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Original research

The WERA cancer center matrix: Strategic management of patient access to precision oncology in a large and mostly rural area of Germany

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ABSTRACT

Purpose: Providing patient access to precision oncology (PO) is a major challenge of clinical oncologists. Here, we provide an easily transferable model from strategic management science to assess the outreach of a cancer center.
Methods: As members of the German WERA alliance, the cancer centers in Würzburg, Erlangen, Regensburg and Augsburg merged care data regarding their geographical impact. Specifically, we examined the provenance of patients from WERA's molecular tumor boards (MTBs) between 2020 and 2022 (n = 2243). As second dimension, we added the provenance of patients receiving general cancer care by WERA. Clustering our catchment area along these two dimensions set up a four-quadrant matrix consisting of postal code areas with referrals towards WERA. These areas were re-identified on a map of the Federal State of Bavaria.
Results: The WERA matrix overlooked an active screening area of 821 postal code areas – representing about 50 % of Bavaria's spatial expansion and more than six million inhabitants. The WERA matrix identified regions successfully connected to our outreach structures in terms of subsidiarity – with general cancer care mainly

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performed locally but PO performed in collaboration with WERA. We also detected postal code areas with a potential PO backlog – characterized by high levels of cancer care performed by WERA and low levels or no MTB representation.

Conclusions: The WERA matrix provided a transparent portfolio of postal code areas, which helped assessing the geographical impact of our PO program. We believe that its intuitive principle can easily be transferred to other cancer centers.

1. Introduction

Precision oncology (PO) has demonstrated substantial clinical benefit for patients, especially in rare and hard-to-treat cancers [1–3]. Yet, equal access to PO is a major challenge for healthcare providers and government authorities. Several countries have established infrastructure to foster patient access to PO – with a particular emphasis on patients from rural areas. Japan and Norway for example have set up nationwide hospital networks with centralized molecular tumor boards (MTBs) [4–8]. For Germany, the "National Decade against Cancer" by the Federal Ministry of Education and Research aims to tackle obstacles in patient access [9,10].

Nevertheless, not only healthcare policymakers are responsible for ensuring patient access – this job also falls within the purview of clinical oncologists. As part of the German NCT (National Center for Tumor Disease) network, the Comprehensive Cancer Centers of Würzburg, Erlangen, Regensburg and Augsburg have established the WERA cancer center alliance. One of WERA's central tasks is providing PO programs including clinical trials to its mainly rural catchment area, which covers the majority of the Federal State of Bavaria. In a first step, this task required capturing the geographical status quo of PO participation. As there is limited evidence on fostering PO in a community oncology setting [11,12], we chose an intuitive and hands-on approach, which already revealed several "white spots" in our catchment area [13].

Here, we substantially extended our approach and added general cancer care data from our four cancer centers. Merging both datasets allowed us to employ a four-quadrant matrix model from portfolio theory known as the Growth-Share Matrix [14]. Using the WERA matrix enables our clinicians and cancer center representatives to better understand their regional impact and identify regions in our catchment area, which potentially are not adequately covered.

2. Material and methods

2.1. Data sources

We merged postal code areas of the residences of WERA's MTB patients between 2020 and 2022. Following harmonized standard operating procedures, our MTBs discuss patients diagnosed with an advanced cancer disease and no or limited treatment options left according to guidelines. Except for few patients with external diagnostics performed by programs such as MASTER (Molecularly Aided Stratification for Tumor Eradication Research) [2], most of the MTB patients received in-house next generation sequencing. Regarding further characteristics, the WERA sites Regensburg and Erlangen already performed in-depth analyses of their MTB cohorts [15,16]. Eligible for analysis were MTB patients with known postal code areas and residences in Germany. Additionally, we merged postal code areas of all patients receiving cancer care at the WERA centers. Using data from our four local cancer registries, we termed these referrals Total Cancer Care (TCC). To obtain a stable TCC catchment area and reduce the influence of outliers from single years, we calculated an average TCC across three years (ø 2018–2020). Table 1 summarizes the datasets finally included and examined in our study.

Absolute MTB and TCC patient numbers per postal code area were divided by local population numbers – resulting in MTB and TCC patient numbers per 100,000 inhabitants and postal code area. Population densities per postal code area were collected from a freely accessible source (https://www.suche-postleitzahl.org/downloads). This database combines information from German statistical offices ("Zensus 2011″ initiative, https://www.zensus2011.de) with geospatial information from OpenStreetMap (https://www.openstreetmap.org).

Due to the retrospective nature and the exclusive utilization of anonymized data, analysis of MTB and TCC patients was in accordance with German General Data Protection Regulation (GDPR) and legislation, specifically the Bavarian Hospital Act ("Bayerisches Krankenhausgesetz").

2.2. Formal analysis and graphical illustration

We merged the residences of MTB and TCC patients by using Microsoft® Access® 2016 (version 16.0.5224.1000, Redmond, WA, USA). For visualization, we employed QGIS, an open-source information system (QGIS Development Team; under license of GNU General Public License, Version 3.26.3). Color-coding of QGIS maps employed the Jenks optimization, which aims to minimize variance within groups while maximizing variance between groups [17]. The WERA matrix was visualized using Microsoft® PowerBI® (version 2.118.621.0 32-bit (June 2023), Redmond, WA, USA).

2.3. Portfolio analysis and strategic assessment of outreach measures

We compared two dimensions: the regional distribution of MTB patients and the regional distribution of TCC patients from WERA. The latter reflects established and comparably stable streams of cancer patients towards our four centers. Originally, the Growth-Share Matrix (Fig. 1A) helped enterprises visualizing and managing their product portfolios – by combining the market share of a product with the dynamics (growth perspective) of its market environment [14]. While the x-axis reflects the current strength of a product in a given market, the y-axis reflects its innovative capability. Adopting this management tool from a portfolio of consumer goods to a portfolio of postal code areas (Fig. 1B), we combined WERA's share in total cancer care (x axis) with

Table 1
Cohorts included in this study. (A) Molecular tumor board (MTB) patients per WERA site and year analyzed. (B) Average number of patients receiving cancer care (termed Total Cancer Care, TCC) and number of postal code areas covered by each WERA site. TCC numbers were calculated as an average of the years 2018, 2019 and 2020.

A MTB Patients per Site and Year included in our Study

	2020	2021	2022	Total
Würzburg	171	182	284	**637**
Erlangen	228	289	283	**800**
Regensburg	90	151	193	**434**
Augsburg	144	98	130	**372**
	633	**720**	**890**	**2243**

B TCC Patients per Site and Year (ø 2018-2020) and Postal Code Areas covered

	Patients per Year (ø 2018-2020)	Postal Code Areas
Würzburg	4223	1345
Erlangen	6136	1428
Regensburg	4314	941
Augsburg	3968	695
	18,641	**2931**[a]

[a] In case of patient referral to more than one WERA Site: Counted only once

the local representation of MTB patients (y axis).

3. Results

3.1. Longitudinal screening of patient access to WERA MTBs

Building upon our earlier analysis [13], we screened the geographical development of our WERA-wide MTB program by mapping relative MTB representation (patients per 100,000 inhabitants and postal code area). While the years 2020 to 2022 still represented a limited database, the resulting map (Fig. 2) already provided insights into the longitudinal evolution of our PO program. Regarding "white spots" from the years 2020 and 2021, some regions newly emerged as MTB referrals in 2022 (indicated by bright blue frames around postal codes areas) – demonstrating an organic growth of our program. For example, regions close to Ingolstadt (Fig. 2, *) and Straubing (Fig. 2, §) were newly established. Contrariwise, some areas not covered within our previous analysis still did not appear in our updated analysis – such as regions near the Czech Border (Fig. 2, #).

Subsequently, we explored the extent to which patients from these remaining "white spots" availed cancer care from WERA, irrespective of tumor type, clinical stage, and treatment modalities. For this, we merged cancer care data sourced from our cancer registries and represented the relative prevalence of TCC patients (per 100,000 inhabitants and postal code area) on a map encompassing the Federal State of Bavaria and adjoining regions. Empirically setting a visualization threshold of 15 TCC patients per 100,000 inhabitants, postal code area, and year, we delineated a coherent catchment area (Fig. 3). Therefore, our analysis focused on the primary region where WERA provides cancer care. With the exception of Upper Bavaria, the region surrounding Munich and the southeastern area proximate to the Alps (Fig. 3, *), WERA's catchment area encompassed a significant portion of Bavaria and certain neighboring regions—specifically, the northern part of Baden-Württemberg (Fig. 3, §).

When comparing MTB and TCC representation on the level of postal code areas, we detected substantial discrepancies between both variables. For example, the eastern rim (Fig. 2, #) was weakly covered in terms of MTB representation but well represented in terms of TCC (Fig. 3). These findings led us to establish a broader graphical approach for all postal code areas of our pre-defined catchment area. We adopted the Growth-Share Matrix from strategic portfolio management [14] for this procedure (Fig. 1).

3.2. Illustrating regional imbalances in MTB and TCC representation: the WERA matrix

For the WERA matrix (Fig. 4), we plotted postal code areas (size of the dots depending on population size) along the two dimensions TCC representation and MTB representation. Dots on the x-axis (Fig. 4, $y = 0$) represented $n = 920$ postal code areas with TCC > 15 patients per 100k inhabitants and year but no MTB referral. In contrast, dots on the y-axis (Fig. 4, $x = 0$) described $n = 128$ postal code areas with MTB referrals but no TCC referrals – which mostly represented MTB referrals from beyond our catchment area. Our graphical approach included $n = 821$ postal code areas with simultaneous TCC and MTB referrals – overall representing a screening area of 34,458.7 square kilometers (about 50 % of the Federal State of Bavaria) and 6367,915 inhabitants.

As we aimed to assess MTB representation in WERAs TCC catchment area, we excluded postal code areas with TCC referrals lower than 15/100,000 inhabitants. The remaining postal code areas of the WERA matrix belonged to one of four quadrants – with median TCC representation and median MTB representation serving as cut-off values. Moreover, this semi-quantitative approach allowed us to re-identify the postal code areas of each quadrant on a map of Bavaria and its surrounding regions (Fig. 5).

Areas characterized by low TCC and low MTB representation (lower left quadrant I, depicted in dark blue) mainly lay in the periphery of our catchment area. Other areas lay halfway between WERA sites. Quadrant II postal code areas (upper left, depicted in orange) had a relatively low TCC combined with a high MTB representation. This quadrant contained cities like Bad Mergentheim (Fig. 5 *) and Bayreuth (Fig. 5 §), where collaboration partners of our network are based. In contrast, postal codes areas from quadrant III (upper right, depicted in green) usually were located near WERA centers. Quadrant IV (lower right, depicted in light blue) finally contained postal code areas with a strong TCC representation along with a relatively weak MTB representation. Several of these regions were located in the periphery of our catchment area. However, some quadrant IV areas also emerged near our cancer centers – indicating potential gaps in terms of PO coverage.

Regarding the overall distribution of the WERA matrix dot plot (Fig. 5), many areas clustered close to the center. This central clustering potentially limits the validity of our graphical approach, which exclusively assigns regions towards one of four quadrants. Therefore, we improved the granularity of our approach by introducing customized gates to identify sub-clusters (Fig. 6). For these bona fide gates, we applied the following coordinates (in x / 100,000 inhabitants and year):

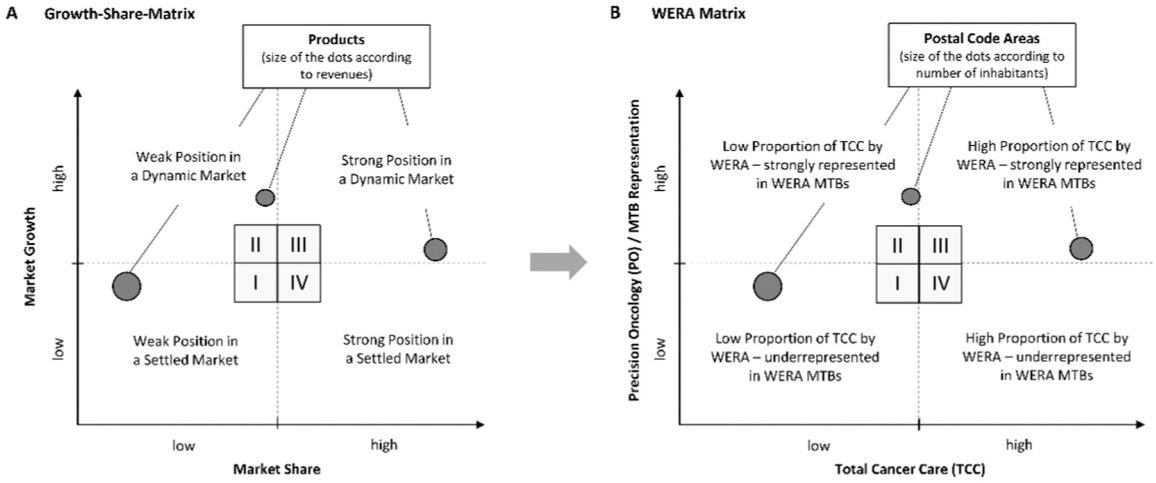

Fig. 1. The WERA matrix adopted from Strategic Portfolio Management. (A) Growth-Share Matrix depicting market shares and market growth rates for specific products. (B) Merging WERAs proportion in Total Cancer Care (TCC, x-axis) with the local MTB (molecular tumor board) representation (y-axis) for each outreach postal code area.

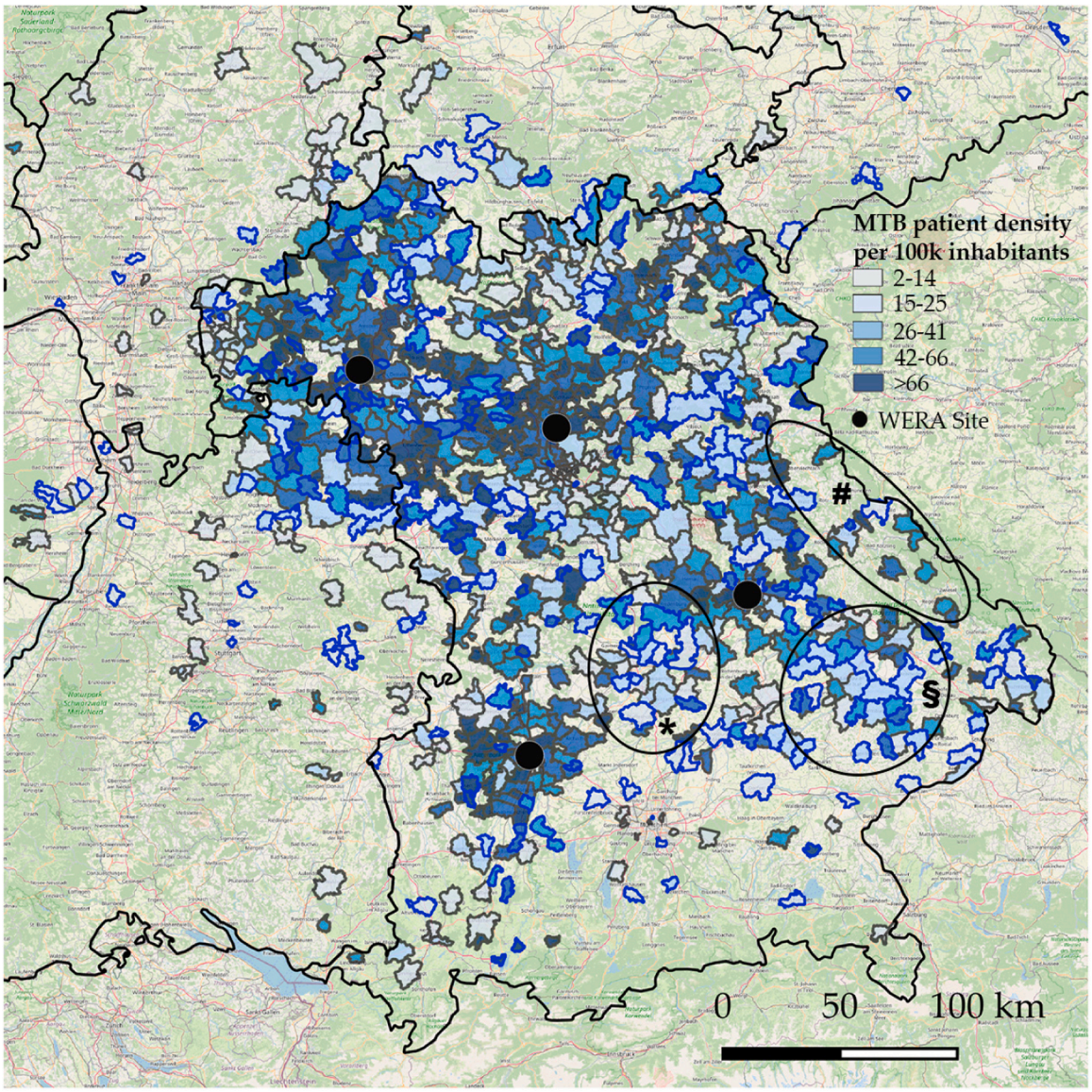

Fig. 2. Federal State of Bavaria with neighboring regions and color-coded development of MTB (molecular tumor board) representation per 100,000 inhabitants and postal code area. Bright blue frames around postal code areas indicate first appearance in the year 2022 – such as regions close to Ingolstadt (*) and Straubing (§). # indicates a weakly covered part of eastern Bavaria close to the Czech border ("Bayerischer Wald").

- Gate A (Orange): 27 < TCC < 104; 13 < MTB < 80
- Gate B (Green): 379 < TCC < 1200; 12 < MTB < 160
- Gate C (Light Blue): 315 < TCC < 600; 2 < MTB < 8,5
- Gate D (Dark Blue): 220 < TCC < 1000; 0 < MTB < 1

As described for quadrant II, Gate A regions lay close to outreach partner sites. As a sub-cluster of quadrant III, Gate B mainly re-identified urban regions next to WERA hubs – with a strong TCC and MTB representation. Regarding imbalances in Patient Access, the remaining gates C and D appeared most interesting. Of note, gate D represented the clearest discrepancy – with regions characterized by strong TCC representation while having no MTB patients. After mapping, these regions were not randomly distributed across our catchment area. Instead, some of these areas such as the eastern rim (Fig. 6 #, "Bayerischer Wald") also clustered geographically, implying that regional socioeconomic determinants could contribute to the imbalance between TCC and MTB representation. However, "white spots" were not only located in rural areas far away from WERA centers – we detected them in urban regions and suburbs of Würzburg (Fig. 6 *) and Regensburg (Fig. 6 §).

Last, we aimed to analyze the regional distribution of external patients, which were referred to our MTBs from beyond our university hospitals (Fig. 7). We identified 669 external patients, representing 29.8 % of our total MTB cohort. We found 444 postal code areas with at least one external MTB patient between the years 2020 and 2022 (indicated in blue). Having a closer look at the regional distribution patterns of external patients´ residences (Fig. 7A), we found clusters of postal code areas, especially in the northern part of Bavaria closer to the WERA sites Würzburg and Erlangen. Moreover, many of the postal code areas with external referrals were located near sites of established WERA collaboration partners, e.g. regions around Bayreuth and Kulmbach (Fig. 7A *) as well as Ansbach (Fig. 7A §).

When merging data of external and internal (in-house) MTB patients (Fig. 7B), the eastern rim (#) again delivered interesting results. While underrepresented in terms of MTB patients in general, the remaining referrals from this area were mainly caused by WERAs in-house patients – as indicated by the yellow painted areas in Fig. 7B #.

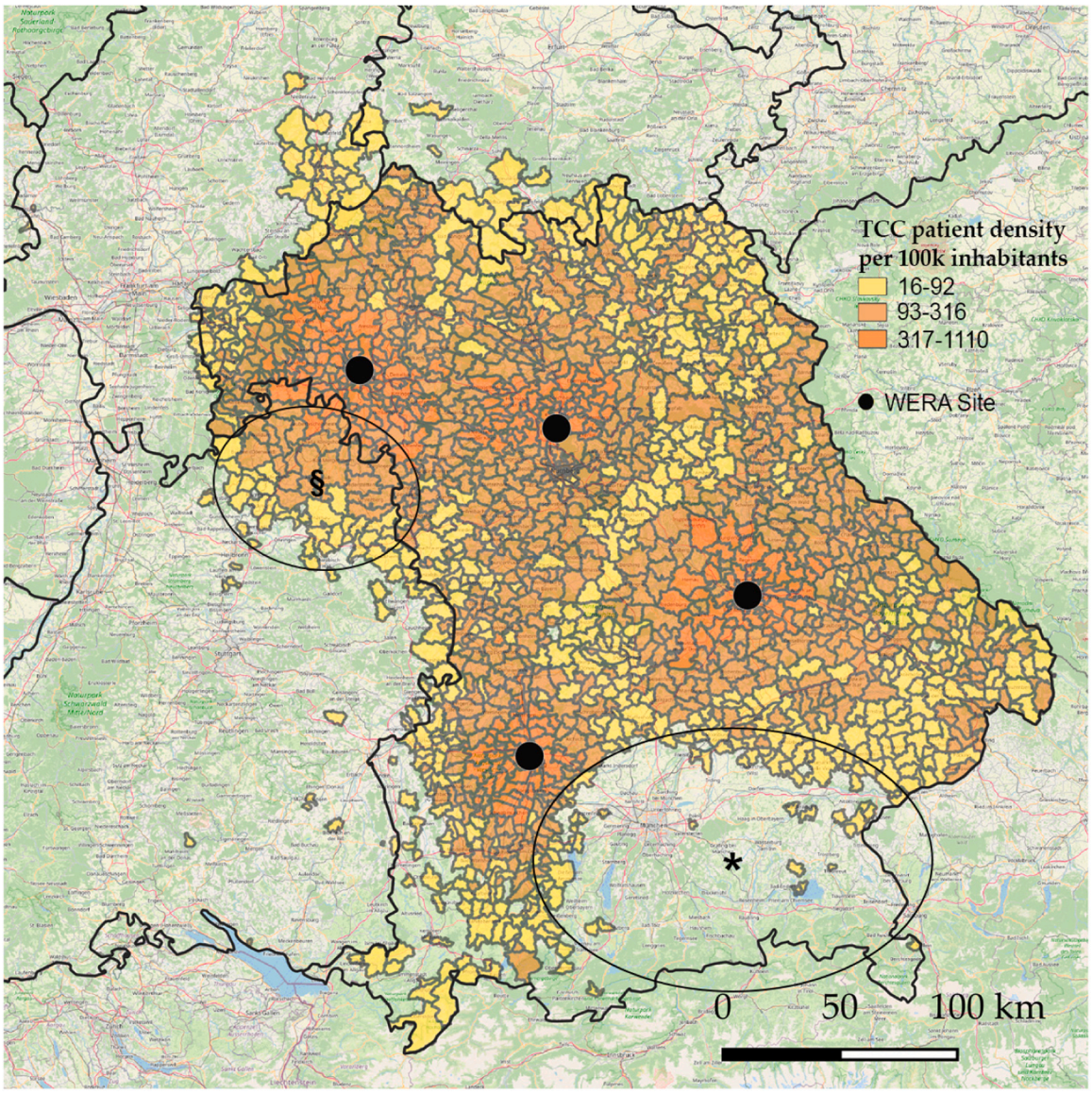

Fig. 3. Total cancer care (TCC) performed by the WERA cancer centers – Regional visualization (per postal code area) of cancer care patients weighted with local population densities; patient density is depicted as patients treated at a WERA center per 100,000 inhabitants and year. § indicates the northern part of the federal state of Baden-Württemberg. * indicates Upper Bavaria including the region around Munich ("Oberbayern").

4. Discussion

4.1. Longitudinal assessment of geographical PO coverage

We previously defined the joint PO coverage area of our cancer centers by merging patient care data from our four MTBs [13]. Thus, we showed successful outreach structures but also regional "white spots" in terms of MTB representation. Here, we assessed the geographical development of our PO coverage by adding MTB patient data from 2022. Upon closer examination of former "white spots" [13], we discovered that some of them were filled recently, particularly in regions close to Ingolstadt and Straubing – thereby reflecting the growth of our PO program. In contrast, some "white spots" such as the eastern rim of our catchment area ("Bayerischer Wald") maintained to be uncovered. To find out whether filling these gaps is merely a question of organic growth and thus a question of time or whether there are systemic obstacles to patient access, we needed to expand and modify our previous approach. Consequently, we added regional information on general cancer care (TCC) performed by WERA.

4.2. The WERA matrix as a strategic outreach management tool

To merge PO and TCC coverage, we adopted the Growth-Share Matrix from strategic portfolio planning [14] to assess the development of local MTB representation not only regarding local population, but also regarding established patient streams receiving cancer care in the WERA network. The resulting WERA matrix attributed postal code areas to one of four quadrants – each representing a potential real-life scenario (Fig. 8).

Geographical re-identification of postal code areas from each quadrant allowed us to draw conclusions about local determinants of patient access. For example, postal code areas belonging to quadrant II could serve as an example for successful and efficient outreach structures in community oncology – with general cancer care mainly performed locally but PO performed in collaboration between local care providers and WERA – reflecting functioning PO outreach. In contrast, postal code areas from quadrant IV appear promising for future outreach activities – as this quadrant contains regions with strong and established patient referral towards WERA centers in terms of TCC, while being

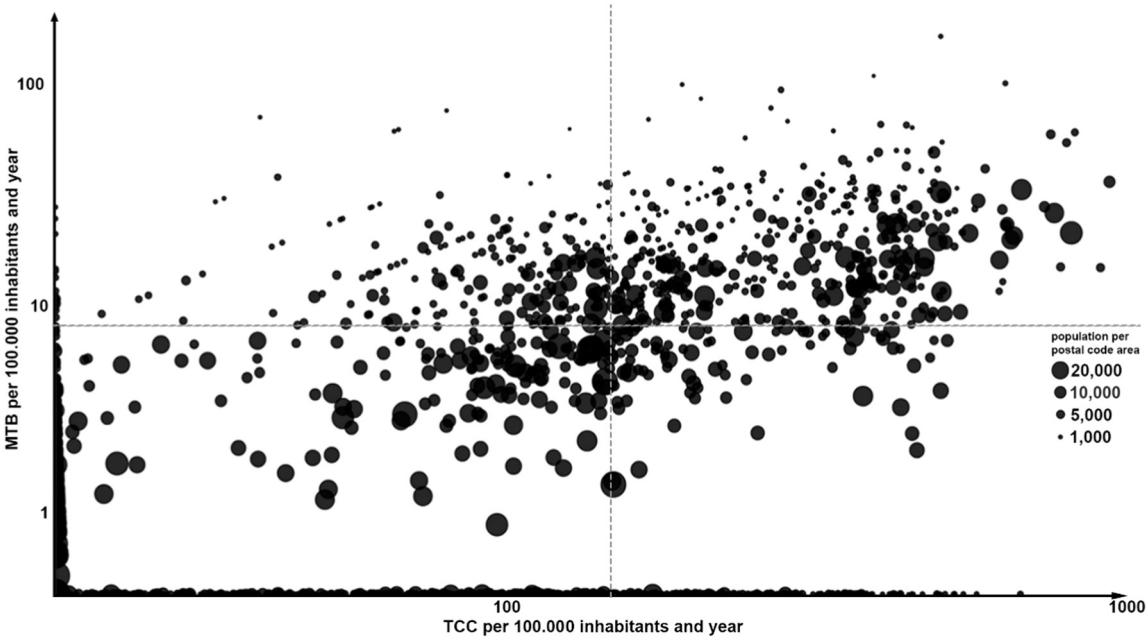

Fig. 4. The WERA matrix - dot plot of postal code areas with patient referral towards the WERA cancer centers along the two dimensions Total Cancer Care (TCC) and molecular tumor board (MTB) representation (per 100,000 inhabitants and year). Each dot describes one postal code area – with dot sizes depending on local population. TCC and MTB representation are depicted on a logarithmic scale. Dashed grey lines describe median TCC and MTB representation for both datasets.

underrepresented in terms of PO (MTB) representation. Part of the explanation for this discrepancy may lie in insufficient information and awareness among local physicians and patients. Moreover, technical and organizational obstacles could be responsible for this discrepancy. Another reason could be that MTB candidates from these regions are referred to other cancer centers or use PO services from commercial suppliers.

To add further granularity to our semi-quantitative matrix approach, we selected clusters of postal code areas within a given quadrant. Thus, we identified "urgent white spots" – regions with a strong referral of patients towards our centers for TCC but no MTB representation at all. Most importantly, these areas were not exclusively located far away from our centers. Instead, we also detected them in close vicinity to our hubs. Moreover, these "urgent white spots" were not evenly distributed across our catchment area but clustered in specific areas, implying that common socioeconomic determinants could prevent patients from accessing suitable PO measures. In the future, we have to examine each of these "white spots" to understand local factors contributing to imbalances between MTB and TCC representation.

In a final step, we investigated the regional distribution of MTB patients depending on whether they were referred from external physicians or from in-house. Thus, we identified several regional clusters representing external MTB referrals. Of note, these clusters frequently were located close to WERA network partners – potentially implying that these are best-practice regions in terms of PO collaboration. At the same time, the few MTB referrals from the eastern rim of our catchment area, one of our most prominent "white spots", mainly represented WERA in-house patients. Altogether, we need a better understanding of the local determinants of patient access within our "white spots", which contribute to the scarcity of external referrals from there. This better understanding could also help explaining why WERA cancer patients from these regions potentially aren't adequately represented in WERA MTBs.

4.3. Strengths and limitations of our approach

Our study has several limitations. For example, established streams of cancer patients do not necessarily reflect a PO need – as some cancers currently have a limited spectrum of druggable targets. Moreover, certain subgroups such as patients with a localized disease, or patients in palliative care might not benefit from PO measures. Yet, we did not use TCC as a surrogate for immediate PO need. Instead, it reflects the willingness of local patients – and physicians – to receive cancer care from WERA centers. Next, a lack of MTB referrals towards WERA from a given region does not necessarily mean a regional lack of PO performed – as local patients and physicians surely can decide to use the services of other cancer centers or commercial suppliers.

Methodically, the Growth-Share Matrix [14] has had a huge impact on strategic management especially in the last century. Yet, later research has questioned its applicability in a business setting partly due to inherent over-simplification [18]. Yet, portfolio management techniques, including the Growth-Share Matrix, are still used in companies, especially in setting strategic goals and visualizing the strategic status quo [19]. In this light, we are convinced that a certain degree of simplification and catchiness helps introducing a management tool as a novel frame of thinking in our clinical setting. Finally, we wanted to stress that delivering patient access to PO represents a considerable management task for clinical oncologists and cancer center representatives [11,20,21] – which should be supported by transparent and easily accessible tools.

Ethical Approval

Ethical approval was obtained by the Ethics Committee of the University of Regensburg, Germany, (Molecular Tumor Board Registry Study, protocol code 20–1682-101). Due to the retrospective nature and the exclusive utilization of anonymized data, this study was also in accordance with German General Data Protection Regulation (GDPR) and legislation.

Funding Statement

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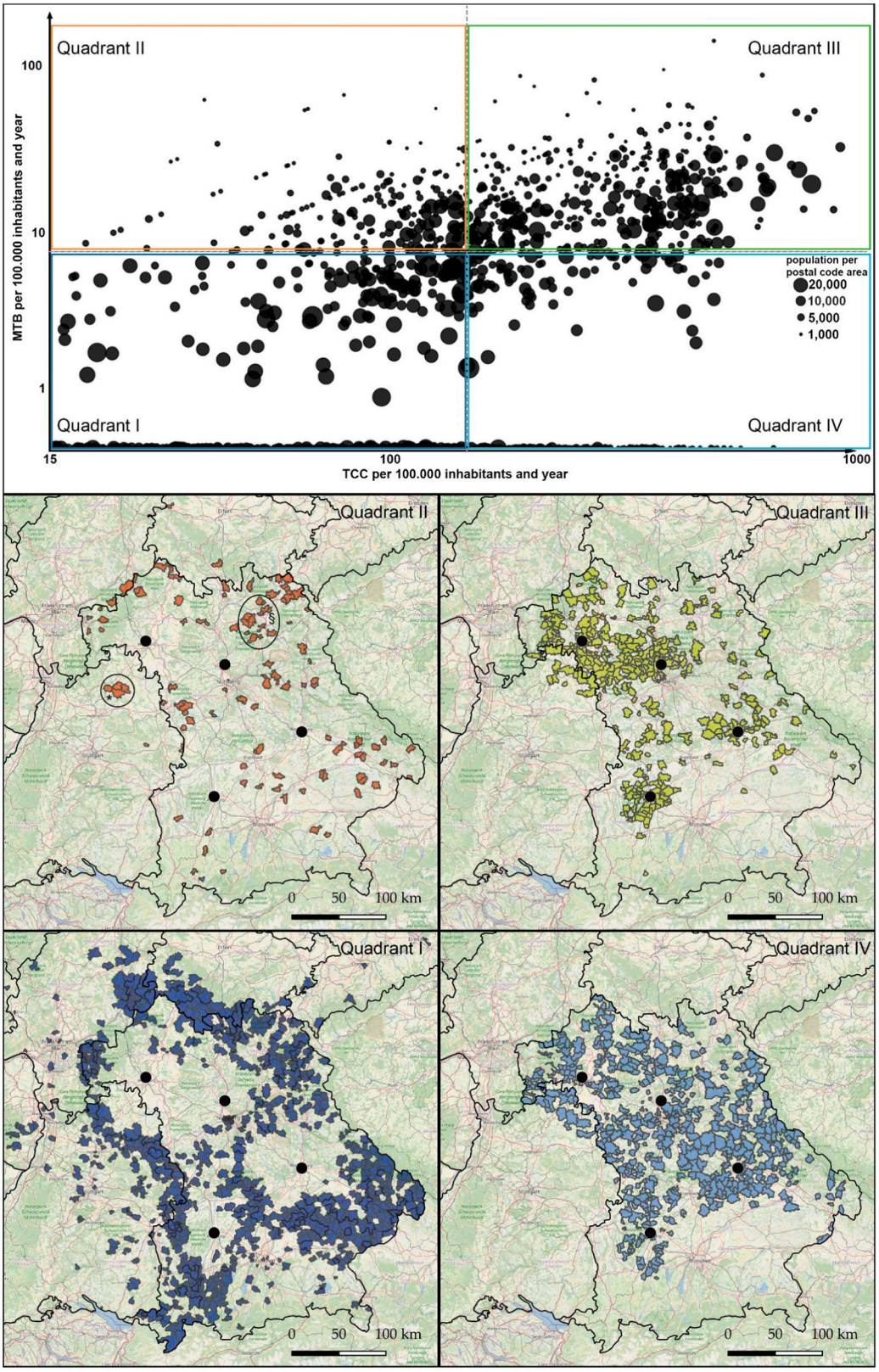

Fig. 5. The WERA matrix – assignment of postal code areas to one of four quadrants and geographical re-identification on a map of the Federal State of Bavaria with surrounding regions. Quadrant I: TCC low (local TCC representation < median TCC representation) and MTB low (local MTB representation < median MTB representation). Quadrant II: TCC low (local TCC representation < median TCC representation) and MTB high (local MTB representation > median MTB representation). Quadrant III: TCC high (local TCC representation > median TCC representation) and MTB high (local MTB representation > median MTB representation). Quadrant IV: TCC high (local TCC representation > median TCC representation) and MTB low (local MTB representation < median MTB representation). * describes quadrant II areas close to Bad Mergentheim. § describes quadrant II areas close to Bayreuth.

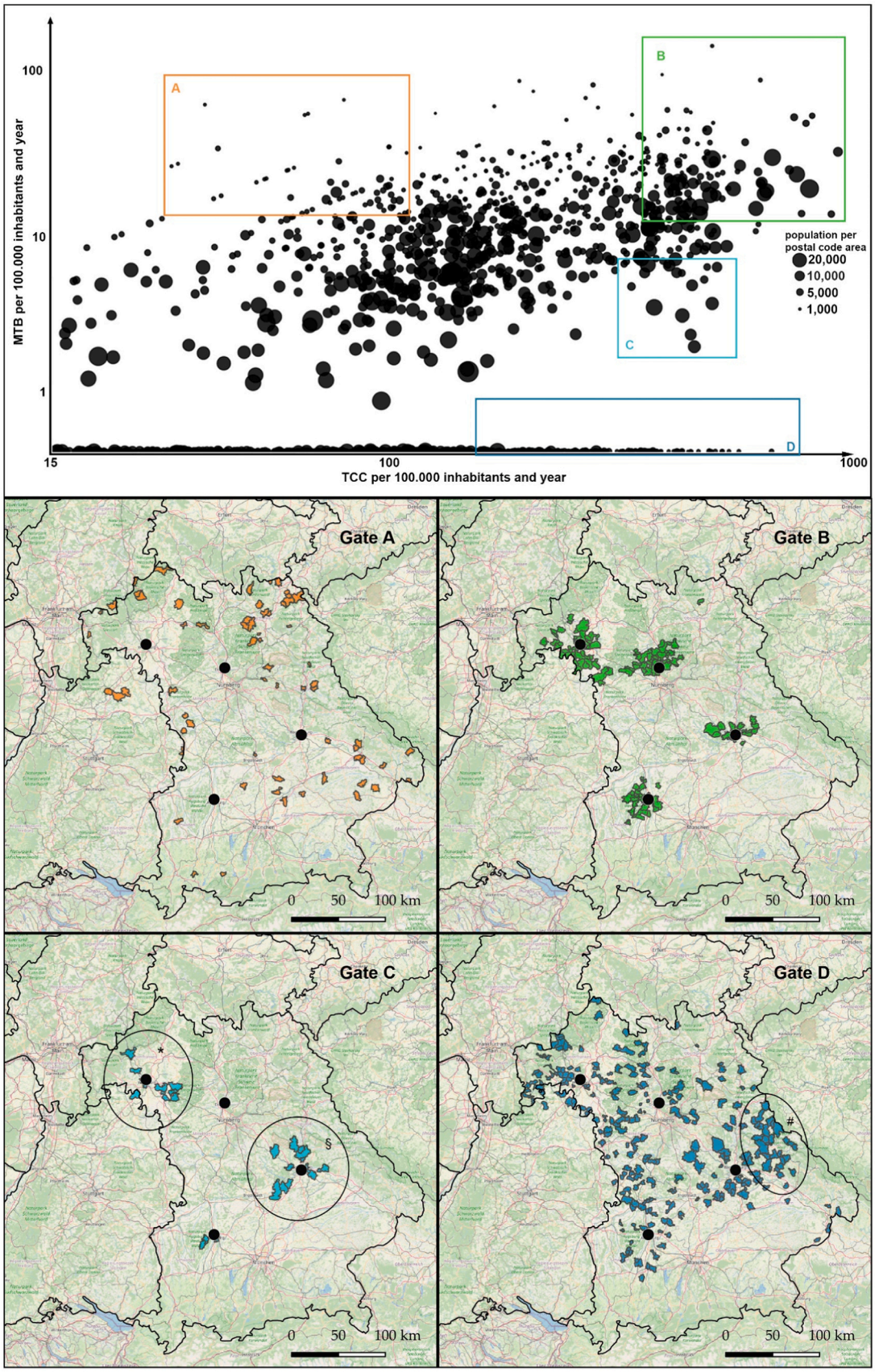

Fig. 6. The WERA matrix – assignment of postal code areas to predefined Gates / sub-clusters and geographical re-identification on a map of the Federal State of Bavaria with surrounding regions. Quadrant C specifically contained areas close to Würzburg (*) and Regensburg (§). The eastern rim of our catchment area ("Bayerischer Wald", #) was particularly represented within gate D.

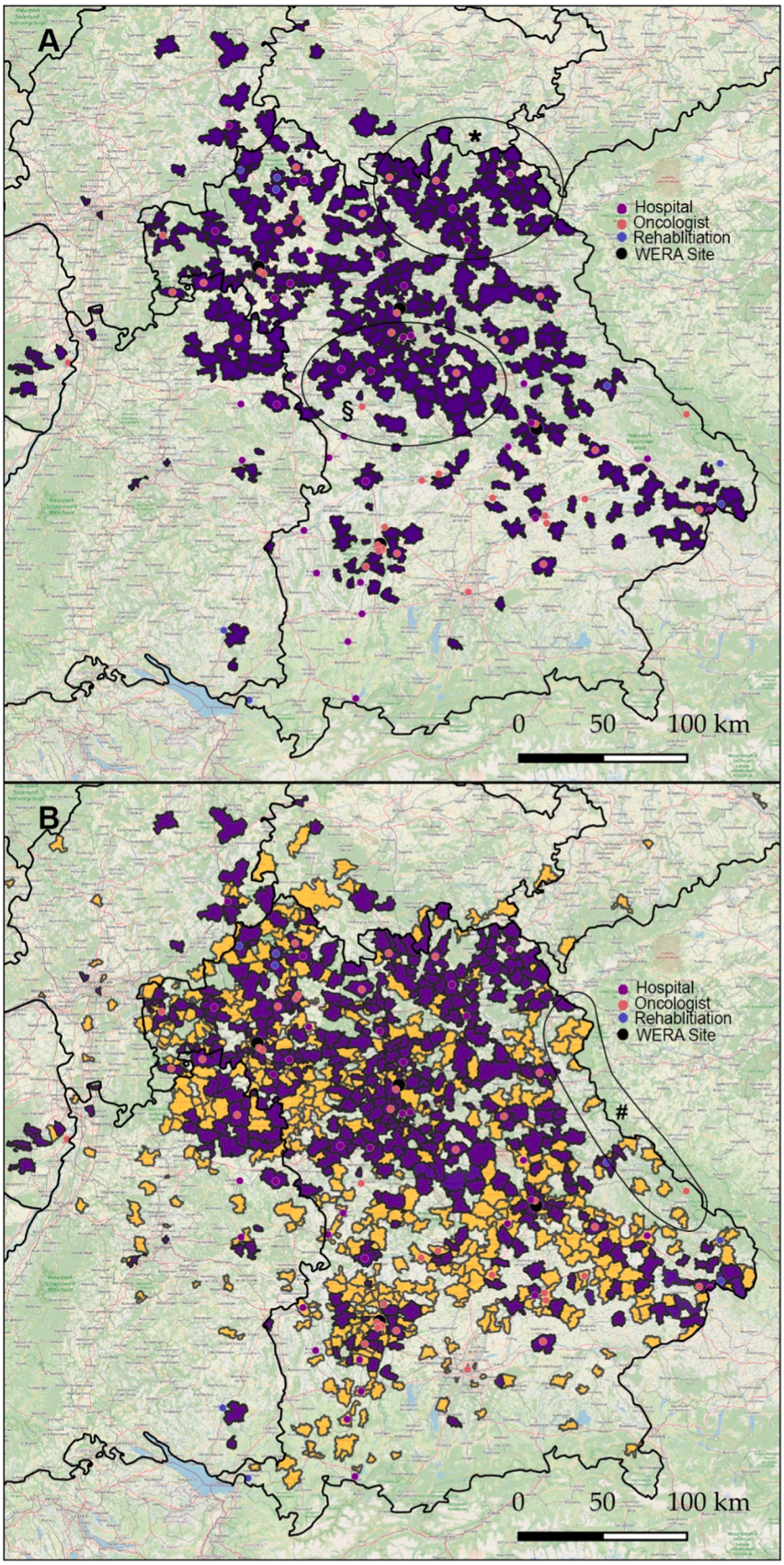

Fig. 7. Regional visualization (per postal code area) of MTB patients depending on their referral status. The colored dots represent sites of WERA collaboration partners. (A) Postal code areas with a least one external MTB referral within our study are indicated in blue. * describes areas close to Bayreuth and Kulmbach, § describes areas near Ansbach. (B) All postal code areas with MTB referrals included in our study. Beyond areas already highlighted in A, yellow-colored regions represent additional in-house referrals to our MTBs. # indicates the eastern rim of our catchment area close to the Czech border.

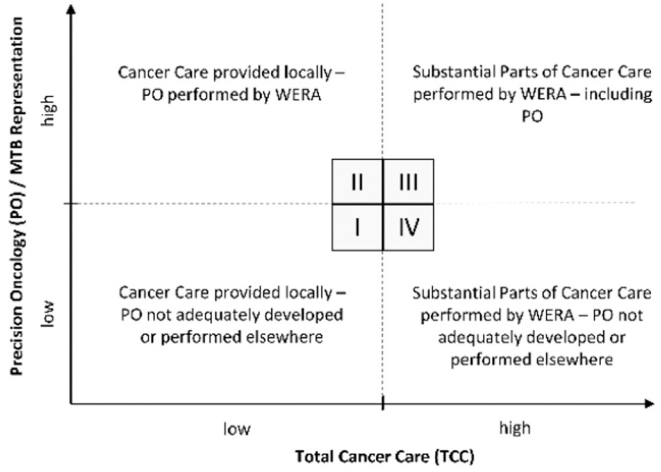

Fig. 8. Potential real-life scenario for each quadrant of the WERA matrix.

CRediT authorship contribution statement

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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