European Journal of Cancer 226 (2025) 115602

Contents lists available at ScienceDirect

European Journal of Cancer

journal homepage: www.ejcancer.com

Original research

Navigating rare cancer care: Patient-reported insights into patient journeys, time to diagnosis, decision-making and care coordination from a national cross-sectional study in Germany

Laura Oestreich [a,*], Friederike Mumm [a,b], Theresia Pichler [a,b], Myrto Boukovala [a], Vanessa Colonna [b], Dorit Di Gioia [a,b,c], Theres Fey [b,i], Volker Heinemann [a,b], Jana Hinneburg [d], Julia Lühnen [e], Maximilian Reichert [f,i,j], Michael Schoenberg [g], Anton Seitz [g], Karsten Spiekermann [a,i], Christine Spitzweg [h], Anke Steckelberg [d], Sebastian Theurich [a], C. Benedikt Westphalen [a,b], Sandro Zacher [d], Danmei Zhang [a], Karin Berger-Thürmel [a,b,i,j,1], Michael von Bergwelt-Baildon [a,b,i,j,1], on behalf of the TARGET group

[a] Department of Medicine III, LMU University Hospital, Ludwig-Maximilians-University of Munich, Munich, Germany
[b] Comprehensive Cancer Center (CCC Munich LMU), LMU University Hospital, Ludwig-Maximilians-University of Munich, Munich, Germany
[c] SarKUM, Center of Bone and Soft Tissue Tumors, LMU University Hospital, Ludwig-Maximilians-University of Munich, Munich, Germany
[d] Institute of Health, Midwifery and Nursing Science, Medical Faculty of Martin Luther University Halle-Wittenberg, Halle (Saale), Germany
[e] Institute of Clinical Nursing Science, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Berlin, Germany
[f] Department of Medicine II, TUM University Hospital, Technical University of Munich, Munich, Germany
[g] Patient Advisory Board of the Comprehensive Cancer Center Munich, Munich, Germany
[h] Department of Medicine IV, LMU University Hospital, Ludwig-Maximilians-University of Munich, Munich, Germany
[i] Bavarian Cancer Research Center (BZKF), Munich, Germany
[j] German Cancer Consortium (DKTK), Partner Site Munich, Munich, Germany

ARTICLE INFO

Keywords:
Oncology
Haematology
Rare cancers
Care coordination
Patient journey

ABSTRACT

Background: Evidence on patient pathways, care coordination, and patient needs in rare cancers (RC) is limited but essential for optimising healthcare systems and resource allocation. Addressing these gaps requires country-specific data reflecting national healthcare structures and cultural differences. This is the first study in Germany to explore these dimensions.

Methods: Using methodological triangulation, we combined a literature review, exploratory interviews, and a cross-sectional anonymous online survey. The survey assessed diagnostic intervals, journeys, care coordination (German Care Coordination Instrument [CCI]), and involvement in medical decision-making (adapted Control Preference Scale) among adult patients with cancer in Germany. Diagnostic intervals were analysed using Kaplan–Meier and Cox regressions methods, CCI predictors using multivariate models.

Findings: Patients with RC (338 of 1254 participants) reported longer median times from symptom onset to treatment (109 [IQR: 35–326] vs. common cancers (CC): 70 [35–185] days) and from first consultation to diagnosis (28 [14–90] vs. CC: 14 [7–35] days), particularly in rural areas (21 [7–60] vs. urban: 14 [7–42] days) ($p < 0.001$). Patients with RC more often first consulted general practitioners (65.6 %, CC: 28.1 %), saw more office-based physicians before diagnosis (1.99 [SD: 1.23], CC: 1.66 [0.90]), and were more frequently diagnosed at university hospitals (33.3 %, CC: 11.2 %) ($p < 0.001$). Discrepancies in preferred levels of involvement in decision-making and higher information needs (RC: 62.9 %, CC: 55.9 %, $p = 0.047$) were reported. The CCI varied according to cancer types.

* Correspondence to: Department of Medicine III, Group Oncological Healthcare Research/Health Economics, LMU University Hospital, Marchioninistraße 15, Munich 81377, Germany.
E-mail address: laura.oestreich@med.uni-muenchen.de (L. Oestreich).
[1] Shared last authors.

https://doi.org/10.1016/j.ejca.2025.115602
Received 30 April 2025; Received in revised form 27 June 2025; Accepted 1 July 2025
Available online 5 July 2025
0959-8049/© 2025 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Interpretation: Patients with RC in Germany experience longer diagnostic pathways and fragmented care, highlighting the need for targeted, cross-sectoral care coordination and greater patient empowerment.

1. Introduction

The complexity of cancer diagnosis and treatment often place a significant burden on patients. Understanding the patients' experiences and needs during their journey, from symptom onset to diagnosis and treatment, is essential for identifying gaps in healthcare systems, optimising referral pathways, enhancing multidisciplinary collaboration, and ultimately improving the outcomes and quality of life for affected individuals [1]. Aligning these experiences with patients' preferences for involvement in medical decision-making is crucial, as it plays a key role in empowering patients and enhancing their care experiences.

In Europe, rare cancers (RC) account for approximately 24 % of all new cancer cases [2]. In Germany, approximately 500,000 new cancer cases are diagnosed each year [3], of which approximately 110,000 are RC [4]. The 5-year survival rate for patients with RC (55 %) is lower than the national average for all cancers (men: 62 %, women: 66 %) [4,5]. This aligns with European trends, where patients with RC have significantly lower 5-year survival rates (48.5 % vs. 63.4 %) and often report a reduced quality of life compared to that in patients with common cancers (CC) [2,6]. In addition to the inherently poorer prognosis for some RCs, these disparities are largely attributed to delayed or incorrect diagnoses, limited access to specialists, logistical challenges in coordinating multiple healthcare providers, limited treatment options, and a lack of disease-specific information [7–10].

Ensuring high-quality care for patients with RC requires coordinated collaboration among stakeholders. In many European countries, general practitioners (GPs) or outpatient specialists serve as the first point of contact [11]; however, effective diagnosis and treatment often depend on timely referral to highly specialised cancer centres with multidisciplinary teams [12]. As a result, patients with RC are more likely to receive diagnosis and treatment at different hospitals than patients with CC, which can negatively impact their experience of care [13]. The perceived quality of care coordination varies by setting and cancer type. Hospital-based care is rated more favourably than outpatient care in Germany, and care for haematological cancers is rated more favourably than care for head and neck cancers in the US [14,15].

However, national differences in care experiences are likely due to the unique healthcare landscape of each country. These differences underscore the need for national-level data. Sharing insights across borders can help improve healthcare structures and outcomes for all patients with cancer.

Germany introduced the National Cancer Plan in 2008, aiming to improve cross-sectoral and interdisciplinary cancer care while strengthening patient orientation [16]. Nevertheless, evidence on diagnostic pathways, care coordination, and the specific needs of patients with RC is still limited in Germany.

This study aimed to explore the reported experiences and needs of patients with RC related to their journeys and waiting times from symptom onset to diagnosis and treatment initiation, involvement in medical decision-making, and perceptions of care coordination in Germany.

2. Methods

2.1. Study design and population

This cross-sectional study employed methodological triangulation through a mixed-methods approach with a sequential qualitative-quantitative design. Phase 1 involved exploratory, semi-structured patient interviews informed by a literature review. Phase 2 involved a self-administered anonymous online survey to assess the cancer patients' care experiences and needs in Germany. German-speaking adults aged $\geq$ 18 years with a confirmed cancer diagnosis at any stage were eligible for participation. RC were classified according to the data from the Robert Koch Institute 2019 [5]. The online survey was conducted between February and June 2024 using LimeSurvey (Version 5.6.65) in Germany.

This study adhered to the Declaration of Helsinki and followed the STROBE guidelines for observational studies and the CHERRIES checklist for online surveys [17,18]. Ethical approval was granted by the Ethics Committee of the Medical Faculty of LMU Munich (Reference numbers: 23–0173, 23–0795 KB).

2.2. Survey development

In phase 1 of the study, a semi-structured interview guide was

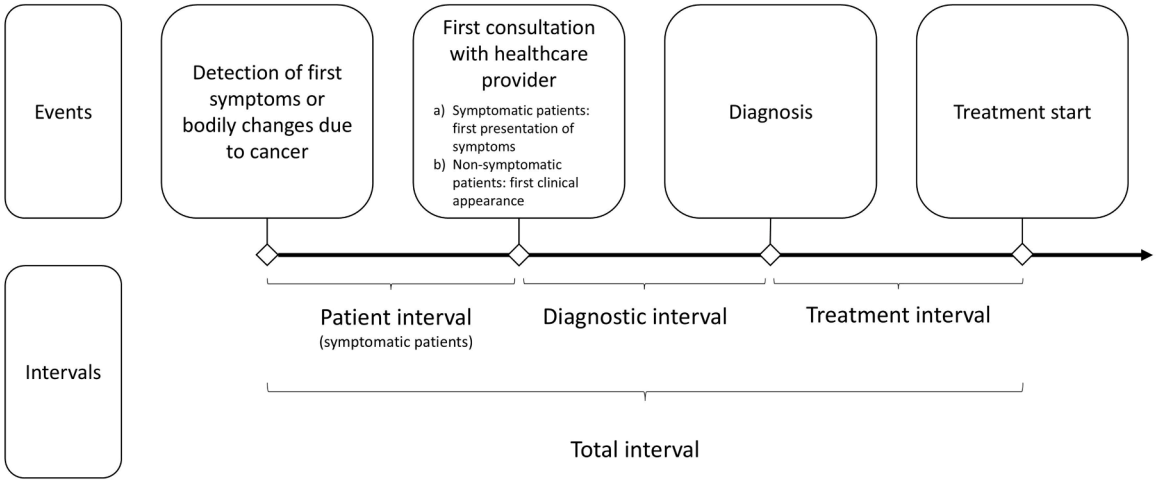

Fig. 1. Conceptual Framework [20–23]: The patient interval refers to the period between the detection of initial symptoms or bodily changes related to cancer and the patient's first consultation with a healthcare provider regarding those symptoms. The diagnostic interval spans the time from the first medical consultation (whether for symptom evaluation or following the incidental detection of cancer during another examination in an asymptomatic individual) to the confirmation of a cancer diagnosis. The treatment interval is defined as the period between receiving a confirmed diagnosis and the initiation of cancer treatment.

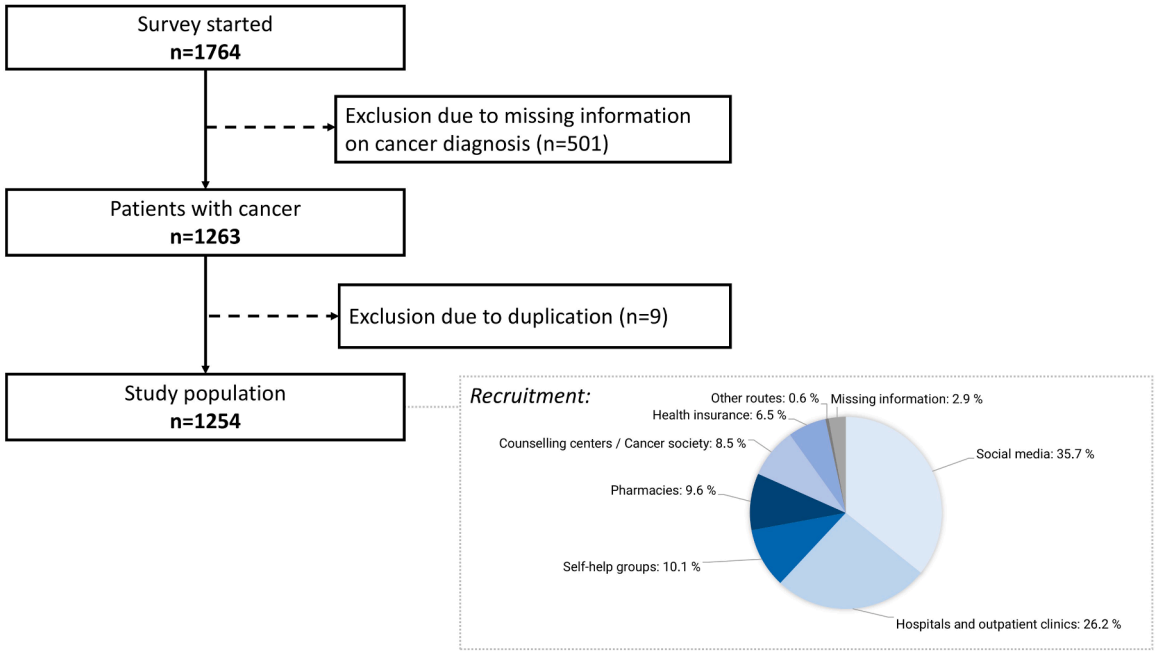

Fig. 2. Study flowchart depicting the selection of the study population.

developed based on a systematic literature review using PubMed, Embase, and Google Scholar. Search terms included “oncology”, “cancer”, “patient journey”, “patient pathways”, “route to diagnosis”, and “participation preferences” in German or English. Between July and September 2023, ten exploratory interviews were conducted with cancer patients via video calls (REDconnect) at the CCC Munich/LMU Hospital to assess their experiences and care related needs. Interviews were analysed using a qualitative content analysis according to Kuckartz [19]. The key concerns identified included the need for faster referrals, better access to specialists, and improved information about suitable hospitals.

Based on the findings from the qualitative phase, a structured questionnaire was developed in phase 2 of the study. The questionnaire was developed collaboratively by an interdisciplinary team of oncologists, psycho-oncologists, social scientists, health and nursing scientists, health economists, and healthcare researchers in close collaboration with patient representatives. The survey was piloted with patients to assess its feasibility, user-friendliness, completeness, and acceptability before dissemination.

2.3. Survey content

In addition to the sociodemographic characteristics of the patients and cancer information, the survey collected data on the route and time to diagnosis and treatment, information needs, participation preferences, care coordination, and desired changes in healthcare experiences (Supplementary Material).

The sociodemographic variables included age, sex, education level, place of residence, and insurance status. Cancer-specific data comprised the number of prior cancer diagnoses, cancer type, date of diagnosis, disease stage, treatment status, and presence of cancer-related symptoms.

Drawing from international consensus statements on diagnostic and treatment intervals and models by Olesen et al. [20,21], Walter et al. [22], and Scott et al. [23], we assessed three patient-reported interval measures: patient, diagnostic, and treatment intervals (Fig. 1).

Patients’ perspectives on care coordination were measured using the validated German version of the Care Coordination Instrument (CCI) for cancer patients [15]. The original CCI version was psychometrically tested [24]. The CCI includes 29 items rated on a four-point Likert scale from strong disagreement to strong agreement. It captures two main dimensions: "Communication/Information" (16 items) and "Need-Based Inter-professional Navigation" (17 items).

Information needs were assessed using items selected from the German version of the validated EORTC QLQ-INFO25 questionnaire [25].

Preferences for involvement in medical decision-making were measured using the adapted German version of the Control Preference Scale (CPS) based on a study by Ernst et al. including eight areas of decision-making [26]. The patients selected one of the following responses: (1) decide independently, (2) decide independently after considering the physician’s opinion, (3) joint decision-making with the physician, (4) physician makes the final decision, but considers the patient’s opinion, or (5) leave the decision to the physician.

2.4. Recruitment

A multi-channel recruitment strategy was implemented to maximise participation. Participants were recruited via social media (Facebook, Instagram, LinkedIn, and WhatsApp), hospitals, outpatient clinics (e.g. GPs, oncologists/haematologists), pharmacies, cancer organisations, health insurers, self-help groups, and patient organisations. Flyers, newsletters, and direct invitations were distributed to raise awareness and encourage participation.

2.5. Statistical analyses

Nominal variables are presented as absolute numbers and percentages, whereas continuous variables are reported as means with standard deviation (SD) for normally distributed data and medians with interquartile range (IQR) for non-normally distributed data. Group differences between patients with RC and those with CC were tested using independent sample t-tests for continuous variables with variance homogeneity, Welch’s test for continuous variables with variance heterogeneity, or Pearson’s chi-square test for categorical variables.

The observed intervals were analysed using the Kaplan–Meier method. For patients whose treatment had not yet begun, the treatment intervals were censored at the time of survey completion. A multivariate

Table 1
Characteristics of the study population by cancer type (total n = 1254).

	Rare cancer n = 338 (27.0 %)	Common cancer n = 916 (73.0 %)	P value
Sociodemographic characteristic			
Age at diagnosis (in years),	n = 333	n = 891	0.177
mean (SD), [min−max]	53.21 (13.37) [11−86]	54.31 (10.81), [12−84]	
Years since diagnosis,	n = 336	n = 900	< 0.001**
median (IQR)	2.28 (0.87−5.45)	1.78 (0.70−3.78)	
Sex, n (%)	n = 333	n = 902	< 0.001**
Female	198 (59.5 %)	778 (86.3 %)	
Male	133 (39.9 %)	122 (13.5 %)	
Divers	2 (0.6 %)	2 (0.2 %)	
Highest education level, n (%)	n = 335	n = 904	< 0.001**
University	124 (37.0 %)	242 (26.8 %)	
Vocational training	103 (30.7 %)	255 (28.2 %)	
Abitur	37 (11.0 %)	114 (12.6 %)	
10th grade	51 (15.2 %)	183 (20.2 %)	
8th/9th grade	18 (5.4 %)	103 (11.4 %)	
No school-leaving certificate	2 (0.7 %)	7 (0.8 %)	
Living area, n (%)	n = 320	n = 873	0.97
Rural	118 (36.9 %)	321 (36.8 %)	
Urban	202 (63.1 %)	552 (63.2 %)	
Health insurance, n (%)	n = 335	n = 906	0.024*
Statutory	237 (70.7 %)	712 (78.6 %)	
Statutory with private supplementary insurance	35 (10.4 %)	85 (9.4 %)	
Private	61 (18.2 %)	104 (11.6 %)	
Other/not insured	2 (0.6 %)	5 (0.5 %)	
Cancer characteristics			
Type of cancer, n (%)			< 0.001**
Breast cancers	3 (1.0 %)[1]	500 (52.5 %)	
Gynaecological cancers	6 (2.0 %)	96 (10.1 %)	
Male genital and urogenital cancers	-	91 (9.5 %)	
Digestive cancers	23 (7.6 %)	106 (11.1 %)	
Melanoma of skin and eye	3 (1.0 %)	27 (2.8 %)	
Neuroendocrine tumours	58 (19.3 %)	-	
Cancers of endocrine organs	2 (0.7 %)	17 (1.8 %)	
Head and neck cancers	18 (6.0 %)	-	
Thoracic cancers	3 (1.0 %)	69 (7.2 %)	
Sarcomas	43 (14.3 %)	-	
Cancers of central nervous system	16 (5.3 %)		
Haematological cancers	157 (46.4 %)	-	
Other	6 (2.0 %)	10 (1.0 %)	
Current phase of the disease, n (%)	n = 335	n = 912	< 0.001**
Initial disease	130 (38.8 %)	360 (39.5 %)	
Recurrence/progression	103 (30.7 %)	190 (20.8 %)	
Cancer-free	61 (18.2 %)	287 (31.5 %)	
Do not know	41 (12.2 %)	75 (8.2 %)	
Phase of treatment, n (%)	n = 335	n = 908	0.027*
Not yet started	19 (5.7 %)	24 (2.6 %)	
First form of treatment	57 (17.0 %)	126 (13.9 %)	
At least second form of treatment	95 (28.4 %)	267 (29.4 %)	
Treatment completed	101 (30.1 %)	327 (36.0 %)	
Palliative/symptom-orientated	27 (8.1 %)	81 (8.9 %)	
Cancellation/pause	20 (6.0 %)	33 (3.6 %)	
Do not know	19 (4.8 %)	50 (5.5 %)	
Number of previous cancer diseases, n (%)	n = 334	n = 902	0.60
0	285 (85.3 %)	757 (82.6 %)	
1	37 (11.1 %)	110 (12.0 %)	
2	8 (2.4 %)	26 (2.9 %)	
3–5	4 (1.2 %)	9 (1.0 %)	
Symptoms prior to cancer, n (%)	n = 328	n = 873	< 0.001**
Yes	237 (72.3 %)	457 (52.3 %)	
No	86 (26.2 %)	409 (46.8 %)	
Do not know	5 (1.5 %)	7 (0.8 %)	

n, number; SD, standard deviation; IQR, interquartile range; min, minimum; max, maximum; [1]: male breast cancer; * $p < 0.05$; ** $p < 0.01$

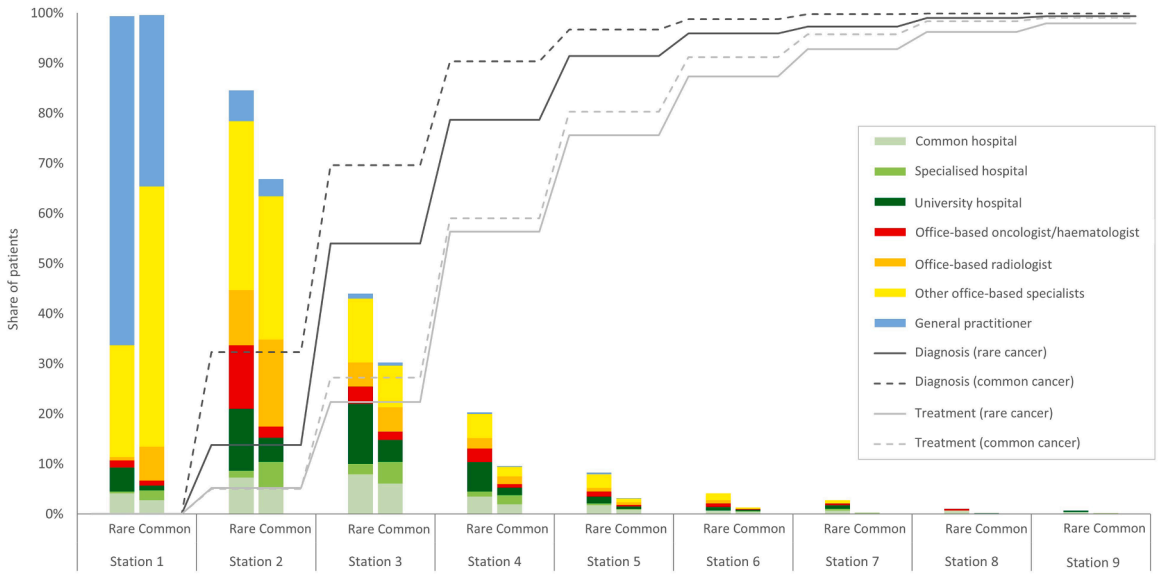

Fig. 3. Pathways to diagnosis in patients with rare and common cancers, and the proportion of patients diagnosed and treated at each stage.

Cox regression analysis was performed to examine the effects of sociodemographic and cancer characteristics on the time to diagnosis, reporting hazard ratios, and 95 % confidence intervals.

Associations between care coordination scores (CCI total score and sub-dimensions) and patient or healthcare characteristics were assessed using multivariate linear regression models. The predictors were selected using forward selection.

Urban and rural classifications were based on the Federal Institute for Research on Building, Urban Affairs, and Spatial Development in Germany as of 31 December 2022 using postal codes and residential area size. Preference for involvement in medical decision-making was grouped into three categories: patient-led (items 1 and 2), shared (item 3), and physician-led (items 4 and 5) decision-making.

For all analyses, a significance level of $\alpha = 0.05$ was considered statistically significant. Data analyses were conducted using RStudio (version 4.3.3) and IBM SPSS Statistics (version 29.0.2.0).

3. Results

3.1. Study population

A total of 1764 participants participated in this study. After excluding respondents with missing information on cancer type or duplicate responses, 1254 patients were included in the final analysis (Fig. 2). The sociodemographic and cancer characteristics of 338 patients with RC (27.0 %) and 916 patients with CC (73.0 %) are shown in Table 1.

3.2. Routes and times to diagnosis and treatment

The route for cancer diagnosis is shown in Fig. 3. On average, patients with RC consulted significantly more physicians before receiving a diagnosis (2.67 [SD: 1.36] vs. 2.08 [SD: 1.05], $p < 0.001$) and treatment (3.68 [SD: 1.71] vs. 3.46 [SD: 1.55], $p = 0.050$) than those with CC. Patients with RC consulted on average 1.99 (SD: 1.23) different office-based physicians before diagnosis (CC: 1.66 [SD: 0.90], $p < 0.001$) and 0.68 hospitals [SD: 0.69] (CC: 0.42 [SD: 0.58], $p < 0.001$). Notably, 43.2 % of patients with RC (CC: 62.2 %) never visited a hospital before diagnosis. The GP was the first point of contact in the diagnostic process for 65.6 % of patients with RC (CC: 28.1 %, $p < 0.001$), whereas patients with CC consulted specialists more often. Notably, 54.4 % of the patients with RC were diagnosed in hospitals, including 33.3 % in university hospitals (CC: 35.9 % and 11.2 %, respectively; $p < 0.001$). Among those diagnosed in hospitals, the majority visited one hospital (RC: 82.1 %; CC: 91.4 %), while smaller proportions visited two (RC: 15.4 %; CC: 7.9 %) or three hospitals (RC: 2.5 %; CC: 0.7 %). Overall, 73.1 % of patients with RC were diagnosed or treated at a university hospital (CC: 38.5 %, $p < 0.001$), and 83.4 % were treated in a hospital (CC: 84.2 %, $p = 0.75$). The detailed diagnostic pathways for the selected RCs are shown in Fig. 4.

The events that led to cancer diagnosis, the number of preliminary diagnoses, received supportive care from other healthcare providers, and information on second opinions are presented in Table 2.

Patient, diagnostic, and treatment intervals are shown in Fig. 5. The median time from awareness of the first symptom to the start of treatment was 109 days (IQR: 35–326) for patients with RC and 70 days (IQR: 35–185) for patients with CC ($p < 0.001$). After 100 days, 24.1 % of patients with RC still had no diagnosis compared with 10.8 % of patients with CC ($p < 0.001$). The median diagnostic intervals were 21 days (IQR: 7–60) in rural areas and 14 days (IQR: 7–42) in urban areas ($p < 0.001$). A multivariate Cox regression analysis confirmed that patients with RC had longer diagnostic intervals than those with CC ($p < 0.001$), and patients with cancer in rural areas had longer diagnostic intervals than those in urban areas ($p = 0.025$; Table 3).

In hindsight, 35.8 % of all the patients preferred different cancer care pathways. The specific preferences for change are illustrated in Fig. 6.

3.3. Assessment of care coordination from the patients' perspective and information needs

The mean perceived care coordination score in the CCI was 48.51 out of 84 (SD: 15.06) overall, 30.60 out of 48 (SD: 9.31) in dimension 1 "communication/information", and 25.57 out of 51 (SD: 8.73) in dimension 2 "need-based inter-professional navigation". Perceptions of care coordination varied according to the cancer type (Fig. 7). Patients' overall perceptions of care coordination were associated with disease stage (cured better than during initial illness), sex (men better than women), type of physician consulted (worse with university hospital or GP), and number of physicians consulted (Table 4).

Overall, 57.7 % of patients with cancer (RC: 62.9 %, CC: 55.9 %, $p = 0.047$) expressed a desire for more information. The specific needs for information are illustrated in Fig. 8. To improve navigation, 22.6 % of all patients (RC: 22.9 %, CC: 22.5 %, $p = 0.40$) expressed the need for a designated care coordinator (oncology navigator).

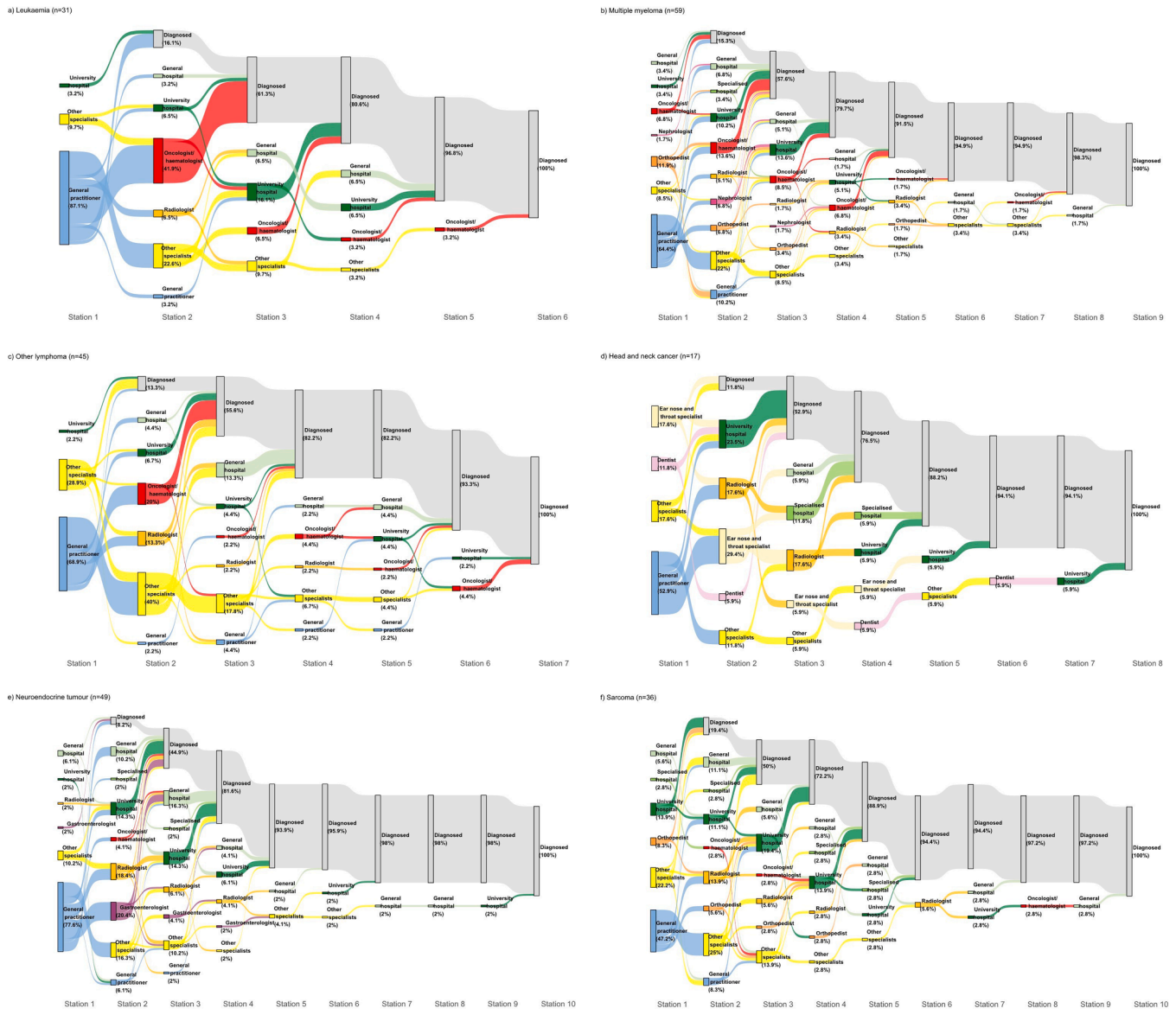

Fig. 4. Sankey diagrams illustrating patient pathways to diagnosis for rare cancers: a) leukaemia, b) multiple myeloma, c) other lymphoma, d) head and neck cancer, e) neuroendocrine tumour, and f) sarcoma.

3.3.1. Involvement in medical decision-making

Patients' preferences regarding their involvement in key medical decisions varied across decisions and was highest in the decision to involve family member and lowest for medication choice (Fig. 9). Regarding the choice of treatment location, patients with RC were less likely to prefer a patient-led decision (51.4 %, physician-led: 12.6 %) than patients with CC (58.6 %, physician-led: 7.6 %, $p = 0.008$). However, in practice, only 34.4 % of patients with RC selected their hospital (57.3 % physician-led) and only 30.5 % chose their office-based specialist themselves (59.6 % physician-led).

4. Discussion

This is the first study in Germany to systematically examine and compare routes and times to cancer treatment, care coordination, information needs, and involvement in medical decision-making among adult patients with RC and CC in a large survey. Our findings highlight disparities in healthcare access, with patients with RC relying more often on GPs as their initial points of contact and receiving a diagnosis and/or treatment in university hospitals. The time to diagnosis depends on the type of cancer and the patient's place of residence, and is approximately twice as long for patients with RC. This study underscores the need for improved cross-sectional care coordination, particularly regarding patient navigation and communication between GPs, specialists, and university hospitals. It also revealed discrepancies in patients' preferred involvement in medical decision-making, along with a strong demand for more cancer-related information.

4.1. Routes and times to diagnosis and treatment

GPs play a central role in the care of patients with RC, with 71.8 % of patients consulting a GP first. As the first point of contact, GPs are often responsible for initiating diagnostic clarification and referring patients to specialists. This mirrors similar trends in other European countries but also highlights the increasing pressure on primary care services, particularly given the aging population and growing GP shortage in Germany [11,27]. With 37 % of GPs in Germany being over 60 years old and a (potential) under-provision in nearly 40 % of districts by 2035 [28,29], ensuring adequate oncological care across regions requires strategic workforce planning, more attractive working conditions for

Table 2
Events leading to diagnosis, preliminary diagnoses, second opinions, and supportive care from other healthcare providers by cancer type (total n = 1254).

	Rare cancer n = 338 (27.0 %)	Common cancer n = 916 (73.0 %)	P value
Events that led to diagnosis, n(%)	n = 314	n = 837	< 0.001**
Symptoms – first visit to physician	149 (47.5 %)	395 (47.2 %)	
Symptoms – first visit to emergency room	24 (7.6 %)	26 (3.1 %)	
Symptoms – first visit to physician, later to emergency room	14 (4.5 %)	14 (1.7 %)	
As part of other examinations	107 (34.1 %)	161 (19.2 %)	
Cancer routine screening	15 (4.8 %)	221 (26.4 %)[1]	
Do not know	5 (1.6 %)	20 (2.4 %)	
Receiving other preliminary diagnoses before final cancer diagnosis, n(%)	n = 297	n = 735	p = 0.46
Yes	140 (47.1 %)	321 (43.7 %)	
No	147 (49.5 %)	394 (53.6 %)	
Do not know	10 (3.4 %)	20 (2.7 %)	
Seeking a second opinion, n(%)	n = 296	n = 740	p = 0.003**
Yes	102 (34.5 %)	221 (29.9 %)	
No	189 (63.9 %)	518 (70.0 %)	
Do not know	5 (1.7 %)	1 (0.1 %)	
If yes: Time of second opinion, n(%)			
Before diagnosis	20 (19.6 %)	34 (15.4 %)	
After diagnosis before treatment	59 (57.8 %)	111 (50.2 %)	
During treatment	27 (26.5 %)	67 (30.3 %)	
After treatment	9 (8.8 %)	28 (12.7 %)	
If yes: Reasons for seeking a second opinion, n(%)			
Confirm diagnosis	40 (39.2 %)	58 (26.2 %)	
Explore (alternative) treatment options	69 (67.7 %)	155 (70.1 %)	
Management of side effects	10 (9.8 %)	16 (7.2 %)	
Participation in clinical studies	8 (7.8 %)	24 (10.9 %)	
Other	18 (17.6 %)	42 (19.0 %)	
Supportive care from other healthcare providers after diagnosis, n(%)	n = 281	n = 660	0.71
None	57 (20.3 %)	141 (21.4 %)	
Psycho-oncological or psychological services	113 (40.2 %)	261 (39.6 %)	
Physiotherapy	89 (31.7 %)	230 (34.9 %)	
Nutritional counselling	75 (26.7 %)	123 (18.6 %)	
Complementary medicine	37 (13.2 %)	106 (16.1 %)	
Alternative practitioners	38 (13.5 %)	87 (13.2 %)	
Self-help groups and patient organisation	97 (34.5 %)	151 (22.9 %)	
Cancer counselling centres	64 (22.8 %)	146 (22.1 %)	
Social services	58 (20.6 %)	168 (25.5 %)	
Pastoral care	5 (1.8 %)	9 (1.4 %)	
Medication analyses in pharmacies	4 (1.4 %)	7 (1.1 %)	
Apps for disease management	-	6 (0.9 %)	
Other	5 (1.8 %)	23 (3.5 %)	

n, number; [1:] highest proportion for cervical (61.5%) and prostate cancer (51.1%); * $p < 0.05$; ** $p < 0.01$.

young physicians, improved remuneration models, and targeted relief measures for GPs. Oncology patient navigators could help ease the initial coordination burden by supporting patients and accelerating the diagnostic and referral process, particularly in complex or ambiguous cases [30].

University hospitals or specialised centres are crucial for diagnosing and treating RCs because of their specialised expertise. International evidence suggests that such referrals can improve patient outcomes. For example, a study from France has linked treatment in sarcoma reference centres to improve survival rates [31], and data from Germany show lower rates of mortality when the initial treatment occurs in certified cancer centres [32]. Therefore, efforts should be made to ensure that the remaining 26.9 % and 16.6 % of patients with RC, who have not yet been treated in a university hospital or hospital, respectively, are referred to such an institution.

The study confirmed that patients with RC, particularly in rural areas, experienced substantial delays during their route to diagnosis. This reflects the often-non-specific symptoms observed in RC and diagnostic uncertainty in primary care [8,33]. Previous international studies have shown that prolonged diagnostic intervals are associated with a lower quality of life, more advanced disease stages at diagnosis, and a higher psychological burden for patients [34–36]. This underscores the need for increased awareness of RCs in primary and specialist care as well as among patients to improve oncological care networks, particularly in rural areas.

4.2. Care coordination

Understanding patients' perceptions of care coordination are essential for adapting healthcare systems in a targeted, patient-centered manner. As shown in our analysis, cancer type specific differences must be considered. In our study, patients who consulted a GP or university hospital rated care coordination more negatively. Further, numerous patients reported a strong demand for more cancer related information. Strategies to improve care coordination could include the broader adoption of shared digital patient records, such as electronic health records, to facilitate information exchange [37]. Low-threshold contact platforms at specialised treatment centres could also enable faster access to specialists and clinical trials, thereby enhancing care coordination. Additionally, patient navigators improved satisfaction and quality of life in previous studies and could help streamline care pathways [38]. Approximately a quarter of our survey respondents expressed a need for such services.

4.2.1. Involvement in medical decision-making

Our findings align with a recent study in Germany showing differences in patients' preferred involvement in decision-making [39]. More than half of the patients in our study reported that the selection of the treatment location was primarily made by the physician. However, when asked about their preferred level of involvement, most patients favoured shared or patient-led decision-making. Similar discrepancies have been observed in previous German studies, particularly among

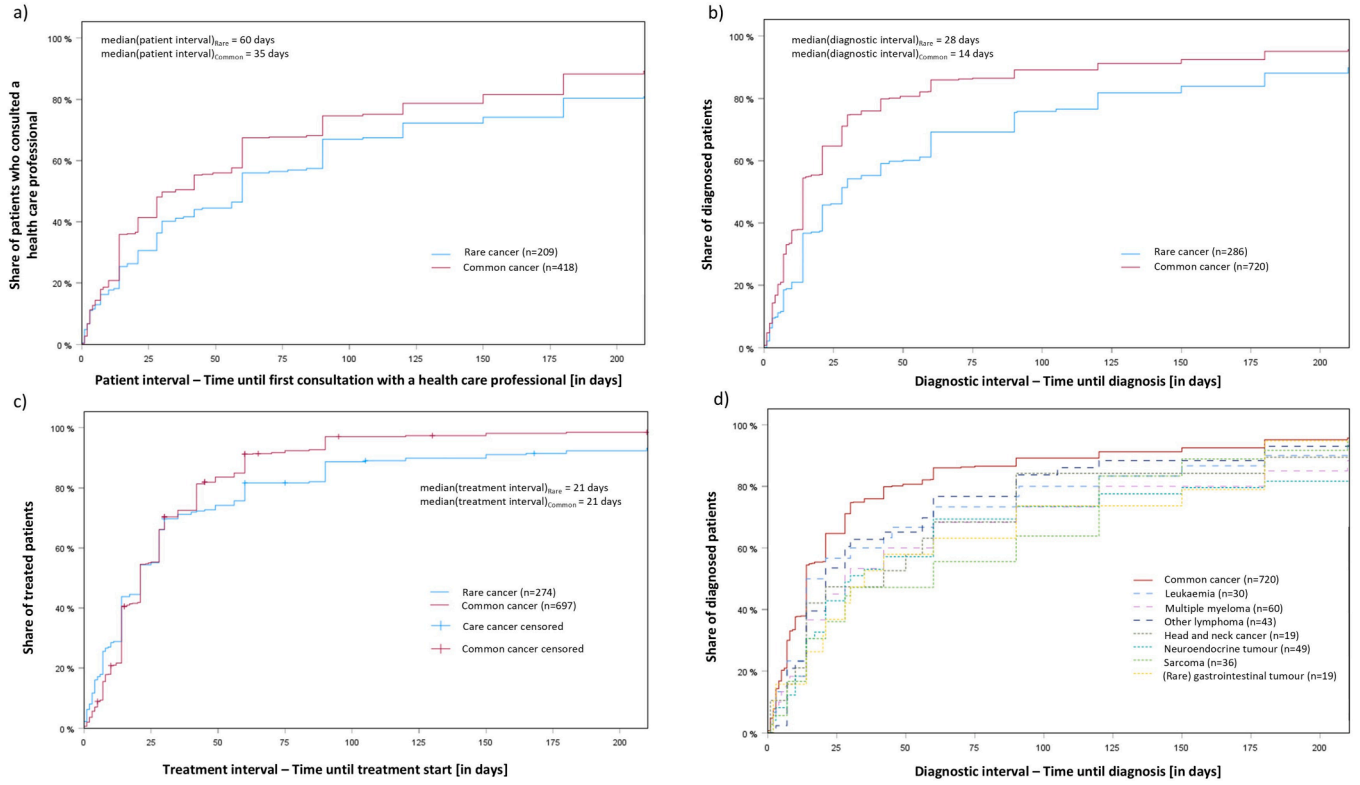

Fig. 5. Kaplan–Meier representation of a) the patient interval (time to first consultation with healthcare provider), b) the diagnostic interval (time from first consultation with healthcare provider to diagnosis), and c) the treatment interval (time from diagnosis to start of treatment) for patients with rare and common cancers, as well as d) the diagnostic interval for patients with various rare cancers.

Table 3
Multivariate Cox regression analysis of the time to diagnosis.

Variable	Hazard ratio [95 % CI]	P value
Rare cancer (common as ref.)	0.72 [0.61 – 0.85]	< 0.001
Age at diagnosis	1.00 [1.00 – 1.01]	0.69
Female (male as ref.)	0.87 [0.73 – 1.04]	0.135
Highest educational level		0.072
University	*ref.*	
Vocational training	1.27 [1.05 – 1.53]	0.013
High school	1.06 [0.84 – 1.35]	0.61
10th grade	1.07 [0.87 – 1.32]	0.52
8th/9th grade	1.22 [0.92 – 1.60]	0.166
No qualification	0.50 [0.21 – 1.23]	0.133
Rural area (urban as ref.)	0.85 [0.73 – 0.98]	0.025
Health insurance		0.70
Statutory	*ref.*	
Statutory with private supplementary insurance	0.95 [0.74 – 1.21]	0.67
Private	1.02 [0.82 – 1.27]	0.85
Other/not insured	0.53 [0.17 – 1.66]	0.27
Current phase of the disease		0.088
Initial disease	Ref	
Recurrence/progression	1.08 [0.90 – 1.31]	0.42
Cancer-free	1.20 [1.02 – 1.41]	0.028
Event that led to diagnosis		0.104
Symptoms – first visit to physician	*ref.*	
Symptoms – first visit to emergency room	1.19 [0.83 – 1.70]	0.35
Symptoms – first visit to physician, later to emergency room	0.87 [0.57 – 1.33]	0.51
As part of other examinations	0.84 [0.70 – 0.99]	0.048
Cancer screening	1.07 [0.89 – 1.29]	0.48
Number of previous cancer diseases	0.95 [0.81 – 1.10]	0.47

CI, confidence interval

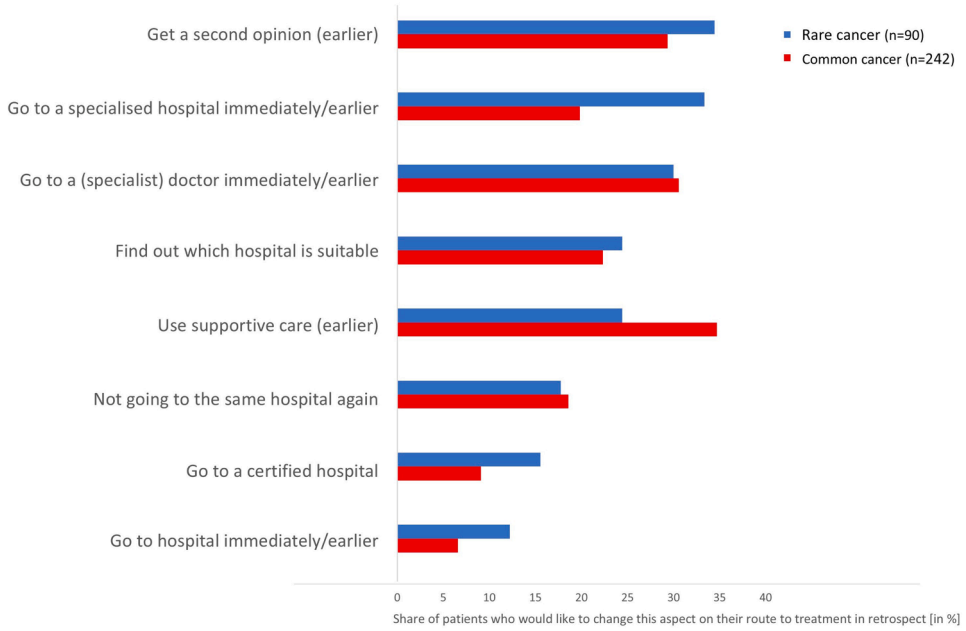

Fig. 6. Preferences for chance in the cancer pathway among patients with rare and common cancers.

patients who indicated a preference for a shared role in the decision-making process [39,40]. In Germany, all patients have the formal right to choose their office-based physicians and hospitals. Occasionally, patient choice can be limited by regional availability, capacity constraints of healthcare providers, and insurance status. For instance, some office-based physicians exclusively treat privately insured patients and limited capacity can disproportionately affect access for statutorily insured patients due to physicians' remuneration and volume constraints. Limited awareness of these rights among patients, combined with insufficient elicitation of preferences by healthcare providers, may further contribute to the observed gap between preferred and actual involvement [41,42]. To better match decision-making processes to individual needs, routine screening of patient preferences using tools, such as the CPS, as proposed by Schuler et al. [43], could be used in routine care to identify and respect patients' desired level of involvement.

4.2.2. Limitations

The survey was not representative of the entire cancer population, and participation bias could not be ruled out. Although diverse patient groups and a large number of participating patients were recruited through different channels, patients with breast cancer were over-represented and patients with prostate cancer were under-represented in the survey compared to population-based cancer registries [3]. Their exclusion did not alter the results. The survey also had a higher participation rate among younger (in Germany, the median onset age of cancer was 69 years for women and 70 years for men) [3] and higher educated individuals, which is common in online surveys [44]. The participants' responses were self-reported and may be subject to recall bias, although no differences were observed between patients diagnosed within or outside the past year. Finally, patients self-reported their cancer types, which were then categorised as rare or common. However, previous studies have indicated that self-reported cancer types are generally accurate [45].

5. Conclusions

The findings of this study underscore the urgent need to enhance patient-centred and cross-sectoral care models and improve patient information in Germany. By analysing the patient perspective to identify system inefficiencies and structural barriers, these insights can inform improvements in cancer care and drive targeted interventions at both the national and European levels. In this study, the use of digital communication channels, including social media, proved to be a fast and effective tool for gathering real-world data on care pathways, and could be further explored in future research.

Future research should focus on developing and evaluating targeted interventions to reduce diagnostic delays, enhance communication between healthcare providers, and optimise patient-centred care models. Regional disparities — such as those between urban or rural areas or potential East–West differences within Germany — should be further investigated to better understand and address structural inequities in care delivery. International comparisons of care coordination strategies could identify the best practices for optimising cancer pathways across healthcare systems, ultimately reducing the disparities in cancer care and ensuring equitable, timely, and high-quality care for all patients.

Ethics committee

The study was approved by the Ethics Committee of the Medical Faculty of the LMU Munich (reference numbers: 23–0173, 23–0795 KB).

CRediT authorship contribution statement

Laura Oestreich: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Friederike Mumm:** Writing – review & editing, Software, Methodology, Investigation. **Theresia Pichler:** Writing – review & editing, Methodology, Investigation. **Myrto Boukovala:** Writing – review & editing, Investigation. **Vanessa Colonna:** Writing – review &

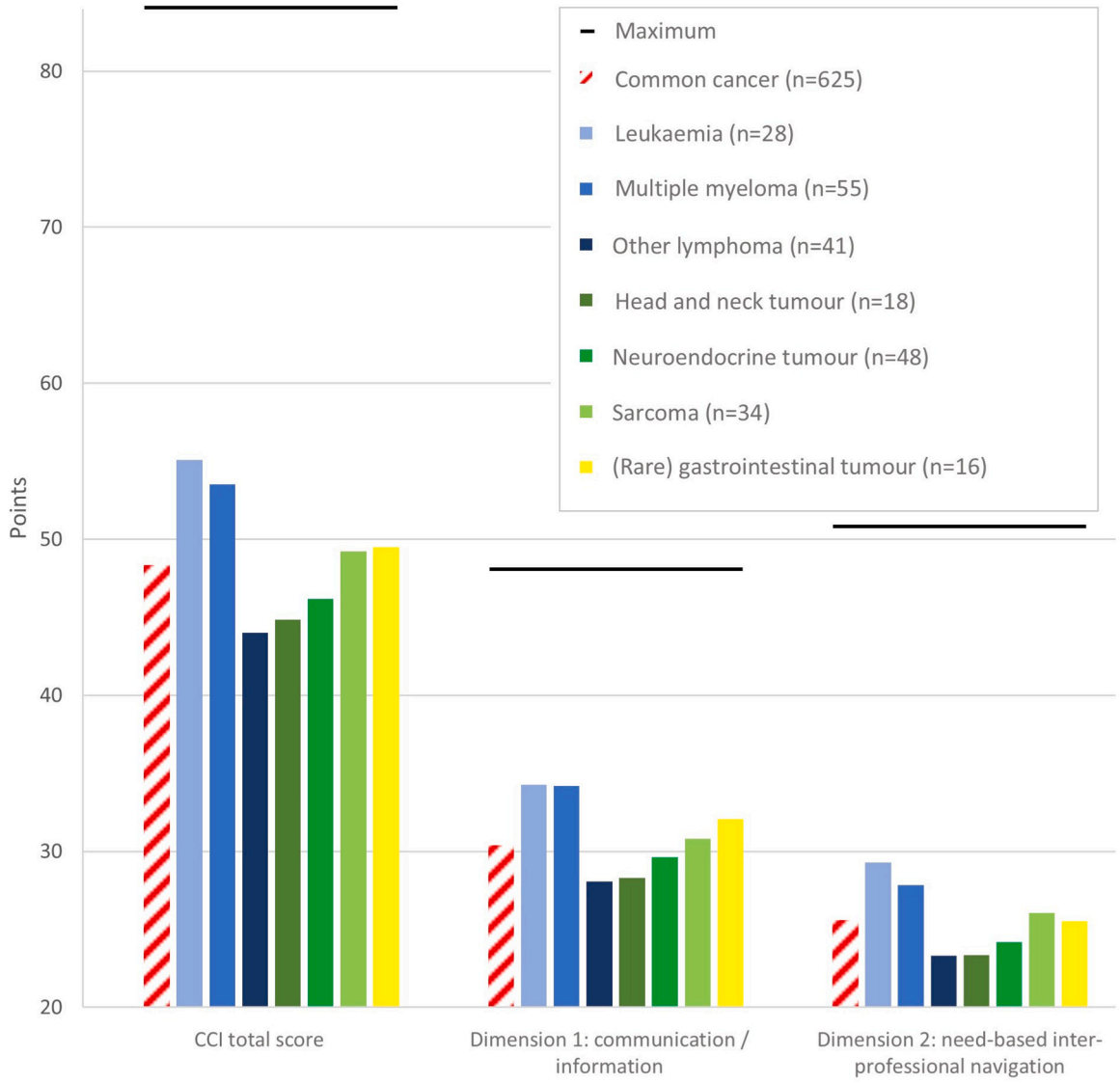

Fig. 7. Overall CCI scores as well as scores for the dimension "communication/information" and dimension "need-based inter-professional navigation" for various rare cancers.

Table 4
Analysis of factors influencing care coordination (total care coordination instrument (CCI), dimension 1: "communication/information", and dimension 2: "need-based inter-professional navigation") using multivariate linear regressions after forward selection (n = 892).

Variable	CCI – total		CCI – dimension 1: communication/ information		CCI – dimension 2: need-based inter-professional navigation	
	β [95 % CI]	P value	β [95 % CI]	P value	β [95 % CI]	P value
Intercept	54.52 [50.76 – 58.29]	< 0.001	34.74 [32.43 – 37.06]	< 0.001	28.97 [26.75 – 31.12]	< 0.001
Rare cancer (common as ref.)	1.64 [-1.10 – 4.38]	0.24	1.46 [-0.23 – 3.14]	0.091	0.6 [-0.96 – 2.23]	0.43
Female (male as ref.)	-3.66 [-6.43 – -0.89]	0.010	-2.90 [-4.60 – -1.19]	< 0.001	-1.76 [-3.37 – -0.14]	0.033
Current phase of the disease (initial disease as ref.)						
Recurrence/progression	2.23 [-0.44 – 4.90]	0.101	1.71 [0.07 – 3.35]	0.042	0.91 [-0.64 – 2.46]	0.25
Cancer-free	4.03 [1.50 – 6.56]	0.002	2.57 [1.02 – 4.13]	0.001	2.11 [0.64 – 3.58]	0.005
Outpatient office-based oncologist visited on the route to diagnosis and treatment (no as ref.)	2.21 [-0.42 – 4.85]	0.100	1.31 [-0.31 – 2.94]	0.112	1.05 [-0.49 – 2.58]	0.181
GP visited on the route to diagnosis and treatment (no as ref.)	-2.62 [-5.06 – -0.18]	0.035	-1.60 [-3.09 – -0.10]	0.037	-1.54 [-2.96 – -0.12]	0.033
University hospital visited on the route to diagnosis and treatment (no as ref.)	-2.49 [-4.75 – -0.22]	0.032	-2.05 [-3.49 – -0.66]	0.004	-1.00 [-2.31 – 0.32]	0.138
Number of different hospitals visited before diagnosis	-0.48 [-2.24 – 1.28]	0.60	-0.53 [-1.61 – 0.55]	0.34	-0.16 [-1.18 – 0.87]	0.76
Number of different office-based physicians visited before diagnosis	-1.61 [-2.75 – -0.47]	0.006	-0.88 [-1.58 – -0.17]	0.015	-1.02 [-1.69 – -0.36]	0.003

CCI: Care coordination instrument; CI, confidence interval

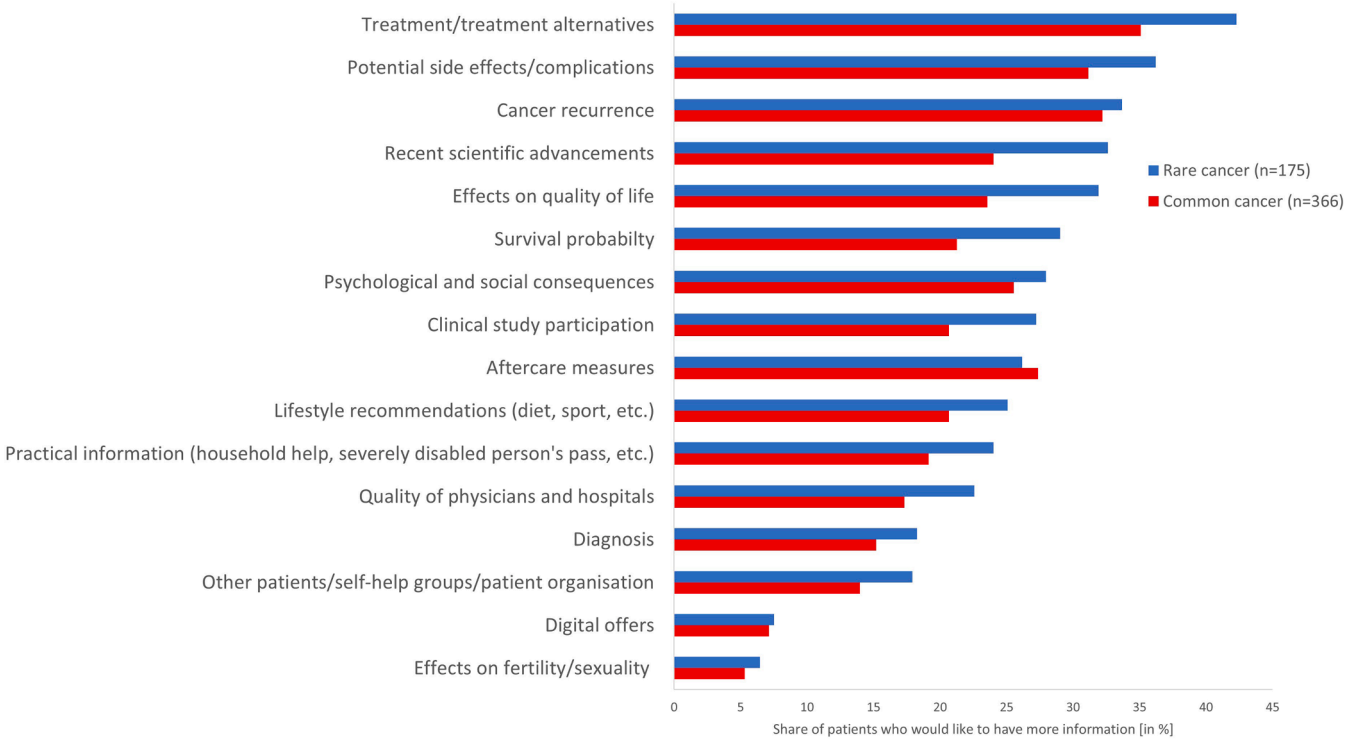

Fig. 8. Preferences for more information among patients with rare and common cancers.

editing, Methodology, Investigation. **Dorit Di Gioia:** Writing – review & editing, Investigation. **Theres Fey:** Writing – review & editing, Methodology, Investigation. **Volker Heinemann:** Writing – review & editing, Investigation, Funding acquisition. **Jana Hinneburg:** Writing – review & editing, Methodology. **Julia Lühnen:** Writing – review & editing, Methodology. **Maximilian Reichert:** Writing – review & editing, Investigation. **Michael Schoenberg:** Writing – review & editing, Methodology. **Anton Seitz:** Writing – review & editing, Software, Methodology, Investigation. **Karsten Spiekermann:** Writing – review & editing, Investigation. **Christine Spitzweg:** Writing – review & editing, Investigation. **Anke Steckelberg:** Writing – review & editing, Methodology. **Sebastian Theurich:** Writing – review & editing, Investigation. **C. Benedikt Westphalen:** Writing – review & editing, Investigation. **Sandro Zacher:** Writing – review & editing, Methodology. **Danmei**

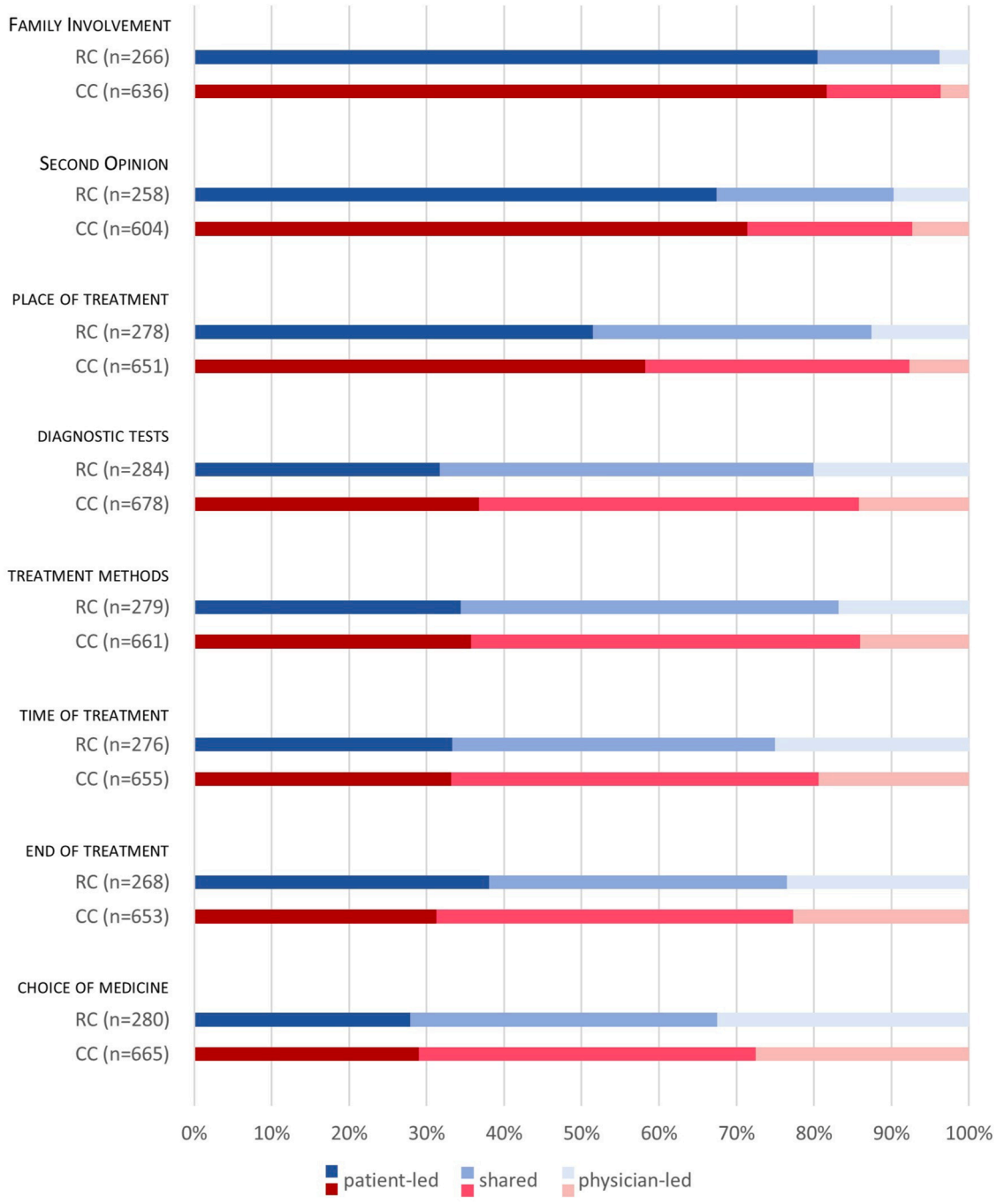

Fig. 9. Distribution of preferences regarding involvement in key medical decisions among patients with rare and common cancers.

Zhang: Writing – review & editing, Investigation. **Karin Berger-Thürmel:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Michael von Bergwelt-Baildon:** Writing – review & editing, Writing – original draft, Resources, Funding acquisition.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: MR has received payments or honoraria for lectures, presentations, and participation in speaker forums from Celgene, Falk, Servier and Roche. All other authors have no conflicts of interest to declare.

Acknowledgments

This work was supported by the Innovation Committee at the Federal Joint Committee (G-BA) (grant number 01NVF20012).

Declaration

The author Volker Heinemann is an Editor of the EJC and was not involved in the editorial review or the decision to publish this article.

Data sharing statement

The data presented in this study are available upon reasonable request from the corresponding author.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ejca.2025.115602.

References

[1] Coulter A, Paparella G, McCulloch A. Listening to people: measuring views. Exp Percept 2020:173–200.
[2] Gatta G, Capocaccia R, Botta L, Mallone S, De Angelis R, Ardanaz E, et al. Burden and centralised treatment in Europe of rare tumours: results of RARECAREnet - a population-based study. Lancet Oncol 2017;18:1022–39.
[3] Robert Koch-Institut, GEKID (Eds.). Krebs in Deutschland für 2019/2020. Berlin 2023 ⟨www.krebsdaten.de/abfrage⟩ [accessed 22 August 2024].
[4] Gatta G, Trama A, Capocaccia R, Hackl M, Eycken EV, Henau K, et al. Epidemiology of rare cancers and inequalities in oncologic outcomes. Eur J Surg Oncol 2019;45:3–11.
[5] Zentrum für Krebsregisterdaten im Robert Koch-Institut. Datenbankabfrage mit Schätzung der Inzidenz, Prävalenz und des Überlebens von Krebs in Deutschland auf Basis der epidemiologischen Landeskrebsregisterdaten. Zentrum für Krebsregisterdaten im Robert Koch-Institut.
[6] Driehuis E, de Heus E, Schrieks M, Engelen V, Buffart TE, Vink GR, et al. Quality of life of patients with rare cancer: a comparison with patients with colorectal cancer and the association with disease trajectory-related factors. J Cancer Surviv 2023;17:986–96.
[7] Drabbe C, Grünhagen DJ, Van Houdt WJ, Braam PM, Soomers VLMN, Van der Hage JA, et al. Diagnosed with a rare cancer: Experiences of adult sarcoma survivors with the healthcare system—results from the SURVSARC study. Cancers (Basel) 2021;13:679.
[8] Duijts SFA, van der Zwan JM. Rare cancers and cancer of unknown primary: Here's what you should know! Eur J Cancer Care (Engl) 2021;30:e13508.
[9] Keat N, Law K, Seymour M, Welch J, Trimble T, Lascombe D, et al. International rare cancers initiative. Lancet Oncol 2013;14:109–10.
[10] Sharifnia T, Hong AL, Painter CA, Boehm JS. Emerging opportunities for target discovery in rare cancers. Cell Chem Biol 2017;24:1075–91.
[11] Jensen H, Tørring ML, Olesen F, Overgaard J, Vedsted P. Cancer suspicion in general practice, urgent referral and time to diagnosis: a population-based GP survey and registry study. BMC Cancer 2014;14:636.
[12] Zaikova O, Sundby Hall K, Styring E, Eriksson M, Trovik CS, Bergh P, et al. Referral patterns, treatment and outcome of high-grade malignant bone sarcoma in Scandinavia—SSG Central Register 25 years' experience. J Surg Oncol 2015;112:853–60.
[13] de Heus E, Engelen V, Dingemans I, Richel C, Schrieks M, van der Zwan JM, et al. Differences in health care experiences between rare cancer and common cancer patients: results from a national cross-sectional survey. Orphanet J Rare Dis 2021;16:249.
[14] Okado I, Cassel K, Pagano I, Holcombe RF. Assessing patients' perceptions of cancer care coordination in a community-based setting. JCO Oncol Pract 2020;16:e726–33.
[15] Werner A, Steckelberg A, Strobel A, Wienke A, Schmidt H, Vordermark D, et al. Translation, adaptation, and validation of the Care Coordination Instrument for cancer patients. BMC Health Serv Res 2025;25:13.
[16] Bundesministerium für Gesundheit (Ed.). Ziele des Nationalen Krebsplans. Bundesministerium für Gesundheit (Hrsg); 2012 ⟨https://www.bundesgesundheitsministerium.de/themen/praevention/nationaler-krebsplan/handlungsfelder/ziele-des-nationalen-krebsplans.html⟩ [accessed 15 September 2024].
[17] Eysenbach G. Improving the quality of web surveys: the checklist for reporting results of internet e-surveys (CHERRIES). J Med Internet Res 2004;6:e34.
[18] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008;61:344–9.
[19] Kuckartz U, Rädiker S. Qualitative Inhaltsanalyse. Methoden, Praxis, Computerunterstützung. Weinheim, Basel: Beltz Juventa; 2022.
[20] Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. Br J Cancer 2009;101:S5–8.
[21] Weller D, Vedsted P, Rubin G, Walter FM, Emery J, Scott S, et al. The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. Br J Cancer 2012;106(7):1262.
[22] Walter F, Webster A, Scott S, Emery J. The Andersen model of total patient delay: a systematic review of Its application in cancer diagnosis. J Health Serv Res Policy 2012;17:110–8.
[23] Scott SE, Walter FM, Webster A, Sutton S, Emery J. The model of pathways to treatment: conceptualization and integration with existing theory. Br J Health Psychol 2013;18:45–65.
[24] Okado I, Cassel K, Pagano I, Holcombe RF. Development and psychometric evaluation of a questionnaire to measure cancer patients' perception of care coordination. BMC Health Serv Res 2020;20:52.
[25] Arraras JI, Greimel E, Chie W-C, Sezer O, Bergenmar M, Costantini A, et al. Information disclosure to cancer patients: EORTC QLQ-INFO25 questionnaire. Expert Rev Pharm Outcomes Res 2011;11:281–6.
[26] Ernst J, Kuhnt S, Schwarzer A, Aldaoud A, Niederwieser D, Mantovani-Löffler L, et al. The desire for shared decision making among patients with solid and hematological cancer. PsychoOncol 2011;20:186–93.
[27] Elliss-Brookes L, McPhail S, Ives A, Greenslade M, Shelton J, Hiom S, et al. Routes to diagnosis for cancer - determining the patient journey using multiple routine data sets. Br J Cancer 2012;107:1220–6.
[28] Nolting H-D, Ochmann R, Zich K, Institut I. Gesundheitszentren für Deutschland - Wie ein Neustart in der Primärversorgung gelingen kann. Stuttgart: Robert Bosch Stiftung; 2021.
[29] Kassenärztliche Bundesvereinigung (KBV). Statistische Informationen aus dem Bundesarztregister. Anzahl Ärzte / Psychotherapeuten nach Alter, 2008-2023 2024 ⟨https://gesundheitsdaten.kbv.de/cms/html/16397.php⟩ [accessed 24 October 2024].
[30] Suazo JM, Mendoza G, Canaynay A, Navarez RA. Role of oncology nurse navigators: an integrative review. World J Cancer Oncol Res 2023;2(1):66–84.
[31] Blay JY, Honoré C, Stoeckle E, Meeus P, Jafari M, Gouin F, et al. Surgery in reference centers improves survival of sarcoma patients: a nationwide study. Ann Oncol 2019;30:1143–53.
[32] Schmitt J, Klinkhammer-Schalke M, Bierbaum V, Gerken M, Bobeth C, Rößler M, et al. Initial cancer treatment in certified versus non-certified hospitals. Dtsch Arztebl Int 2023;120.
[33] Lyratzopoulos G, Neal RD, Barbiere JM, Rubin GP, Abel GA. Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England. Lancet Oncol 2012;13:353–65.
[34] Forster AS, Herbert A, Koo MM, Taylor RM, Gibson F, Whelan JS, et al. Associations between diagnostic time intervals and health-related quality of life, clinical anxiety and depression in adolescents and young adults with cancer: cross-sectional analysis of the BRIGHTLIGHT cohort. Br J Cancer 2022;126:1725–34.
[35] Neal RD, Tharmanathan P, France B, Din NU, Cotton S, Fallon-Ferguson J, et al. Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review. Br J Cancer 2015;112:S92–107.
[36] Mund M, Uhlenbusch N, Rillig F, Weiler-Normann C, Herget T, Kubisch C, et al. Psychological distress of adult patients consulting a center for rare and undiagnosed diseases: a cross-sectional study. Orphanet J Rare Dis 2023;18:82.
[37] Kasprzak J, Goering T, Berger-Thürmel K, Kratzer V, Prompinit W, Wichert SP, et al. Bridging the gap: Leveraging telemedicine and IT infrastructure to connect outpatient oncology practices with specialized expert teams in the management of rare tumors. Digit Health 2024;10:20552076241272709.
[38] Budde H, Williams GA, Winkelmann J, Pfirter L, Maier CB. The role of patient navigators in ambulatory care: overview of systematic reviews. BMC Health Serv Res 2021;21:1166.
[39] Grabbe P, Gschwendtner KM, Gaisser A, Kludt E, Wild B, Eich W, et al. Preferred and perceived participation roles of oncological patients in medical decision-making: Results of a survey among users of the German Cancer Information Service. Z FüR Evidenz Fortbild und Qualät Im Gesundh 2022;172:40–8.

[40] Noteboom EA, May AM, van der Wall E, de Wit NJ, Helsper CW. Patients' preferred and perceived level of involvement in decision making for cancer treatment: A systematic review. PsychoOncol 2021;30:1663–79.
[41] Brom L, De Snoo-Trimp JC, Onwuteaka-Philipsen BD, Widdershoven GA, Stiggelbout AM, Pasman HR. Challenges in shared decision making in advanced cancer care: a qualitative longitudinal observation and interview study. Health Expect 2017;20(1):69–84.
[42] Kunneman M, Marijnen CA, Baas-Thijssen MC, van der Linden YM, Rozema T, Muller K, et al. Considering patient values and treatment preferences enhances patient involvement in rectal cancer treatment decision making. Radio Oncol 2015; 117(2):338–42.
[43] Schuler M, Schildmann J, Trautmann F, Hentschel L, Hornemann B, Rentsch A, et al. Cancer patients' control preferences in decision making and associations with patient-reported outcomes: a prospective study in an outpatient cancer center. Support Care Cancer 2017;25:2753–60.
[44] Alessy SA, Davies EA, Rawlinson J, Baker M, Lüchtenborg M. How representative are colorectal, lung, breast and prostate cancer patients responding to the National Cancer Patient Experience Survey (CPES) of the cancer registry population in England? A population-based case control study. BMJ Open 2019;9:e034344.
[45] Bergmann MM, Calle EE, Mervis CA, Miracle-McMahill HL, Thun MJ, Health CW. Validity of self-reported cancers in a propsective cohort study in comparison with data from state cancer registries. Am J Epidemiol 1998;147:556–62.