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# Systemic anticancer treatment in the Netherlands: Few hospitals treat many patients, many hospitals treat few patients

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ARTICLE INFO ABSTRACT Introduction: The correlation between patient volume and clinical outcomes is well known for various oncological Keywords: Patient volume treatments, especially in the surgical field. The current level of centralisation of systemic treatment of (hemato-) Oncology oncology indications in Dutch hospitals is unknown. Centralisation Objectives: The aim of this study was to gain insight in patient volumes per hospital of patients treated with Concentration systemic anticancer treatment in the Netherlands. Care quality Methods: National claims data (Vektis) of all 73 Dutch hospitals that provide systemic anticancer medication in Anticancer medication the Netherlands for the time period 2019 were used. The distribution of volumes of patients treated with anticancer medication for 38 different haematological or oncological indications was analysed. Hospitals were categorized into academic/specialised, general, and top clinical. Two volume cut off points (10 and 30 patients) were used to identify hospitals treating relatively few patients with anticancer medication. Four indications were investigated in more detail. Results: A wide distribution in patient volumes within hospitals was observed. Top clinical hospitals generally treated the most patients per hospital, followed by general and academic/specialised oncology hospitals. The volume cut off points showed that in 19 indications (50%) the majority (>50%) of all hospitals treated less than 10 patients and in 25 indications (66%) the majority of all hospitals treated less than 30 patients with anticancer medication. Four case studies demonstrated that relatively few hospitals treat many patients while many hospitals treat few patients with anticancer medication. Conclusion: In the majority of oncology indications, a large proportion of Dutch hospitals treat small numbers of unique patients with anticancer medication. The high level of fragmentation gives ground for further exploration and discussion on how the organisation of care can support optimization of the efficiency and quality of care. Professional groups, policy makers, patients, and healthcare insurers should consider per indication whether centralisation is warranted.

# 1. Introduction

Universal healthcare systems usually aim to supply all insured inhabitants with an equally high quality of care. High quality of care may be perceived differently by different people, but within the field of oncology quality of care is often associated with factors such as survival, quality of life, shared decision-making, appropriate treatment discontinuation and end-of-life care [1-3]. To deliver high quality of care, it is essential for healthcare professionals to have sufficient expertise and experience within certain indications, as studies have shown that greater experience –through concentration of care– can benefit its quality [4-18]. For example, high-volume hospitals have been shown to have a

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lower mortality rate as compared to low-volume hospitals for surgeries in multiple indications [4–8]. For systemic treatments, including in the palliative setting, longer survival and more timely systemic treatment discontinuation have been demonstrated for several tumour types in high-volume hospitals compared to low-volume hospitals [9–14]. Similarly, in higher volume hospitals it is often easier to provide access for patients to ongoing clinical trials. Multiple other studies have shown a relation between care quality and care volume [15–20].

In order to make healthcare sufficiently accessible and at the same time ensure the quality of care, the care around some diseases in the Netherlands is concentrated to a limited number of hospitals or specialised healthcare hospitals [21–23]. On a European scale, the European Society for Medical Oncology (ESMO) strives to improve the quality of care in the field of oncology by promoting an alternative to centralisation, connecting multidisciplinary professionals with diverse expertise and experience [24].

Minimum volume norms can be used in the organisation of care and are already used in multiple countries including the Netherlands [25, 26]. Most of the volume requirements are set within the range of 10 to 100 patients per indication or per treatment per year [25–27]. At the moment, most of these norms are focused on complex surgeries, but in light of the insights provided by recent studies, requirements for systemic treatments are emerging. In the Netherlands, professional groups of physicians of several therapeutic areas cooperate to publish criteria for quality of care. One of these states that systemic treatment of hepatocellular carcinoma, intrahepatic cholangiocarcinoma and perihilar cholangiocarcinoma should only be conducted in hospitals that treat at least 10 patients with cholangiocarcinoma or primary hepatocellular carcinoma per year [26,27]. Another example states that systemic treatment for renal cell carcinoma may only be applied in hospitals that treat at least 10 patients annually with systemic treatment for this indication [27].

Clearly, volume norms for systemic treatments within the field of oncology may be used more in the future as one of several methods for improving the quality of care [9-14,25-27]. At the moment very little is known about patient volumes for systemic anticancer medication use. To diminish this global knowledge gap, we provide a case study, depicting the current status in the Netherlands. This study aims to provide insight in hospital volumes for patients treated with systemic oncology medication in the Netherlands.

# 2. Materials and methods

# 2.1. Inclusion and data collection

A Dutch claims database (Vektis database) covering the time period 2019 was used. The Vektis database contains all claims for all healthcare costs that are reimbursed by healthcare insurance companies falling within the scope of the Dutch health insurance law [28]. Only the claims for systemic (hemato)oncolytic medication paid to hospitals (so-called 'add-on' medication) were used. Hospitals with a total of less than ten declarations were excluded (N = 2). Furthermore, two other hospitals were excluded because one is a specialised hospital for children oncological care, which is already centralised in the Netherlands, and the other one because the hospital was shut down in 2019.

#### 2.2. Data preparation

Declarations for a single drug on a patient level were clustered per indication and treatment hospital, providing a total number of patients treated within a single hospital with systemic oncolytic medication within a certain indication. Thus, per indication multiple drugs were clustered, as we were interested in the number of patients treated per indication rather than patients treated with a specific single drug. The indications were based on the main indications included with the claims dataset (on the level of lung cancer, renal cancer, etc.), and further specified through expert opinion, resulting in a total of 38 indications being included (Table 1). Further specification, for example in haematological cancers, was considered in case of variability in systemic treatment between sub-indications, or to give a more detailed insight in high-volume indications. Gastric/cardia/oesophagus cancer, and ovarian/tuba/peritoneal cancer were already combined in the claims database and were therefore each analysed as one indication. Vaginal cancer and vulvar cancer were combined together based on indicational resemblance and comparable systemic treatments.

Hospitals were categorised in 'Academic/Specialised', 'General' and 'Top clinical' (Table 1). In total, 73 hospitals were included. Hospital names were blinded to ensure anonymity. For that same purpose, we clustered academic hospitals with the specialised hospitals into the category 'Academic/Specialised'.

Patients with declarations for the same drug for multiple indications were allocated in the most apparent indication, specified by which indication was most often recorded. For example, when a patient has 3 declarations for treatment A of indication X and 1 declaration for treatment A of indication Y, we included the patient for indication X. The underlying assumption was that it is much more likely that a wrong indication was entered once than that the patient was really treated with the same drug for multiple indications. When patients were treated with systemic treatment in two hospitals in 2019, they were counted for each hospital (being the conservative approach as this increases the number of treated patients per hospital relative to counting patients only for one hospital).

In total, the data of 2019 consisted of 145,846 medication declarations for 89,481 unique patients. After excluding declarations that were missing at least one field of information (N = 9; 0.006%), the total number of declarations was 145,837 for 89,480 unique patients.

# 2.3. Data analysis

We performed three analyses. First, we analysed the number of patients per hospital for each indication. This analysis provided a comprehensive overview of hospital volumes for patients treated with systemic oncology drugs in the Netherlands. Two hypothetical volume cut off points were introduced (10 and 30 patients per year), set within the range of existing norms, to assess the distribution of patients over hospitals. To show measures of concentration, the mean and standard deviation (SD) were calculated. Second, four indications were chosen to analyse the patient volume distribution between hospitals in the Netherlands in more detail, namely renal cell cancer, bile duct cancer, and hepatocellular cancer mainly because they have existing volume norms. However, they also depict an overview of indications of different rarities and use of new specialised medication. We added insights on gastric, cardia & oesophagus cancer to complete the overview with a high volume indication in which a large variety of systemic treatments is used. Third, an overview of the centralisation of care throughout the different hospitals in the Netherlands was made to show the number of indications treated in low volume by a certain number of hospitals. Microsoft Excel (Redmond, WA) and R (version 4.0.4) were used for analyses.

Table 1

Information on number of declarations, patients, drugs, indications and hospitals included in the dataset.

	Number
Total medication declarations	145,837
Unique patients	89,480
Medications	131
Number of indications	38
Number of hospitals:	73
Academic/Specialised	10
General	37
Top clinical	26

# 3. Results

## 3.1. Data characteristics

The indications with the most unique patients in 2019 were breast cancer, non-small cell lung cancer (NSCLC), and colorectal cancer

#### Table 2

Number of unique patients treated with medication for a specific indication. Sorted by number of unique patients.

	sorted by number of unique patients.					
	Number of unique	Number of medication	Number of	Average number of		
	patients	declarations	hospitals	patients per		
	I			hospital (with		
				standard		
				deviation)		
Total	89,480	145,837	73	1226 (764)		
Hospitals						
Top clinical	41,907	67,044	26	1612 (417)		
General	27,375	43,475	37	740 (340)		
Academic/ specialised	22,274	35,318	10	2227 (1090)		
Indications						
Breast	14,500	25,623	73	200 (116)		
Lung: NSCLC	9681	17,769	72	142 (132)		
Colorectal	9090	15,588	72	127 (62)		
Haematological: Myeloproliferative	7748	12,182	71	111 (55)		
neoplasm						
Bladder	7136	8269	72	100 (53)		
Haematological:	6517	8175	71	96 (54)		
Lymphoma						
Prostate	6469	7992	72	91 (51)		
Haematological: Leukaemia	5265	7706	72	75 (63)		
Haematological:	4759	7643	71	71 (46)		
Multiple myeloma Haematological:	3911	5425	71	57 (36)		
Lymphoma /	5511	3423	/1	37 (30)		
Myeloma:						
unknown						
Gastric / cardia /	3036	4975	72	42 (39)		
oesophagus						
Ovarian / tuba /	2613	4290	72	39 (25)		
peritoneal	0455	0.407	01	110 (100)		
Dermal: melanoma Lung: other	2455	3497	21 72	118 (139)		
Renal cell	2292 1597	3076 3052	72 56	32 (19) 29 (35)		
Pancreatic	1562	2096	50 72	22 (18)		
Neurological	1460	1817	36	41 (50)		
Gastro intestinal	787	1050	41	19 (38)		
stromal tumour						
Head/Neck	766	869	24	32 (37)		
squamous cell						
Cervix	511	827	36	14 (19)		
Primary tumour unknown	495	672	63	8 (13)		
Neuroendocrine	422	630	59	7 (10)		
Germ cell	417	579	19	22 (22)		
Bile duct	355	515	66	5 (5)		
Lung: mesothelioma	337	339	65	5 (4)		
Sarcoma: bone / soft tissue	222	273	20	11 (14)		
Hepatocellular	176	213	23	8 (12)		
Sarcoma	149	185	25	6 (8)		
Thyroid	125	136	18	7 (9)		
Dermal: non-	86	105	9	10 (10)		
melanoma Gall bladder	72	86	36	2 (2)		
Vaginal / vulvar	72 45	86 46	30 20	2 (2)		
Adrenal	38	38	9	4 (2)		
Uterus	30	31	21	1 (1)		
Histiocytosis	24	25	16	2 (1)		
Choriocarcinoma	11	19	5	2(1)		
Neurological:	9	17	7	2 (2)		
blastoma Solivory glond	7	7	5	1 (1)		
Salivary gland	/	/	3	1 (1)		

(Table 2). Academic/specialised hospitals (N = 10) treated on average 2227 (SD = 1090) patients with medication spread over all 38 indications. Top clinical hospitals (N = 26) treated 1612 (SD = 417) patients over 36 indications and general hospitals (N = 37) treated 740 (SD = 340) patients spread over 33 indications.

# 3.2. All indications

Fig. 1 shows the variability in number of patients treated with systemic medication per hospital for indications with at least 500 unique patients in 2019. The total number of hospitals treating each indication (with medication) is widespread. Most of the higher volume indications are treated in about 71 to 72 (of 73) hospitals, while lower volume indications like thyroid, adrenal and uterus cancer are treated in 18, 9, and 21 hospitals, respectively.

The overall average number of patients per hospital is lowest for general hospitals and highest for academic/specialised hospitals. Within most indications, the hospitals that treat the most patients per hospital with medication are the academic/specialised hospitals.

An overview of patient volumes per hospital for the rarer indications (unique patients < 500) can be seen in Fig. 2. A relatively high number of hospitals is seen in bile duct cancer, lung: mesothelioma,neuroendocrine, and primary tumour unkown(N = 66, 65, 59, and 63). In contrast, choriocarcinoma, neurological: blastoma, and salivary gland cancer were treated in 7, 5 and 5 hospitals, respectively. A higher spread in unique patients per hospital is seen in higher volume indications, with academic/specialised hospitals clearly treating the most patients per hospital in most indications. The split between general and top clinical hospitals is less apparent in these smaller indications as compared to Fig. 1.

The proportion of hospitals treating a number of patients with medication that is below the volume marks becomes larger as the total volume of patients within the indication becomes smaller. In the indications gall bladder cancer, vaginal / vulvar cancer, adrenal cancer, uterus cancer, histiocytosis, neurological: blastoma, choriocarcinoma, and salivary gland cancer all hospitals treated less than 10 unique patients for each indication in 2019. The volume marks in Fig. 1 and 2 show that throughout all indications, the proportion of hospitals treating less than either 10 or 30 unique patients with systemic treatments within an indication (including multiple drugs) varied greatly, exceeding 50% in multiple indications. In 19 of 38 (50%) indications the majority (>50%) of all hospitals treated less than 10 patients and in 25 (65.8%) indications the majority of all hospitals treated less than 30 patients. In other words, in almost two-thirds of all oncology indications in the Netherlands, a majority of all treating hospitals treats less than 30 unique patients with systemic treatment annually.

# 3.3. Specific indications

#### 3.3.1. Gastric, Cardia, Oesophagusl cancer

For this indication, a total of 3059 patients were treated systemically by 72 hospitals (Fig. 3). Out of the 72 hospitals, 38 hospitals (52.8%) treated less than 30 patients and 8 hospitals (11.1%) treated less than 10 patients with medication. Most of the high-volume hospitals were academic/specialised and top clinical, although two of these treated less than 30 patients with medication. Treatments consisted of one or more of the following drugs: capecitabine, cisplatin, docetaxel, epirubicin, etoposide, gemcitabine, irinotecan, oxaliplatin, paclitaxel, ramucirumab, tegafur (combinations), trastuzumab, and trifluridine/tipiracil.

# 3.3.2. Renal cell cancer

A total of 1640 patients were treated, split over 56 hospitals (Fig. 4). Out of the 56 hospitals, 37 hospitals (66.0%) treated less than 30 patients and 18 hospitals (32.1%) treated less than 10 patients with medication. The order in volume of hospital categories was very clear for this indication, with academic/specialised hospitals treating the

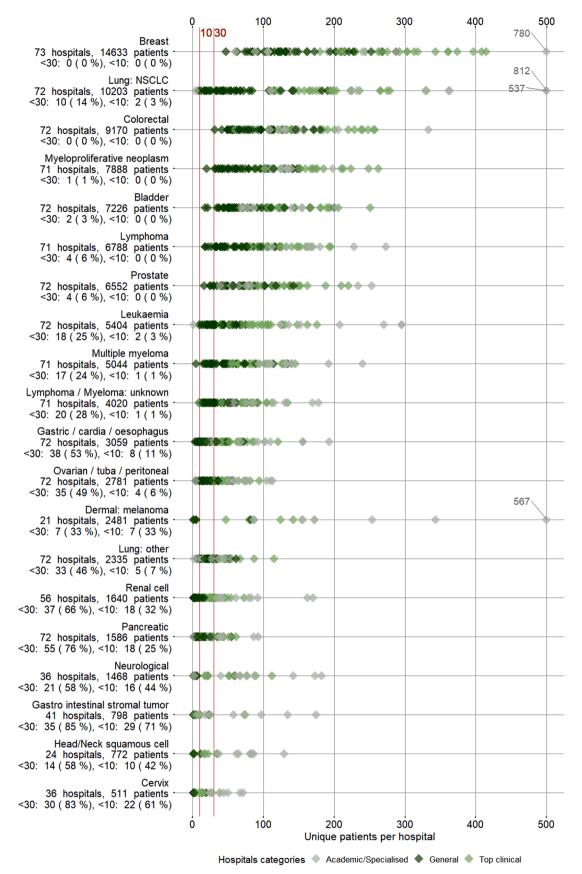


Fig. 1. Overview of the volume of patients treated with medication for each indication per hospital (indications with at least 500 unique patients treated with systemic anti-cancer medication in 2019). Sorted by total number of unique patients treated. Volume cut off points were added on 10 and 30 (line in red), with the number and percentage of hospitals below them displayed on the y-axis. Datapoints which exceeded 500 unique patients per hospital were shown on the end of the x-

axis with the amount of unique patients accordingly. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

most patients followed by top clinical and then general hospitals. Treatments consisted of one or more of the following drugs: axitinib, bevacizumab, cabozantinib, everolimus, lenvatinib, nivolumab, pazopanib, sorafenib, sunitinib, and temsirolimus.

# 3.3.3. Bile duct cancer

For this indication, a total of 357 patients were treated with medication, split amongst 66 hospitals (Fig. 5). Out of the 66 hospitals, all hospitals (100%) treated less than 30 patients and 55 hospitals (83.3%) treated less than 10 patients with medication. Most patients were treated in academic/specialised oncology hospitals. Treatments consisted of one or more of the following drugs: cisplatin or gemcitabine.

# 3.3.4. Hepatocellular cancer

A total of 176 patients were treated with medication, split over 23 hospitals. 21 hospitals (91.3%) treated less than 30 patients and 17 hospitals (73.9%) treated less than 10 patients with medication. Academic/specialised hospitals were the main locations for treatment (Fig. 6). Only very small numbers of patients were treated in other hospitals. Treatments consisted of one or more of the following drugs: cabozantinib, lenvatinib, regorafenib, and sorafenib.

# 3.4. Overview of indications below thresholds per hospital

As Fig. 7 shows, 60 hospitals treat <10 patients with systemic therapy in at least six indications and treat <30 patients with systemic therapy in at least ten indications. The most indications in which <10 patients are treated by a single hospital is 14 (left side of the Figure). One specialised breast cancer hospital does not treat any indications in low volume, explaining why the Figure only goes up to 72 (out of 73) hospitals. All other 72 hospitals treated at least in four indications less than 10 patients and in at least six indications less than 30 patients (the right side of the Figure).

# 4. Discussion

In this nationwide quantitative study based on all systemic anticancer medication hospital declarations of the year 2019, a large spread in patient volumes treated with systemic medication between hospitals across the Netherlands was observed. The order of types of hospitals treating the largest patient volumes showed that academic/specialised hospitals have the highest patient volumes per hospital for most indications. In more than half of the indications the majority of all hospitals treated less than 10 patients annually and in almost two-thirds of indications the majority of all hospitals treated less than 30 patients with systemic treatments. In the four case studies it was further demonstrated that relatively few hospitals treated many patients while many hospitals treated few patients.

Despite the volume norms set for the systemic treatment of hepatocellular, renal cell, and bile duct cancer [26,27], we observed that even in the best case of these indications (renal cell cancer) one-third of the hospitals did not treat the norm of at least 10 patients with systemic therapy. Moreover, in the other two indications more than three-quarter of hospitals did not meet this patient volume norm. It should however be noted that for hepatocellular and bile duct cancer the norms for systemic treatment volumes, were set by the Dutch Society of Surgery (NVvH), not by the medical oncology society [26]. Furthermore, the Foundation of Oncological Collaboration (SONCOS) report, in which the norm for renal cell cancer in case they collaborated with an expertise hospital, regardless of the number of patients [27]. Unfortunately, (the number and details of) collaborations –for example multidisciplinary consultations– between hospitals could not be extracted from our data. Data of patients not treated with systemic treatment were not included in our dataset. Thus, conclusions about meeting this volume criterium should be interpreted with caution.

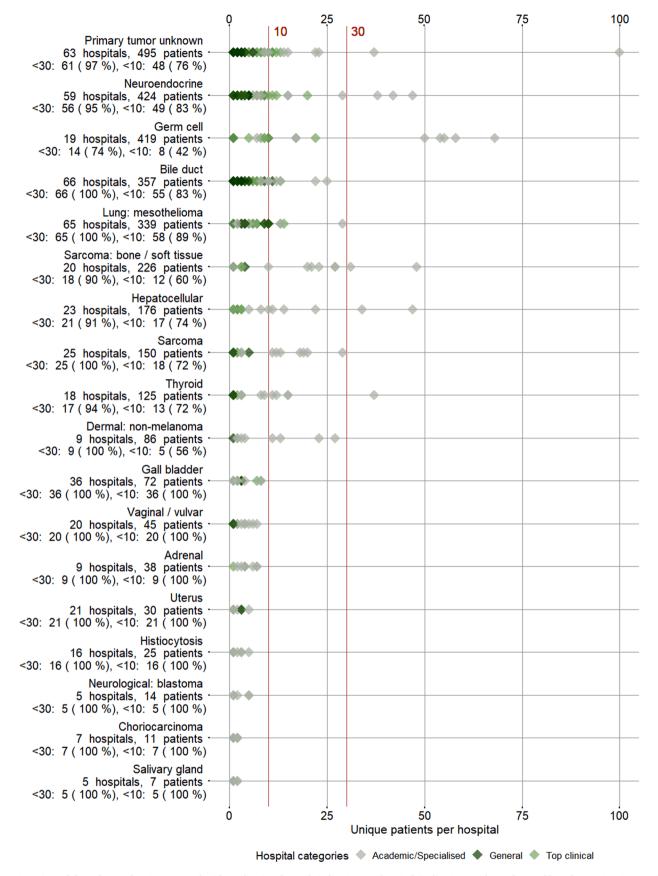
Our results clearly indicate that it is very common for hospitals to treat relatively few patients with systemic oncolytic medication for a specific indication. For some indications, small patient numbers may not constitute such a problem if they are treated with shared care, together with help of expert hospitals, or if the quality of care is guaranteed in some other way. Some may argue that it may not be necessary to treat many patients in a specific indication as medication may be relatively simple to apply, or the same drug may be applied throughout multiple indications which would mitigate the need for higher patient numbers within a single indication. The latter could explain why patients with some indications are treated in a relatively high number of hospitals. For example, there are almost a 5-fold more patients with renal cell cancer as opposed to bile duct cancer, but these renal cell cancer patients are treated in a lower number of general hospitals. A possible explanation for this could be that the treatment for renal cell cancer is more specialised and is thus used in less hospitals. On the other hand, gemcitabine and cisplatin, the standard treatment option for bile duct cancer, are indicated and therefore used in many more types of cancer. This phenomenon may hold true for other indications where classic chemotherapy plays a large role in standard care. However, indication-specific aspects of certain systemic treatments may suggest the opposite. For example, the decision between treatments or the choice to defer treatment may be based on potential side effects in relation to indicationspecific prognosis or alternative treatment options [27]. Additionally, many indications defined within this study consist of multiple subtypes, further complicating the (systemic) treatment of these patients. Another benefit of a certain extent of concentration is that high volume hospitals can contribute to clinical research more efficiently and easily.

Concentration of care may have benefits for patients [4–21], but also the disadvantage that travelling time and expenses are increased. Not only when a patient is treated for one indication, but also in the case a patient has to be treated for multiple indications by multiple different expert hospitals. In addition, especially older patients may have comorbidities treated for many years by several physicians in their local hospital. That patients are willing to travel for higher quality care has been found in research conducted in Sweden, the United Kingdom as well as in the Netherlands [24,29,30]. Travel costs and additional burden for patients and informal caregivers should be considered when organizing concentration of care.

#### 4.1. International perspective

One could argue that the high occurrence of low patient volumes (treated with systemic medication) may be because of the high density of hospitals in the Netherlands. However, in fact, according to international data on the density of hospitals, the Netherlands has a relatively low number of hospitals per 100.000 inhabitants compared to for example Germany, France or Europe overall (1.62 versus 3.89, 4.85, and 3.09 respectively) [31]. A low hospital density would suggest more patients per hospital in the Netherlands relative to other countries. Importantly, this could imply that other countries, depending on their (lack of) concentration policy, may even have lower numbers of patients treated with systemic oncology treatments within these indications per hospital.

Although international data on the relation between surgery and care volume and care quality is available [4–20], studies investigating patient volumes of systemic anticancer treatment in other countries are lacking. It would thus be interesting if further research in other countries



**Fig. 2.** Overview of the volume of patients treated with medication for each indication per hospital (indications with a volume of less than 500 unique patients treated with systemic anti-cancer medication in 2019). Sorted by total number of unique patients treated. Volume cut off points were added on 10 and 30 (line in red), with the number and percentage of hospitals below them displayed on the y-axis. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

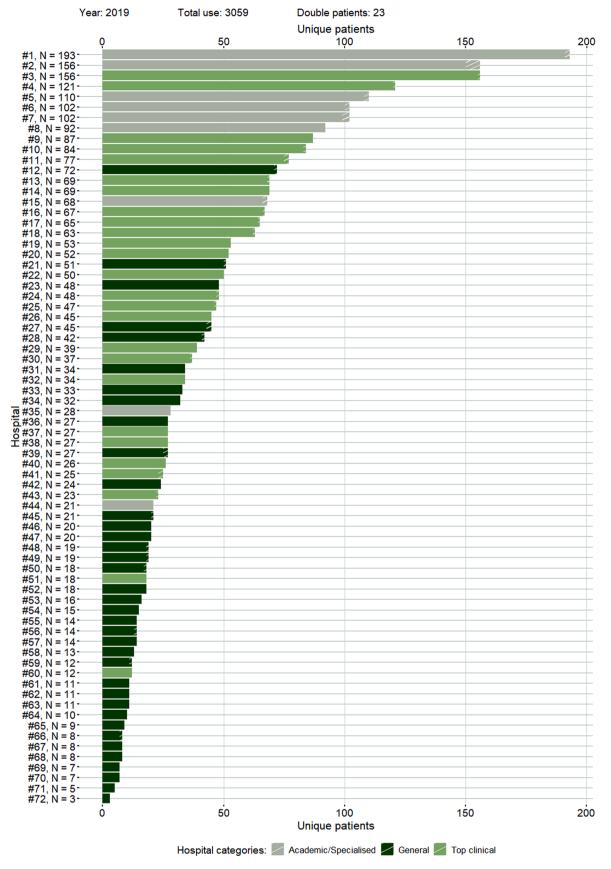


Fig. 3. Patient volume (treated with medication) per hospital for gastric, cardia, oesophagus cancer. Hospitals are displayed in colour of their category. Striped parts indicate unique patients who were treated in multiple hospitals (double patients).

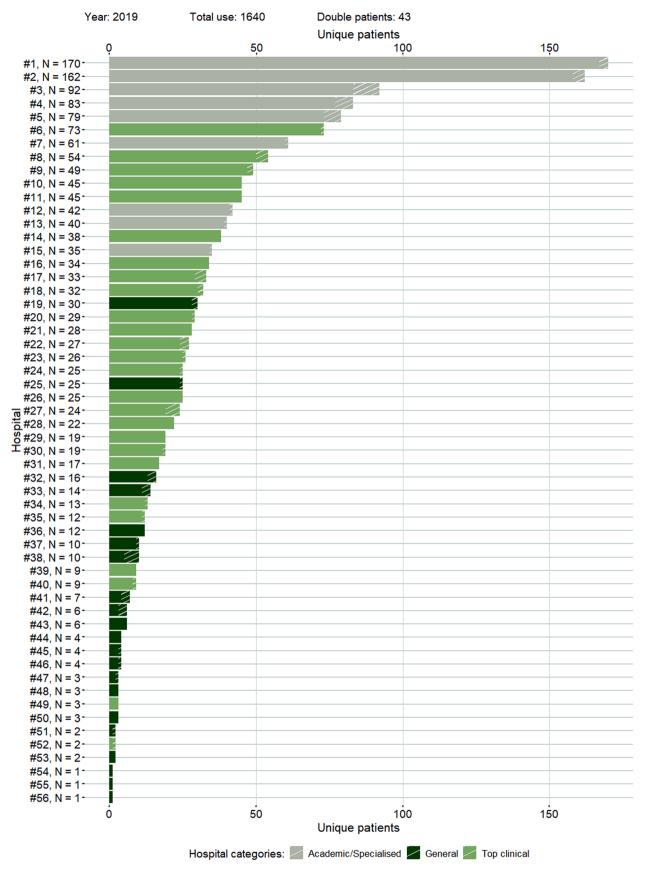


Fig. 4. Patient volume (treated with medication) per hospital for renal cell cancer. Hospitals are displayed in colour of their category. Striped parts count unique patients who were treated in multiple hospitals (double patients).

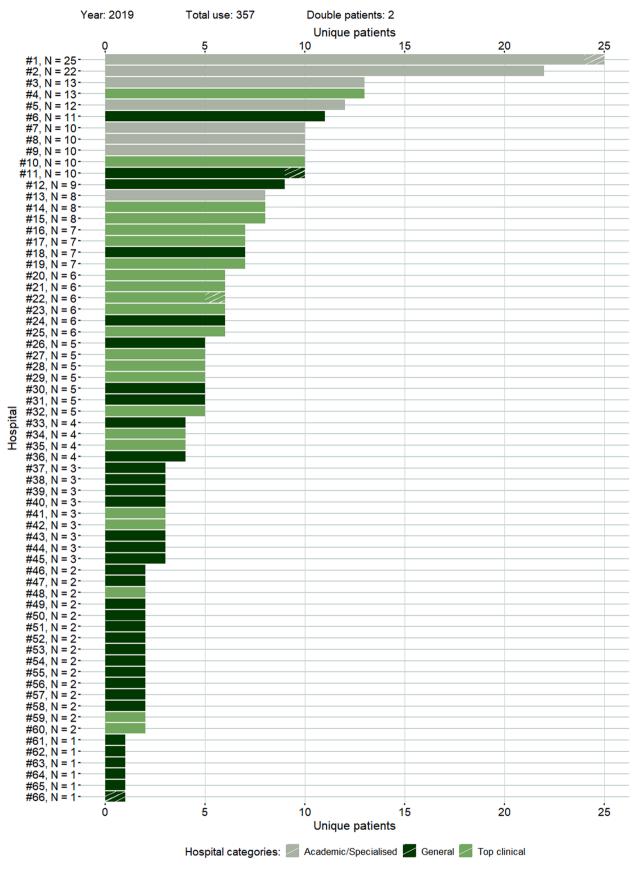


Fig. 5. Patient volume (treated with medication) per hospital for bile duct cancer. Hospitals are displayed in colour of their category. Striped parts count unique patients who were treated in multiple hospitals (double patients).

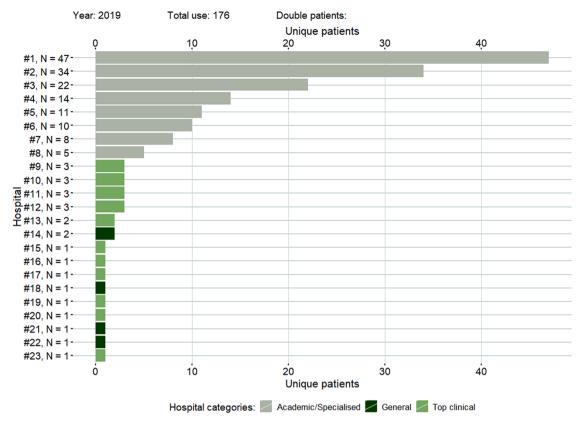
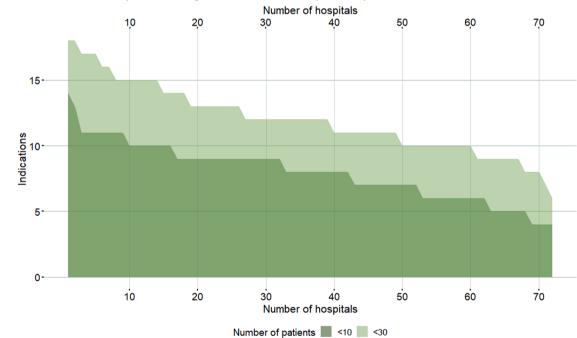


Fig. 6. Patient volume (treated with medication) per hospital for hepatocellular cancer. Hospitals are displayed in colour of their category.



Number of hospitals treating a certain number of patients per indication

**Fig. 7.** Overview of the organisation of care in the Netherlands shown by the number of indications (N = 38) treated in volumes <10 and <30 patients by a certain number of hospitals (N = 73).

would focus on the concentration of systemic anticancer treatment. Subsequently, the results of our study could be placed into context relative to the results in other countries. One could then ultimately strive to establish international health policy advices. All in all, the prevalence of hospitals treating very few numbers of patients with systemic anticancer treatment indicates that healthcare professionals, patients, and other stakeholders should discuss whether there is a need for action based on the indication. Preferably, this is done not only nationally, but also internationally. In case action is needed, volume norms for systemic anticancer treatment could be considered. The direct comparison between patient volumes and clinical outcomes should be investigated for systemic therapy. Furthermore, the quantity and complexity of multidisciplinary collaboration between centers should be taken into account when practical advices to stakeholders are given on both a national and global scale.

#### 4.2. Strengths and limitations

The strength of this study lies in the usage of a complete dataset of all national declarations in the Netherlands. However, the use of this data source also introduces some limitations. Only declarations of systemic medications as so-called 'add-on' therapies were included, thus, we did not have total patient volumes of indications per hospital, including e.g. patients having only supportive care or surgery. Only including treatments that are reimbursed by health insurance companies also adds a limitation, missing out on study medication. Additionally, claims data may contain administrative faults which cannot be corrected for. The data was from 2019. It is expected that in other years the exact numbers of patients treated will be different. However, it is likely that the overall picture of a lack of concentration will be similar, and data from 2020 to 2021 would have been confounded by the COVID-19 pandemic. Finally, the data on use of systemic therapy did not provide us any information on underlying collaboration between centres -for example multidisciplinary consultations-.nor on the outcome of treatment. Given the limitations inherent to the data no conclusions can be drawn on the current state of care quality in any indication.

#### 5. Conclusions

In the majority of oncology indications, a large proportion of Dutch hospitals treat small numbers of unique patients with systemic medication. The high level of fragmentation gives ground for further exploration and discussion on how the organisation of care can support optimization of the efficiency and quality of care. Professional groups, policy makers, patients, and healthcare insurers should consider per indication whether the introduction of and compliance to volume norms is warranted.

#### **Contributor statement**

NWLP, RAV, HvL and LT conceived the study. RAV and LT provided the data. NWLP and RAV analysed the data. NWLP, RAV, GC, MJK, HVL and LT interpreted the data. NWLP and RAV drafted the manuscript. All authors revised the manuscript. All authors approved the final manuscript. LT is the guarantor.

#### **Declaration of Competing Interest**

HvL reported conflicts of interest as consultant of Bristol Myers Squibb, Dragonfly, Lilly, Merck, Nordic Pharma, Servier. HvL also received research funding and/or medication supply from Bayer, BMS, Celgene, Janssen, Incyte, Lilly, Merck, Nordic Pharma, Philips, Roche, Servier. MJK reported conflicts of interest as consultant of Bristol Myers Squibb, Celgene, Kite, a Gilead Company, Miltenyi Biotech, Novartis, and Roche; MJK also received research funding from Kite, Roche, Takeda, and Celgene and travel support from Kite, Miltenyi Biotech, Novartis, and Roche

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#### Data availability statement

Restrictions apply to the availability of these data, which were used under license for this study. Data are available on request from the corresponding author with the permission of Zorginstituut Nederland.

#### Glossary

Patient volume, anticancer medication, drugs, oncology, centralisation, concentration, quality of care

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#### References

- Fiteni F, Westeel V, Pivot X, et al. Endpoints in cancer clinical trials. J Visc Surg 2014;151(1):17–22. https://doi.org/10.1016/j.jviscsurg.2013.10.001. Epub 2014 Jan 14. PMID: 24440056.
- [2] Kilickap S, Demirci U, Karadurmus N, et al. Endpoints in oncology clinical trials. J BUON 2018;23(7):1–6. PMID: 30722104.
- [3] Crawford GB, Dzierżanowski T, Hauser K, et al. ESMO guidelines committee. Care of the adult cancer patient at the end of life: ESMO clinical practice guidelines. ESMO Open 2021;6(4):100225. https://doi.org/10.1016/j.esmoop.2021.100225. Epub 2021 Aug 17. PMID: 34474810; PMCID: PMC8411064.
- [4] de Haas J, Heida JP, Stoop T, et al. Concentratie van complexe ingrepen kan meer dan 200 sterftegevallen vermijden. SiRM. Accessed 2022:2022. https://www.sirm. nl/docs/Concentratie-complexe-behandelingen.pdf.
- [5] Llorente C, Guijarro A, Hernandez V, et al. Effect of hospital volume on 90-day mortality after radical cystectomy for bladder cancer in Spain. World J Urol 2020; 38(5):1221–8. https://doi.org/10.1007/s00345-019-02874-9. Epub 2019 Jul 13. PMID: 31302754.
- [6] Greenup RA, Obeng-Gyasi S, Thomas S, et al. The effect of hospital volume on breast cancer mortality. Ann Surg 2018;267(2):375–81. https://doi.org/10.1097/ SLA.000000000002095. PMID: 27893532; PMCID: PMC5994238.
- [7] Diers J, Wagner J, Baum P, et al. Nationwide in-hospital mortality following colonic cancer resection according to hospital volume in Germany. BJS Open. 2019;3(5):672–7. https://doi.org/10.1002/bjs5.50173. PMID: 31592096; PMCID: PMC6773649.
- [8] Clark PR, Dambrino RJ, Himel SM, et al. The impact of craniotomy for brain tumor case volume on patient safety indicators and in-hospital mortality. Clin Neurol Neurosurg 2020;196:106043. https://doi.org/10.1016/j.clineuro.2020.106043. Epub 2020 Jun 24. PMID: 32653799.
- [9] Haj Mohammad N, Bernards N, van Putten M, et al. Volume-outcome relation in palliative systemic treatment of metastatic oesophagogastric cancer. Eur J Cancer 2017;78:28–36. https://doi.org/10.1016/j.ejca.2017.03.008.
- [10] Dijksterhuis WPM, Verhoeven RHA, Meijer SL, et al. Increased assessment of HER2 in metastatic gastresophageal cancer patients: a nationwide population-based cohort study. Gastric Cancer. 2020;23(4):579–90. https://doi.org/10.1007/ s10120-020-01039-7.
- [11] Dijksterhuis WPM, Verhoeven RHA, Pape M, et al. Hospital volume and beyond first-line palliative systemic treatment in metastatic oesophagogastric adenocarcinoma: a population-based study. Eur J Cancer 2020;139:107–18. https://doi.org/10.1016/j.ejca.2020.08.010.
- [12] Besseling J, Reitsma J, Van Erkelens JA, et al. Use of palliative chemotherapy and ICU admissions in gastric and esophageal cancer patients in the last phase of life: a nationwide observational study. Cancers (Basel) 2021;13(1):145. https://doi.org/ 10.3390/cancers13010145.
- [13] Haj Mohammad N, Bernards N, Besselink MG, et al. Volume matters in the systemic treatment of metastatic pancreatic cancer: a population-based study in the Netherlands. J Cancer Res Clin Oncol 2016;142(6):1353–60. https://doi.org/ 10.1007/s00432-016-2140-5. PMID: 26995276; PMCID: PMC4869755.
- [14] Besseling J, Reitsma J, Van Erkelens JA, et al. Use of palliative chemotherapy and ICU admissions in gastric and esophageal cancer patients in the last phase of life: a nationwide observational study. Cancers (Basel) 2021;13(1):145. https://doi.org/ 10.3390/cancers13010145.
- [15] Hillner BE, Smith TJ, Desch CE, et al. Hospital and physician volume or specialization and outcomes in cancer treatment: importance of quality of cancer care. J Clin Oncol 2000;18:2327–40.

- [16] Chen AY, Fedewa S, Pavluck A, et al. Improved survival is associated with treatment at high-volume teaching facilities for patients with advanced stage laryngeal cancer. Cancer 2010;116:4744–52.
- [17] Lin JF, Berger JL, Krivak TC, et al. Impact of facility volume on therapy and survival for locally advanced cervical cancer. Gynecol Oncol 2014;132:416–22.
- [18] Wang EH, Rutter CE, Corso CD, et al. Patients selected for definitive concurrent chemoradiation at high-volume facilities achieve improved survival in stage III nonsmall-cell lung cancer. J Thorac Oncol 2015;10:937–43.
- [19] Wuthrick EJ, Zhang Q, Machtay M, et al. Institutional clinical trial accrual volume and survival of patients with head and neck cancer. J Clin Oncol 2015;33:156–64.
- [20] Eaton BR, Pugh SL, Bradley JD, et al. Institutional enrollment and survival among NSCLC patients receiving chemoradiation: NRG Oncology Radiation Therapy Oncology Group (RTOG) 0617. J Natl Cancer Inst 2016;108:1–8.
- [21] Morche J, Renner D, Pietsch B, et al. International comparison of minimum volume standards for hospitals. Health Policy (New York) 2018;122(11):1165–76. https:// doi.org/10.1016/j.healthpol.2018.08.016. Epub 2018 Aug 31. PMID: 30193981.
- [22] Ministerie van VWS. Passende Zorg [Zorginstituut+NZa, nov 2020]. Programma de juiste zorg op de juiste plek. Accessed on 06 September 2022. www.dejuistezorgo pdejuisteplek.nl.
- [23] Vonlanthen R, Lodge P, Barkun JS, et al. Toward a consensus on centralization in surgery. Ann Surg 2018;268(5):712–24. https://doi.org/10.1097/ SLA.000000000002965. PMID: 30169394.

- Health policy 135 (2023) 104865
- [24] NFK. (2019). Een ziekenhuis kiezen bij kanker: wat vind jij belangrijk? Accessed on 6 September 2022. https://nfk.nl/media/1/191205-DJE-Expertzorg\_rapportage FINAAL.pdf.
- [25] European Society for Medical Oncology. About ESMO. Accessed on 6 September 2022. https://www.esmo.org/about-esmo.
- [26] Nederlandse Vereniging voor Heelkunde. Normering Chirurgische Behandelingen 8.1. Accessed on 6 September 2022. https://assets.heelkunde.nl/p/491520/none /Normen%208\_1%20versie%20april%202021.pdf.
- [27] Stichting Oncologische Samenwerking. Multidisciplinaire Normering Oncologische Zorg in Nederland. Accessed on 6 September 2022. https://www.soncos.org/ wp-content/uploads/2021/03/SONCOS-normeringsrapport-versie-9-2021.pdf.
   [28] Vektis. Accessed on 6 September 2022. www.vektis.nl.
- [29] Svederud I, Virhage M, Medin E, et al. Patient perspectives on centralisation of low volume, highly specialised procedures in Sweden. Health Policy (New York) 2015; 119(8):1068–75. https://doi.org/10.1016/j.healthpol.2015.01.016. Epub 2015
- Feb 19. PMID: 25773506.
  [30] Vallejo-Torres L, Melnychuk M, Vindrola-Padros C, et al. Discrete-choice experiment to analyse preferences for centralizing specialist cancer surgery services. Br J Surg 2018;105(5):587–96. https://doi.org/10.1002/bjs.10761. Epub 2018 Mar 7. PMID: 29512137; PMCID: PMC5900867.
- [31] European Health Information Gateway. Accessed on 6 September 2022. https://gat eway.euro.who.int/en/indicators/hfa\_470-5010-hospitals-per-100-000/