from the group consisting of internists, oncologists and haematologists, and even more so from the group of vascular medicine specialists and cardiologists, were more inclined to deprescribe antiplatelet therapy than other medical specialities. Conversely, the model did not identify any significant associations for other types of ATT, nor for the group comprising general practitioners, palliative care specialists, nursing home physicians and geriatricians vs. healthcare professionals from other specialties. In addition, no significant differences

Table 4
Consultation and advice from colleagues when deciding to deprescribe or prescribe antithrombotic therapy in patients with cancer considered in end-of-life care.

Do you actively seek consultation and advice from your colleagues when deciding to deprescribe or prescribe antithrombotic therapy in patients with cancer considered in end-of-life care?		
Frequency	Deprescribing (n = 161)	Prescribing (n = 202)
Never	18 (11)	24 (12)
Sometimes	92 (57)	118 (58)
Often	36 (22)	50 (25)
Always	15 (9.3)	10 (5.0)

Data are presented as numbers (n, % in brackets).

Table 5
Determinants influencing antithrombotic therapy decisions in patients with cancer considered in end-of-life care.

Factors	Deprescription (n = 202)	Prescription (n = 202)
ATT type	97 (48)	117 (58)
ATT indication	142 (70)	172 (85)
Bleeding risk	186 (92)	172 (85)
Thrombotic risk	115 (57)	160 (79)
Sex	6 (3.0)	5 (2.5)
Age	46 (23)	39 (19)
Patient's performance status	149 (74)	144 (71)
Patient's preference	143 (71)	141 (70)
Other factor[a]	10 (5.0)	9 (4.5)
- Actual life expectancy (i.e., short vs. relatively long)	6	4
- Pain relief	–	2
- Swallowing capability vs. swallowing inability	3	1
- Symptomatology/expected impact on QoL	2	2

Data are presented as numbers (n, % in brackets). Abbreviations: ATT, antithrombotic therapy; QoL, quality of life.
Note: healthcare professionals were given the option to select multiple factors.
[a] This could involve multiple factors per healthcare professional.

were observed at the geographical level between participants from Eastern or Southern Europe and those from the reference region of Northern/Western Europe. Female healthcare professionals exhibited a higher inclination to deprescribe DOACs or VKAs compared to their male colleagues. Apart from significance of single levels (e.g., high vs. low), all these categorical covariates also proved significant as a whole, according to the likelihood ratio tests we performed. Furthermore, there appears to be a positive association between the number of patients with cancer receiving ATT seen or treated per year and the likelihood of considering deprescribing DOACs or VKAs as part of end-of-life care for these patients. An association to the degree of professional experience, however, was not found.

Actual cases

Respondents to the flash-mob survey collectively shared 131 case decisions in patients with active cancer who were considered to receive end-of-life care (Tables S4–S6). In 107 (82 %) cases, the reporting healthcare professionals chose to deprescribe the ATT, while in the remaining 24 cases (18 %), the decision was to maintain the ATT. Healthcare professionals primarily reported a high thrombotic risk as the reason for maintaining the ATT, whereas the key factors driving ATT deprescription were a high bleeding risk, poor performance status and poor prognosis.

Discussion

The findings of our study, one of the first to specifically explore healthcare professionals' views, preferences and practices regarding the use of ATT in the end-of-life care of patients with cancer, confirm that deprescription of ATT is not routinely undertaken in the context of end-of-life care for patients with advanced cancer. Although not limited to ATT and patients with cancer, a questionnaire study showed that although physicians indicate to be willing to stop medication when life expectancy is limited (approximately three months), in practice they maintain medication more regularly than they deprescribe it [22]. Based on the statements presented to the physicians, the authors did not identify any possible reasons why medication is continued. Not surprisingly, the main reason reported by participating healthcare providers in our study was the perceived thrombotic risk (i.e., high). Other less frequently reported factors contributing to continuation of ATT were inexperience with deprescribing, low bleeding risk and favourable performance status of the patient.

Despite a growing body of literature on deprescribing general medications in patients with cancer at the end of life, there is a lack of specific research on ATT in this population [23–29]. In addition to this, most studies focus primarily on the incidence of “Potentially Inappropriate Medications” but do not report on actual management and decision-making factors [24–29]. To date, only one study has focused on the perspective of healthcare professionals and reported on the use of ATT and factors influencing deprescribing of such medications [30].

While there is general consensus about the importance of end-of-life care and reducing polypharmacy, there remains ambiguity as to what constitutes end-of-life. It is clear that end-of-life care ends with the death of a person, but when it begins or what it involves is hard to determine [31]. Several criteria are used to conceptualise this phase, such as rapid tumour progression, significant decline in a patient's physical and cognitive functioning and failed curative treatment options [32,33]. Besides these disease- and patient-centred criteria, time-based criteria are also used. The National Institute for Health and Care Excellence (NICE) for End of Life Care describes end-of-life care as care provided in the final weeks and months of life [34]. Despite this, end-of-life care is commonly referred to as the care individuals receive in their final weeks or days of life. The ambiguity surrounding the term ‘end-of-life’ and the challenge of defining this phase is underscored by the considerable variation observed in the perspectives of the participating healthcare professionals on the time frame denoting end-of-life care, both overall and within distinct professional groups.

Some limitations of our study should be kept in mind when interpreting our results. First, the overall response rate to the survey was lower than anticipated, particularly in some countries and among certain specialties. This happened despite using multiple channels for the distribution of the survey and increasing the likelihood of reaching a

Table 6
Healthcare professionals' responses to the discrete choice experiment choice sets.

Choice set		Choice set description			Scenario			
		ECOG-PS[a]	Thrombotic risk[b]	Bleeding risk[c]	DOAC or VKA	LMWH	AA	None
1	n = 191	↑	↑	↑	0 (0.0)	168 (88)	0 (0.0)	23 (12)
2	n = 190	↑	↑	↓	36 (19)	41 (22)	26 (14)	87 (46)
3	n = 190	↑	↓	↑	99 (52)	47 (25)	16 (8.4)	28 (15)
4	n = 189	↑	↓	↓	40 (21)	71 (38)	23 (12)	55 (29)
5	n = 184	↓	↑	↑	56 (30)	41 (22)	30 (16)	57 (31)
6	n = 185	↓	↑	↓	28 (15)	23 (12)	21 (11)	113 (61)
7	n = 184	↓	↓	↑	93 (51)	43 (23)	18 (9.8)	30 (16)
8	n = 183	↓	↓	↓	37 (20)	55 (30)	15 (8.2)	76 (42)

Abbreviations: DOAC, direct oral anticoagulant; VKA, vitamin K antagonist; LMWH, low-molecular-weight heparin; AA, antiplatelet agent; ECOG-PS, Eastern Cooperative Oncology Group performance status.
[a] ECOG-PS ↑ indicates an ECOG-PS score of 3 or higher, ECOG-PS ↓ indicates an ECOG-PS score of 2 or lower.
[b] Thrombotic risk ↑ indicates a high risk of thrombosis, thrombotic risk ↓ indicates a low risk of thrombosis, as judged by the healthcare professional.
[c] Bleeding risk ↑ indicates a high risk of bleeding, bleeding risk ↓ indicates a low risk of bleeding, as judged by the healthcare professional.

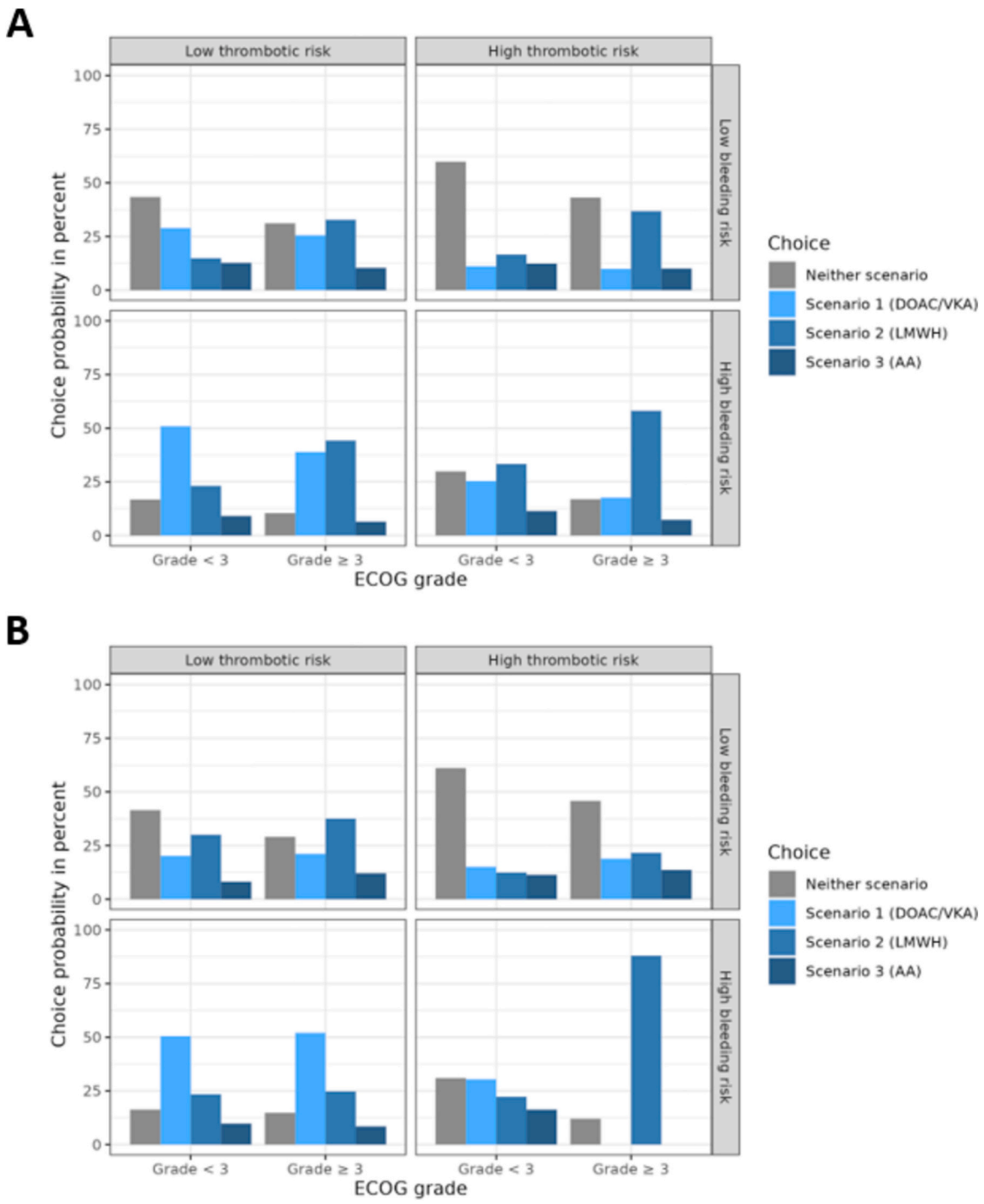

Fig. 1. The estimated and observed choice probabilities of the discrete choice experiment.
To explore preferences regarding deprescribing in routine practice, all healthcare professionals were presented with various hypothetical scenarios containing information on patient's performance status, antithrombotic therapy, and the risk of bleeding and thrombosis. They were asked to select the scenario in which they would consider deprescribing the antithrombotic medication as part of end-of-life care for patients with cancer to be the most appropriate choice. If deprescription of the antithrombotic therapy was deemed inappropriate in any scenario, healthcare professionals could select 'neither scenario'.
Panel A illustrates the estimated choice probabilities relative to the logistic regression model and panel B the observed choice probabilities.
Abbreviations: DOAC, direct oral anticoagulant; VKA, vitamin K antagonist; LMWH, low-molecular-weight heparin; AA, antiplatelet agent.

wide audience. The heterogeneous response rate may reflect a lack of awareness of this topic or unfamiliarity with deprescribing ATT in the end-of-life setting. This also means that healthcare professionals who did respond to the survey may represent a select group which is more familiar with and/or may has had more interest in this topic. Accordingly, our findings may overestimate the propensity of healthcare professionals to consider deprescribing of ATT. Second, DCE analyses offer only a limited choice of factors affecting decisions. Thus, aiming to minimise complexity of the hypothetical scenarios and decision fatigue from an overwhelming number of choice sets and a large number of possible combinations, the number of factors and levels presented in the DCE was limited to those that were deemed clinically realistic and

Table 7
Odds ratios with 95 % confidence intervals and p-values of deprescribing a certain type of antithrombotic therapy as opposed to maintaining antithrombotic therapy regardless of type estimated from the multinomial logistic regression model.

Predictor	Level	Scenario		
		DOAC or VKA	LMWH	AA
ECOG-PS score	Low	1.00 (reference)	1.00 (reference)	1.00 (reference)
	High	1.23 ([0.92, 1.65], p = 0.163)	3.14 ([2.38, 4.14], p < 0.001 *)	1.13 ([0.78, 1.65], p = 0.511)
Thrombotic risk	Low	1.00 (reference)	1.00 (reference)	1.00 (reference)
	High	0.27 ([0.20, 0.37], p < 0.001 *)	0.81 ([0.62, 1.07], p = 0.133)	0.70 ([0.48, 1.01], p = 0.057)
Bleeding risk	Low	1.00 (reference)	1.00 (reference)	1.00 (reference)
	High	4.68 ([3.47, 6.33], p < 0.001 *)	4.10 ([3.10, 5.42], p < 0.001 *)	1.86 ([1.27, 2.74], p = 0.002 *)
Specialty	Cardiovascular medicine	0.77 ([0.44, 1.35], p = 0.359)	0.86 ([0.52, 1.40], p = 0.539)	3.45 ([1.44, 8.25], p = 0.005 *)
	Haemato-oncology	1.36 ([0.82, 2.26], p = 0.234)	1.17 ([0.73, 1.86], p = 0.518)	2.79 ([1.19, 6.55], p = 0.019 *)
	Primary and elderly care	0.94 ([0.54, 1.66], p = 0.842)	0.69 ([0.41, 1.18], p = 0.173)	1.68 ([0.66, 4.27], p = 0.273)
	Other	1.00 (reference)	1.00 (reference)	1.00 (reference)
Region	Northern/Western Europe	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Eastern Europe	0.74 ([0.43, 1.26], p = 0.269)	1.18 ([0.74, 1.88], p = 0.496)	0.50 ([0.24, 1.03], p = 0.060)
	Southern Europe	0.77 ([0.55, 1.08], p = 0.126)	0.78 ([0.57, 1.07], p = 0.129)	0.83 ([0.54, 1.26], p = 0.384)
	Other region	0.37 ([0.18, 0.76], p = 0.007 *)	0.42 ([0.22, 0.79], p = 0.007 *)	0.48 ([0.19, 1.21], p = 0.117)
Sex of healthcare professional	Male	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Female	1.41 ([1.03, 1.94], p = 0.032 *)	0.80 ([0.60, 1.07], p = 0.129)	1.10 ([0.74, 1.65], p = 0.637)
Patients treated	Per patient per month	1.02 ([1.00, 1.04], p = 0.041 *)	0.99 ([0.97, 1.01], p = 0.387)	1.02 ([1.00, 1.05], p = 0.082)
Professional experience	Per 5 years	1.01 ([0.99, 1.03], p = 0.452)	1.00 ([0.98, 1.02], p = 0.761)	1.00 ([0.97, 1.02], p = 0.840)

Abbreviations: DOAC, direct oral anticoagulant; VKA, vitamin K antagonist; LMWH, low-molecular-weight heparin; AA, antiplatelet agent; ECOG-PS, Eastern Cooperative Oncology Group performance status.
* Predictor level is significant (p-value < 0.05).

meaningful to healthcare professionals. Third, no definitive conclusions regarding the difference in ATT management between female and male healthcare professionals can be made, as our data did not include information that allows direct comparison of cases treated by either sex. Another limitation could be the use of a forced-choice approach in the DCE, meaning that participants did not have the opportunity to select multiple scenarios in each choice set. In reality, healthcare professionals might consider deprescribing to be appropriate in more than one scenario. However, in our opinion forced-choice questions best serve the purpose of the present study because they encourage respondents to reflect on each option more deeply and weigh their preferences. Finally, the observed difference between the frequency of considered and actual ATT deprescription (Table S2) raises the question on how reliable the results of a DCE based on hypothetical decisions can be.

In conclusion, healthcare professionals' perspectives and practice patterns vary, and some preferences appear to be associated with the therapists' professional focus and region of practice. The present study sheds light on the variability of practice patterns among healthcare professionals from different clinical and geographical areas regarding ATT in the end-of-life setting of patients with advanced cancer. Future research will need to investigate ATT management in specific indications, focusing on both prescribing and deprescribing behaviour as well as the timing, motivations and associated outcomes, in order to further dissect the decision-making process in patients with cancer and a short life expectancy. In addition, and importantly, the insights gained from this study will be used in the next steps of the SERENITY project including qualitive interviews with patients, their carers and healthcare professionals on ATT management at the end of life and a Delphi process. These will inform the design of a shared decision support tool (SDST) aimed at supporting informed decision-making about ATT in patients with cancer nearing the end of life. Once the SDST is developed, its implementation and effects will be tested in a randomised controlled trial in five European countries [16]. It is expected that the present study and the entire SERENITY project will inform guidelines to assist healthcare professionals and patients in making evidence-based decisions about optimal use of ATT at the end of life.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) used ChatGPT in order to improve readability. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

CRediT authorship contribution statement

E.S.L. Martens: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Writing – original draft, Writing – review & editing, Visualization, Project administration. **D. Becker:** Conceptualization, Methodology, Investigation, Resources, Writing – original draft, Writing – review & editing, Visualization, Project administration. **C. Abele:** Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Visualization. **D. Abbel:** Methodology, Writing – review & editing. **W.P. Achterberg:** Methodology, Resources, Writing – review & editing. **J.J. Bax:** Methodology, Writing – review & editing. **L. Bertoletti:** Resources, Writing – review & editing. **M.E. Edwards:** Resources, Writing – review & editing. **C. Font:** Resources, Writing – review & editing. **A. Gava:** Resources. **J. Goedegebuur:** Methodology, Resources, Writing – review & editing. **A.A. Højen:** Methodology, Writing – review & editing. **M.V. Huisman:** Methodology, Writing – review & editing. **M.J.H.A. Kruip:** Methodology, Resources, Writing – review & editing. **I. Mahé:** Methodology, Resources, Writing – review & editing. **S.P. Mooijaart:** Methodology, Resources, Writing – review & editing. **M. Pearson:** Methodology, Writing – review & editing. **K. Seddon:** Writing – review & editing. **S. Szmit:** Methodology, Resources, Writing – review & editing. **S.S.I.R. Noble:** Conceptualization, Methodology, Resources, Writing – review & editing, Project administration. **F.A. Klok:** Conceptualization, Methodology, Investigation, Resources, Writing – original draft, Writing – review & editing, Supervision, Project administration. **S.V. Konstantinides:** Conceptualization, Methodology, Investigation, Resources, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.thromres.2024.109205.

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