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# Nowotwory Journal of Oncology







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### Original article

COVID-19

### Breast cancer treatment during the COVID-19 pandemic — a patient's perspective

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**Introduction.** The COVID-19 pandemic has had an impact on healthcare. The aim of the study was to assess how factors related to the COVID-19 pandemic were perceived by breast cancer patients during their anticancer treatment. **Material and methods.** The study was carried out on 154 breast cancer patients. A questionnaire prepared specifically for this analysis was used.

**Results.** The duration of the cancer diagnosis was the same both before and during the COVID-19 pandemic. However, 42.9% of the respondents stated that they waited longer for a visit/examination than before the pandemic. Some patients were proposed a teleconsultation and over half of them were not satisfied with this; most patients claimed that this could have been a good alternative only when they began to feel better.

**Conclusions.** Breast cancer patients treated during the COVID-19 pandemic experienced some inconveniences and were afraid that the pandemic would have a negative impact on their treatment's outcome.

Keywords: breast cancer, COVID-19, anticancer treatment, vaccination, teleconsultations

### Introduction

Breast cancer is one of the most frequently diagnosed cancers in the world [1]. The International Agency for Research on Cancer estimates that there were about 2.3 million new breast cancer cases around the world in 2020. Breast cancer is the most common cause of death from cancer in women [1].

Diagnosis and effective treatment of breast cancer is affected by multiple factors, dependent both on the healthcare system and on the patients themselves. Recently, the healthcare system has been severely affected by the COVID-19 pandemic. Restrictions began to be implemented in Poland

in March 2020, and a pandemic state was ultimately declared [2, 3]. The healthcare system had to face the challenge of a large number of COVID-19 patients, which — on the one hand — forced the decision-makers to introduce organisational changes and to move resources to fight the pandemic and, on the other hand, caused problems with ensuring continuing healthcare to patients with other diseases. During the first period of the pandemic, prevention and screening tests were discontinued, and emergency cases became the priority [4, 5]. Changes in the functioning of the healthcare system forced by the pandemic also affected the diagnostics

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and treatment of cancers. It is known that a longer waiting time for diagnosis and treatment initiation has an adverse impact on the survival rate in cancer patients, including those with breast cancer [6, 7]. Extending the time before the start of breast cancer treatment by three months results in decreasing the 5-year overall survival rate by 5-7% [7]. A number of analyses were conducted based on predictive models. e.g. it is projected that the discontinuation of screening tests for breast cancer for three months because of the COVID-19 pandemic in Canada resulted in a decrease in the number of diagnosed cancer cases by 7% and an increase in the number of advanced cancers [8]. It is estimated in the United Kingdom (UK) that a delay in diagnosing breast cancer will result in a decrease in the 5-year overall survival rate by 9.6% [9]. Patients who were in the middle of anticancer treatment or whose cancer was diagnosed during the pandemic should have been given treatment in accordance with the standard of care. However, it turned out that this was not the case. For example, the number of patients on radiotherapy in various countries decreased during the first year of the COVID-19 pandemic by 6-36% [10-12]. The concerns among healthcare professionals and patients themselves about the spread of the infection and its consequences have led various oncology scientific associations to recommend appropriate actions to reduce the risk of morbidity and death from SARS-CoV-2 infection among cancer patients, which in turn has led to changes in existing procedures [13-16].

The aim of the study was to assess how factors related to the COVID-19 pandemic were perceived by patients with breast cancer during their anticancer treatment.

### **Material and methods**

The study was carried out on 154 breast cancer patients diagnosed between 2019 and 2021. The questionnaire in a Google form was shared on Facebook. A link to the form was provided on the websites of Klub Amazonek, patient associations and oncology-related non-profit organisations. The link to the online survey was active from 1.04.2022 to 4.03.2023. Participation in the study was voluntary and anonymous; filling out the questionnaire was equal to giving consent to participate in the study.

An original questionnaire prepared for this analysis was used. The questionnaire contained demography-related questions (age, place of residence, educational status) and 21 survey questions: twenty close-ended questions (with three multiple-choice questions among them) and one openended question. The questionnaire is presented as Supplementary Materials.

The survey was anonymous, and none of the participants' personal data were processed. Therefore, in accordance with the rules of the Bioethics Committee at the University of Warmia and Mazury in Olsztyn, ethics approval for the study was not required.

### Statistical analysis

Descriptive statistics were used to characterise the patients' group. The chi-square test was used to compare the proportions between subgroups. A p value of < 0.05 was considered to be significant. The data analysis was conducted using Statistica (data analysis software), version 13 — http://statistica. io TIBCO Software Inc., Krakow, Poland (2017).

### **Results**

The study included 154 women diagnosed with breast cancer, aged 25-73 years (mean age 47.3 years). 55.2% of the patients had high education, 44.2% had secondary education, and only one woman had primary education. The patients were from all parts of Poland — the smallest number from the Podlaskie and the Świętokrzyskie Voivodships (3 respondents from each), the largest number from the Mazowieckie Voivodship (18 respondents). A quarter of the respondents lived in villages (26.6%), a third lived in cities with a population exceeding 100 thousand residents (33.8%), and the other third lived in smaller towns (39.6%). Breast cancer had been diagnosed before December 2019 (over three months before the outbreak of the COVID-19 pandemic) in 32 patients (20.8%), 14 women (9.1%) had been diagnosed between December 2019 and March 2020 (immediately before the COVID-19 pandemic outbreak), 41 patients (26.6%) had been diagnosed between April and December 2020 (during the first nine months of the COVID-19 pandemic), and 66 patients (42.9%) had been diagnosed between January 2021 and December 2021 (during the second year of the COVID-19 pandemic).

The time between reporting the first symptoms to the physician or observing worrying results of screening tests and obtaining a result of a histopathological examination was shorter than one month in over half of the patients (65.6%), and it was 2–3 months in a quarter of the patients (24.7%). Only 11 patients (7.1%) waited over three months for the diagnosis after the first symptoms. A majority of the patients had completed chemotherapy and/or radiotherapy at the time of the study (80%). Half of the patients had received three COVID-19 vaccination doses at the time of the study (54.5%), 27.9% had received two doses, and 3.3% of them had received one dose. Eleven women (14.3%) were not vaccinated against COVID-19 at the time of completing the survey (Tab. I).

Demographic factors as age, education and place of residence did not have statistically significant impact on time from reporting the first symptoms to the physician or obtaining a worrying mammography result to the histopathological result (Tab. II). There was no significant relationship between the period during which the patients were diagnosed (over three months before the COVID-19 pandemic, three months immediately before the pandemic, the first nine months of the pandemic, and nine months after the start of the pandemic) and the time between a patient's visit to the physician with cancer symptoms or a worrying results

**Table I.** Characteristics of the study group (n = 154)

Age (range 25–73 years; mean 47.3 ± 10.1):         < 50 years       93       60.4         ≥ 50 years       61       39.6         Education	Group	n	[%]
Education  Primary 1 0.6 Secondary 68 44.2 High 85 55.2 Place of residence — voivodship  Dolnośląskie 8 5.2 Kujawsko-Pomorskie 9 5.8 Lubelskie 7 4.5 Lubuskie 5 3.2 Łódzkie 14 9.1 Małopolskie 12 7.8 Mazowieckie 18 11.7 Opolskie 9 5.8 Podkarpackie 7 4.5 Swiętokrzyskie 15 9.7 Śląskie 15 9.7 Śląskie 15 9.7 Śląskie 12 7.8 Świętokrzyskie 15 9.7 Śląskie 12 7.8 Świętokrzyskie 14 9.1 Wielkopolskie 14 9.1 Wielkopolskie 14 9.1 Vielkopolskie 14 9.1 Zachodniopomorskie 4 2.6 Place of residence Village 41 26.6 City < 20 thousand residents 23 14.9 City 20-100 thousand residents 38 24.7	Age (range 25–73 years; mean 47.3 ± 10.1):		
Education         Primary       1       0.6         Secondary       68       44.2         High       85       55.2         Place of residence — voivodship       Dolnośląskie       8       5.2         Kujawsko-Pomorskie       9       5.8         Lubelskie       7       4.5         Lubuskie       5       3.2         Łódzkie       14       9.1         Małopolskie       12       7.8         Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence       Village       41       26.6         City < 20 thousand residents	< 50 years	93	60.4
Primary       1       0.6         Secondary       68       44.2         High       85       55.2         Place of residence — voivodship       Dolnośląskie       8       5.2         Kujawsko-Pomorskie       9       5.8         Lubelskie       7       4.5         Lubuskie       5       3.2         Łódzkie       14       9.1         Małopolskie       12       7.8         Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence       Village       41       26.6         City < 20 thousand residents	≥ 50 years	61	39.6
Secondary       68       44.2         High       85       55.2         Place of residence — voivodship       5       55.2         Dolnośląskie       8       5.2         Kujawsko-Pomorskie       9       5.8         Lubelskie       7       4.5         Lubuskie       5       3.2         Łódzkie       14       9.1         Malopolskie       12       7.8         Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Education		
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Place of residence — voivodship         Dolnośląskie       8       5.2         Kujawsko-Pomorskie       9       5.8         Lubelskie       7       4.5         Lubuskie       5       3.2         Łódzkie       14       9.1         Małopolskie       12       7.8         Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Secondary	68	44.2
Dolnośląskie       8       5.2         Kujawsko-Pomorskie       9       5.8         Lubelskie       7       4.5         Lubuskie       5       3.2         Łódzkie       14       9.1         Małopolskie       12       7.8         Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	High	85	55.2
Kujawsko-Pomorskie       9       5.8         Lubelskie       7       4.5         Lubuskie       5       3.2         Łódzkie       14       9.1         Małopolskie       12       7.8         Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Place of residence — voivodship		
Lubelskie       7       4.5         Lubuskie       5       3.2         Łódzkie       14       9.1         Małopolskie       12       7.8         Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Dolnośląskie	8	5.2
Lubuskie       5       3.2         Łódzkie       14       9.1         Małopolskie       12       7.8         Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Kujawsko-Pomorskie	9	5.8
Łódzkie       14       9.1         Małopolskie       12       7.8         Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Lubelskie	7	4.5
Małopolskie       12       7.8         Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Lubuskie	5	3.2
Mazowieckie       18       11.7         Opolskie       9       5.8         Podkarpackie       7       4.5         Podlaskie       3       1.9         Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Łódzkie	14	9.1
Opolskie         9         5.8           Podkarpackie         7         4.5           Podlaskie         3         1.9           Pomorskie         15         9.7           Śląskie         12         7.8           Świętokrzyskie         3         1.9           Warmińsko-Mazurskie         14         9.1           Wielkopolskie         14         9.1           Zachodniopomorskie         4         2.6           Place of residence           Village         41         26.6           City < 20 thousand residents	Małopolskie	12	7.8
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Pomorskie       15       9.7         Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Podkarpackie	7	4.5
Śląskie       12       7.8         Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Podlaskie	3	1.9
Świętokrzyskie       3       1.9         Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Pomorskie	15	9.7
Warmińsko-Mazurskie       14       9.1         Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Śląskie	12	7.8
Wielkopolskie       14       9.1         Zachodniopomorskie       4       2.6         Place of residence         Village       41       26.6         City < 20 thousand residents	Świętokrzyskie	3	1.9
Zachodniopomorskie 4 2.6  Place of residence  Village 41 26.6  City < 20 thousand residents 23 14.9  City 20–100 thousand residents 38 24.7	Warmińsko-Mazurskie	14	9.1
Place of residence  Village 41 26.6  City < 20 thousand residents 23 14.9  City 20–100 thousand residents 38 24.7	Wielkopolskie	14	9.1
Village         41         26.6           City < 20 thousand residents         23         14.9           City 20–100 thousand residents         38         24.7	Zachodniopomorskie	4	2.6
City < 20 thousand residents 23 14.9  City 20–100 thousand residents 38 24.7	Place of residence		
City 20–100 thousand residents 38 24.7	Village	41	26.6
<u> </u>	City < 20 thousand residents	23	14.9
City > 100 thousand residents 52 33.8	City 20–100 thousand residents	38	24.7
	City > 100 thousand residents	52	33.8

of screening mammography and the moment when the breast cancer was confirmed by histopathology (Tab. III).

A majority of respondents (85.7%) were vaccinated against COVID-19 (with at least one dose) at the moment of the study. Significantly more women aged  $\geq 50$  years were vaccinated compared to those aged < 50 years (95% vs. 79%, respectively; p = 0.006). The educational level and place of residence did not have any impact on whether they were vaccinated or not (Tab. IV). 60.4% of the women stated that they feared vaccination against COVID-19 (Tab. V). Women

Group	n	[%]
Time between reporting the first symptoms to observing worrying results of screen tests and of the histopathological examination		
< 1 month	101	65.6
1–3 months	38	24.7
> 3 months	11	7.1
No data	4	2.6
Phase of treatment		
During chemotherapy or radiotherapy	21	13.6
During hormonotherapy	123	79.9
During treatment of disease progression	10	6.5
Period of cancer diagnosis		
01.2019–11.2019	32	20.8
12.2019-03.2020	14	9.1
04.2020–12.2020	41	26.6
01.2021–12.2021	66	42.9
No data	1	0.6
Vaccination against COVID-19:		
1 dose	5	3.3
2 doses	43	27.9
3 doses	84	54.5
Not vaccinated	22	14.3

± Standard deviation

living in cities with a population of over 100,000 the least fear vaccination against COVID-19 (p = 0.005). Neither age nor educational status was shown to affect the fear of vaccination (Tab. SI). The women could not state whether they had become more susceptible to COVID-19 or its severe course after being diagnosed with cancer (Tab. V). Women with breast cancer living in large cities believed more often that they were at a higher risk of infection/severe course of COVID-19 (p = 0.04). Other demographic factors, such as age or educational level, did not affect the feelings of insecurity (Tab. SI). Only half of the patients (47.4%) said they felt/feel less at risk of severe COVID-19 after receiving the vaccination (Tab. V). There was no significant differences in feeling less threatened with a severe bout of COVID-19 after being vaccinated according to demographic factors (Tab. SI).

In total, 43.5% of the respondents felt safe in a hospital//clinic environment in terms of risk of SARS-CoV-2 infection, although in most of them (86.4%) an epidemiological history was taken and their body temperature was measured before

**Table II.** The relationship between demographic factors and the time between reporting the first symptoms to the physician or observing worrying results of screen tests and obtaining a result of histopathological examination

Group	The time bet			toms to the phys result of histopa			esults of scre
	< 1 r	nonth	1–3 n	nonths	> 3 m	nonths	p value
		[%]		[%]		[%]	
Age							
< 50 years	60	67.4	22	24.7	7	7.9	0.94
≥ 50 years	41	67.2	16	26.2	4	6.6	
Education							
Secondary	44	65.7	18	26.9	5	7.4	0.94
High	56	68.0	20	25.0	6	7.0	
Place of residence							
Village	23	57.0	14	35.0	3	8.0	0.19
City < 20 thousand residents	19	86.4	1	4.5	2	9.1	
City 20–100 thousand residents	24	64.9	9	24.3	4	10.8	
City > 100 thousand residents	35	68.6	14	27.5	2	3.9	

**Table III.** The relationship between the period of cancer diagnosis (based on the pandemic period) and the time between reporting the first symptoms to the physician or observing worrying results of screen tests and obtaining a result of the histopathological examination

Period of cancer diagnosis	The time b	oetween repo				cian or observ athological ex		g results of	screen tests
	< 1 n	nonth	1–3 n	nonths	> 3 m	nonths	no	data	p value*
		[%]		[%]		[%]		[%]	
01.2019–11.2019	21	65.6	6	18.8	3	9.4	2	6.2	0.85
12.2019-03.2020	9	64.3	3	21.4	2	14.3	0	0.0	
04.2020–12.2020	26	63.4	10	24.4	3	7.3	2	4.9	
01.2021–12.2021	44	66.7	19	28.8	3	4.5	0	0.0	
No data	1								

<sup>\*</sup>No data was excluded from analysis

the visit. 37% of the women said it was impossible to maintain appropriate social distancing while waiting for the visit to the clinic or hospital admission. Nearly half of the respondents (48.7%) knew that they could use free tests to detect SARS-CoV-2 (in case of symptoms or contact with an infected person) (Tab. V).

During COVID-19 pandemic-related restrictions, the breast cancer study participants noticed changes in the functioning of healthcare that had an impact on their contacts with oncology centres. 42.9% of the respondents claimed that they waited for the visit or an examination longer than they would have before the pandemic. Difficulty in contacting the attending physicians was declared by 16.2% of the patients, while 8.4% had their planned visit cancelled with no information on when and where the visit would be rescheduled. According to 10 patients, the visits at the clinic were discontinued and/or the ward where they were treated

had been closed. 15.6% of the respondents had problems with having imaging examinations performed, and 9.1% had problems collecting results of already performed tests. For some patients (38.9%), a visit to the clinic was replaced with a teleconsultation and over half of the patients were not satisfied with the change (Fig. 1A).

Only 21% of patients expressed the view that the health-care system during the COVID-19 pandemic made them feel safe. 10.4% of the respondents needed more frequent meetings with the physician, and 21% mentioned the need to meet with a psychologist. Most of the patients received great support from their families and/or friends (72.1%) and their husband/partner (71.4%) (Fig. 1B).

Half of the respondents (53.2%) thought that the COVID-19 pandemic had an adverse impact on diagnosis and treatment of cancer (Tab. V). There were no significant correlations between demographic factors, such as age,

Table IV. The relationship between demographic factors and being vaccinated

Group	Vacci	nation	p value
	n	[%]	
Age			
< 50 years	73	79.3	0.006
≥ 50 years	59	95.2	
Education			
Secondary	61	89.7	0.20
High	70	82.4	
Place of residence			
Village	35	85.4	0.99
City < 20 thousand residents	20	87.0	
City 20–100 thousand residents	33	86.8	
City > 100 thousand residents	44	84.6	

educational status, or place of residence and this opinion

(Tab. SII). A majority of the respondents (72.8%) expressed

Table V. Patients' opinion on factors related to the COVID-19 pandemic

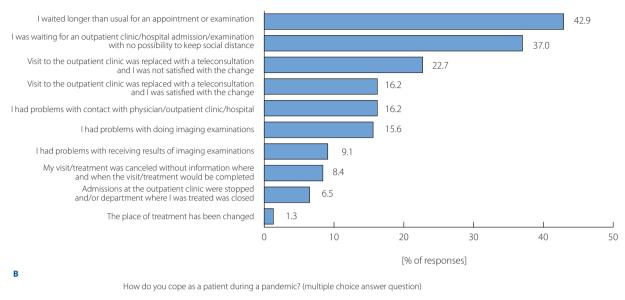
Patients' opinion	n	[%]
Do/Did you fear vaccination against COVID-19?		
Yes	93	60.4
No	61	39.6
In your opinion, do you have a higher risk of COVID-course of COVID-19?	19 infectior	n/severe
Yes	55	35.7
No	49	31.8
I have no opinion	50	32.5
Did you feel/Would you have felt a lower risk of seve being vaccinated?	re COVID-1	19 after
Yes	73	47.4
No	42	27.3
I have no opinion	39	25.3
In your opinion, what is the impact of the COVID-19 diagnosis and treatment of cancer in Poland?	pandemic	on
It is worse than before the pandemic	82	53.2
It is better than before the pandemic	6	3.9
It is the same as before the pandemic	66	42.9
Are/Were you afraid that isolation/quarantine may re the effectiveness of your treatment?	duce	
Yes	112	72.8
No	27	17.5
I have no opinion	15	9.7

concern that isolation/quarantine could have decreased the effectiveness of their treatment (Tab. V). This concern was reported significantly more often by patients living in villages and in small towns compared to those living in large cities (p = 0.004) (Tab. SII).

A teleconsultation as an alternative to an in-person clinic visit was regarded as a good option by 46.1% of the patients. but only when they felt well. According to 31.8% of the respondents, the physician may have incomplete insight into overall health status during a teleconsultation. According to 51.7% of the patients who used teleconsultation, it did not meet their expectations, and 71.7% of the patients who had teleconsultations claimed that they strongly preferred in-person visits to the clinic. Only 20% of the women who had teleconsultations definitely liked them. Some patients thought that with teleconsultation they had avoided contact with those suffering from COVID-19, and saved time and money (53.5%, 63.3% and 41.7% of the respondents who had such consultations, respectively) (Tab. VI). No differences were demonstrated regarding opinion on teleconsultations based on such demographic factors as age, educational status, or place of residence.

Patients' opinion		[%]
Did you feel safe in a hospital/clinic with respect infected with SARS-CoV-2?	to the threat o	fbeing
Yes	67	43.5
No	58	37.7
I have no opinion	28	18.2
No data	1	0.6
In your opinion, were treatment and diagnostic to treat and diagnose patients during the COVID		
Yes	48	31.2
No	53	34.4
I have no opinion	53	34.4
Was your visit to the hospital preceded by an an health condition and an epidemiological interviemeasurement, interview or questionnaire on prepeople or symptoms of infection)?	ew (temperatur	
Yes	133	86.4
Seldom/occasionally	10	6.5
No	11	7.1
Did you have the option to use tests to detect So of symptoms or exposure to an infected person)		(in case
Yes	75	48.7
No	11	7.1
I have no opinion	68	44.2

Did any of the following situations happen to you during your treatment during the pandemic? (multiple choice answer question)



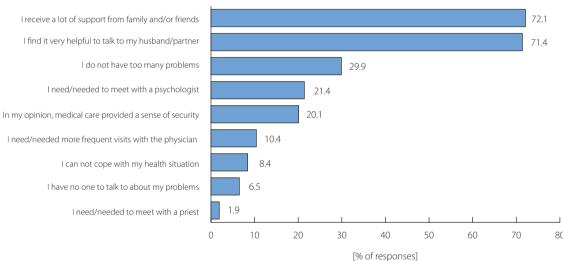


Figure 1. Patients' problems (A) and needs (B) related to treatment during the COVID-19 pandemic

### **Discussion**

Analyses performed in various countries have shown that the COVID-19 pandemic, particularly in its initial stage, had an impact on cancer diagnostics and treatment [17–19]. Some societies (e.g. the American Society for Clinical Oncology) recommended that screening tests like mammography should be postponed [20]. It was found that the number of new cancers detected decreased by 40–50% compared to the same months in previous years [21, 22]. Afterwards, the number of detected cancers in more advanced stages increased, which also applies to breast cancer [23, 24]. It seems that this may have been affected by an extension of the diagnosis time. In a very large United States (U.S.) population study (over 6 mil-

lion insured), a decrease in the number of breast biopsies performed was shown by 71% in April 2020 and by 31% in July 2020 compared with the same months of the previous year [25]. The period in the current study during which patients were diagnosed (over three months before the COVID-19 pandemic, three months immediately before the pandemic, the first nine months of the pandemic, and nine months after the start of the pandemic) did not have a significant impact on the duration of the cancer diagnosis. 65.6% of all the analysed patients got a histopathological diagnosis within one month of reporting the first symptoms to the physician or obtaining a worrying mammography result. In fact, this study did not analyse the time between the histopathologi-

Table VI. Patients' opinion on teleconsultations

Patients' opinion	n	[%] (n = 154)*	[%] (n = 60)**
Do you think teleconsultations are a good alternative to an in-person visit? (multiple choice answer question)			
Yes, teleconsultations met my expectations	28	18.2	46.7
No, teleconsultations did not meet my expectations	31	20.1	51.7
Yes, teleconsultations saved my time	38	24.7	63.3
Yes, teleconsultations saved my money	25	16.2	41.7
Yes, owing to teleconsultations it is possible to avoid being exposed to contact with those with COVID-19	32	20.8	53.3
No, in my opinion, the physician may not have full insight into my health status during a teleconsultation	49	31.8	-
No, I don't think I can convey all my problems and concerns to the physician during the teleconsultation	0	0.0	0.0
Yes, I definitely like the teleconsultations	12	7.8	20.0
No, I definitely prefer in-person visits	43	27.9	71.7
No, teleconsultation is regarded as a good option only when I feel well	71	46.1	-
I have no opinion	4	2.6	6.7

<sup>\*</sup>All patients; \*\*Patients, who have had teleconsultation

cal result and the start of treatment. The Netherlands Cancer Registry reported that the number of women who started breast cancer treatment within three months of the cancer diagnosis decreased in the first months of the COVID-19 pandemic compared to the previous year [26]. A considerable decrease in the number of visits to oncology clinics — both for first and subsequent visits — was recorded in the U.S. at the beginning of the pandemic (March–July 2020) compared to the previous year [25]. The decline was greatest in April 2020 (by 74%). The number of hospitalised cancer patients decreased by more then 30% [25]. Similar observations on the difficulty of accessing oncology consultations were also shown by other authors [27, 28]. 42.9% of the respondents in this study stated that they waited for a visit or an imaging examination longer than usual during the COVID-19 pandemic. The appointments of 13 patients were cancelled without any information about when or where the visit would be rescheduled, and ten patients reported that the admission to the clinic, outpatient clinic and/ /or department where they were treated was discontinued. This was probably a result of organisational changes in healthcare, a reallocation of resources to fight the pandemic, and a desire to reduce the risk of SARS-CoV-2 infection in cancer patients.

A new form of healthcare — a teleconsultation — was introduced to reduce social contact to limit the spread of the pandemic. Teleconsultations were liked by only 20% of the respondents in the current study, and this was not influenced by their age, educational and place of residence. 32% of all patients thought that the physician could not provide a full view of the patient's situation during the teleconsultation, and 46% of the respondents stated that a teleconsultation was a good option only if the patient was

feeling well. Half of the patients for whom the in-person clinic visit was replaced by a teleconsultation were dissatisfied with the change. In a study by Wehrle et al. [29], 68% of cancer patients preferred personal visits. However, other authors reported a higher satisfaction rate with teleconsultations among cancer patients [30-32]. Bizot et al. [31] examined 1,300 breast cancer patients and noted that those who used teleconsultations showed concerns about the fact that their breasts were not physically examined by a physician. After the teleconsultations were discontinued, 63% of the respondents, as shown in the study by Wehrle et al. [29], were satisfied with the return to the in-person visits to the clinic, mainly because of the physical examinations being carried out. The patients who had a teleconsultation in the current study believed that this form of contact with the physician, saved time and money, and they were not exposed to contact with those suffering from COVID-19. Similarly, patients examined by Wehrle et al. [29] also mentioned the benefits of teleconsultations, such as convenience and time saving (52% of those using teleconsultations) and reducing the risk of COVID-19 infection (48%). Nearly all the patients with breast and gynecological cancers in the U.S (92%) in the Zimmerman et al. study [32] were satisfied with teleconsultations during the COVID-19 pandemic, and they mentioned time-saving as the main benefit of such visits. Less than half of the respondents in the current study declared that they felt safe during the pandemic in a hospital/clinic with regard to potential SARS-CoV-2 infection, although most patients claimed that their hospitalisation was preceded by an analysis of their health and epidemiological history. In general, the patients did not know whether, in their case — a cancer patient — there might be an increased risk of infection and/or a severe course of COVID-19. In a study by Erdoğan et al. [33] in Türkiye, 66.8% of cancer patients were scared of COVID-19 infection and the associated risk of death.

A Danish study found that 80% of cancer patients were afraid of SARS-CoV-2 infection, and 9% of them avoided visits to the clinic or to the hospital because of it [34]. According to an analysis of more than one million COVID-19 patients in the U.S., those diagnosed with cancer had a 14% higher risk of pulmonary complications and a 21% higher risk of hospital death compared to the general population [35]. Nearly half of the patients in this study declared that they would be less afraid of a severe course of the disease after being vaccinated against COVID-19. Karatas et al. [36] showed that a fear of negative consequences of a COVID-19 infection was relatively low in vaccinated cancer patients. However, 60.4% of the women in this study were afraid of vaccination against COVID-19. Vaccines against COVID-19 were not available during the first months of the pandemic. After the introduction of vaccines, there were no clear guidelines concerning the vaccination of cancer patients. Media reports have been inconsistent and may have caused fear and even panic. This particularly concerned the quick introduction of new vaccines and uncertainty regarding their side effects [37, 38]. However, most patients under the current study had themselves vaccinated against COVID-19. This study showed that significantly more women aged ≥ 50 years were vaccinated compared to those aged < 50 years. Karataş et al. [36] showed that fears related to the COVID-19 virus in cancer patients (breast cancer, lung cancer, colorectal cancer) were associated with age — individuals over 45 years were more afraid. In a study conducted in England in 2020, 72% of the general population were ready to be vaccinated against COVID-19, and there were no differences regarding the respondents' ages [37]. An analysis by Cochran Library from 2022 [38] showed that the acceptance of vaccination fluctuated across various countries. For example, it was close to 100% in Malaysia and Indonesia, nearly 60% in France and only 30% in the U.S. 53.2% of breast cancer patients in this study believed that the COVID-19 pandemic had a negative impact on cancer diagnosis and treatment in Poland. As many as 72.8% of the respondents thought that the pandemic restrictions could affect the effectiveness of their treatment.

There are some limitations to the study: the online questionnaire was made available via social media and patient organization websites, which may have contributed to patients' selection; sample size was relatively small; the questionnaire was prepared only for this study and had not been validated; the study refers only to patients' subjective impression and has not been verified based on medical records.

### Conclusions

Breast cancer patients treated during the COVID-19 pandemic experienced inconveniences and fears related to the pandemic; they had doubts about whether the pandemic would

negatively affect the effectiveness of their treatment. It is necessary to monitor the objective impact of the COVID-19 pandemic on breast cancer treatment outcomes.

### **Article information and declarations**

### Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

### **Ethics statement**

The survey was anonymous, and no participants' personal data were processed. Therefore, in accordance with the rules of the Bioethics Committee at the University of Warmia and Mazury in Olsztyn, ethic approval for the study was not required.

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None.

### Conflict of interest

None declared.

### Supplementary material

- 1. Questionnaire.
- 2. Table SI. The relationship between demographic factors and patients' opinion on factors related to COVID-19 pandemic.
- Table SII. The relationship between demographic factors and patients' opinion on treatment during COVID-19 pandemic.

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### SUPPLEMENTARY MATERIAL

### Questionnaire

Ag	e: years	□ October
		□ November
Ed	ucation	□ December
	Primary	
	Secondary	How long did it take from the time you reported the first
	High	symptoms to the physician or observing worrying results
		of screen tests and obtaining a result of histopathological
Pla	ace of residence — voivodship	examination?
	Dolnośląskie	□ <1 month
	Kujawsko-Pomorskie	□ 1−3 months
	Lubelskie	□ > 3 months
	Lubuskie	□ I do not know
	Łódzkie	
	Małopolskie	What phase of treatment are you in?
	Mazowieckie	<ul> <li>During chemotherapy or radiotherapy</li> </ul>
	Opolskie	□ During hormonotherapy
	Podkarpackie	<ul> <li>During treatment of disease progression</li> </ul>
	Podlaskie	
	Pomorskie	Are you vaccinated against COVID-19?
	Śląskie	□ Yes — 1 dose
	Świętokrzyskie	□ Yes — 2 doses
	Warmińsko-Mazurskie	□ Yes — 3 doses
	Wielkopolskie	□ No
	Zachodniopomorskie	
		Do/Did you fear vaccination against COVID-19?
Pla	ace of residence	□ Yes
	Village	□ No
	City < 20 thousand residents	
	City 20–100 thousand residents	Did you feel/would have felt less threatened with a severe
	City > 100 thousand residents	course of COVID-19 after being vaccinated?
		□ Yes
Ye	ar of breast cancer diagnosis	□ No
	2019	□ I have no opinion
	2020	
	2021	Have you or your household members been infected with
		COVID-19?
Mo	onth of breast cancer diagnosis	<ul><li>Yes, only I have been infected</li></ul>
	January	Yes, someone in the household has been infected
	February	<ul> <li>No, no one in my household has been infected</li> </ul>
	March	
	April	In your opinion, do you have a higher risk of COVID-19
	May	infection/severe course of COVID-19?
	June	□ Yes
	July	□ No
	August	□ I have no opinion

□ September

	your opinion, what is the impact of the COVID-19 pan- mic on diagnosis and treatment of cancer in Poland?		as your visit to the hospital preceded by an analysis your health condition and an epidemiological interview
	It is worse than before the pandemic	(te	emperature measurement, interview or questionnaire
	It is better than before the pandemic	on	previous exposure to sick people or symptoms of in-
	It is the same as before the pandemic		ction)? Yes
	s your treatment or diagnosis been postponed or		Seldom/occasionally
ca	nceled due to the COVID-19 pandemic?		No
	Yes		
	No		d you have possibility to use tests to detect SARS-CoV-2
		vir	rus (in case of symptoms or exposure to an infected
If t	the answer in the previous question was yes, please	pe	rson)?
ind	dicate how often		Yes
	Once		No
	Twice		I have no opinion
	Several times		
	Many Times	Ar	e/Were you afraid that isolation/quarantine may reduce
	It is difficult to establish		e effectiveness of your treatment?
			Yes
Di	d any of the following situations happen to you during		No
	ur treatment during the pandemic? (multiple choice		I have no opinion
-	swer question)		Thave no opinion
	I waited longer than usual for an appointment or exami-	Do	you think teleconsultations are a good alternative
	nation		an in-person visit? (multiple choice answer question)
	I had problems with contact with physician/outpatient		Yes, teleconsultations met my expectations
	clinic/hospital		No, teleconsultations did not meet my expectations
	Visit to the outpatient clinic was replaced with a telecon-		Yes, teleconsultations saved my time
	sultation and I was satisfied with the change		Yes, teleconsultations saved my money
	Visit to the outpatient clinic was replaced with a telecon-		Yes, owing to teleconsultations it is possible to avoid being
	sultation and I was not satisfied with the change		exposed to contact with those ill with COVID-19
	My visit/treatment was canceled without information		No, in my opinion, the physician may not have full insight
	where and when the visit/treatment would be completed		into my health status during a teleconsultation
	I had problems with doing imaging examinations		No, I don't think I can convey all my problems and concerns
	I had problems with receiving results of imaging exami-		to the physician during the teleconsultation
	nations		Yes, I definitely like the teleconsultations
	Admissions at the outpatient clinic were stopped and/or		No, I definitely prefer in-person visits
	department where I was treated was closed		No, teleconsultation is regarded as a good option only
	The place of treatment has been changed		when I feel well
	I was waiting for an outpatient clinic/hospital admission/		I have no opinion
	/examination with no possibility to keep social distance		
			ow do you cope as a patient during a pandemic? (mul-
Di	d you feel safe in a hospital/clinic with respect to	tip	ole choice answer question)
th	e threat of being infected with SARS-CoV-2?		I receive a lot of support from family and/or friends
	Yes		I find it very helpful to talk to my husband/partner
	No		I have no one to talk to about my problems
	I have no opinion		In my opinion, medical care provided a sense of security
			I do not have too many problems
In	your opinion, are treatment and diagnostic centers		I can not deal with what's going on in my life
	ell prepared to treat and diagnose patients during		I need/needed more frequent visits with the doctor
	e COVID-19 pandemic?		I need/needed to meet with a psychologist
	Yes		I need/needed to meet with a priest
	No	_	

□ I have no opinion

What are your feelings about anticancer treatment in

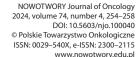
Poland during the pandemic?

 Table SI. The relationship between demographic factors and patients' opinion on factors related to COVID-19 pandemic

Group	Do/	Oid you fe	fear vaccina COVID-1 <i>9</i> ?	Do/Did you fear vaccination against COVID-19?	ainst		In your o	pinion, o	In your opinion, do you have a higher risk of COVID-19 infection/severe course of COVID-19?	re a high ourse of	er risk of COVID-19	ć(	Didy	ou feel/wo	ould have	Did you feel/would have felt less threatened with a severe course of COVID-19 after being vaccinated?	threaten oeing va	ed with a ccinated?	severe
	N N		Yes	Ş	p value	N N	0	Yes	S	I have no opinion	e no ion	p value	No	0	Yes	Ş	I have no opinion	e no iion	p value
	c	[%]	۵	[%]		<u> </u>	[%]	۵	[%]	_	[%]		<u> </u>	[%]	_	[%]	_	[%]	
Age																			
< 50 years	36	39.1	26	6.09	0.88	33	35.9	34	37.0	25	27.1	0.20	30	32.6	37	40.2	25	27.2	0.07
≥ 50 years	25	40.3	37	59.7		16	25.8	21	33.9	25	40.3		12	19.4	36	58.0	41	22.6	
Education																			
Secondary	25	36.8	43	63.2	0.48	20	29.4	21	30.9	27	39.7	0.25	19	27.9	34	20.0	15	22.1	0.67
High	36	42.4	49	57.6		29	34.1	33	38.8	23	27.1		23	27.1	38	44.7	24	28.2	
Place of residence																			
Village	41	34.1	27	62.9	0.005	6	22.0	4	34.1	18	43.9	0.04	41	34.1	13	31.8	41	34.1	0.35
City < 20 thousand residents	4	17.4	19	82.6		5	21.7	∞	34.8	10	43.5		5	21.7	11	47.8	7	30.5	
City 20–100 thousand residents	13	34.2	25	65.8		14	36.8	10	26.4	14	36.8		10	26.3	20	52.6	∞	21.1	
City > 100 thousand residents	30	57.7	22	42.3		21	40.4	23	44.2	<sub>∞</sub>	15.4		13	25.0	29	55.8	10	19.2	

 Table SII.
 The relationship between demographic factors and patients' opinion on treatment during COVID-19 pandemic

Group	In your opin	iion, what is th	e impact of th of ca	of the COVID-19 par of cancer in Poland?	In your opinion, what is the impact of the COVID-19 pandemic on diagnosis and treatment of cancer in Poland?	agnosis and tı	eatment	Are/V	Vere you afra	id that isola 0	lation/quarantine n of your treatment?	ntine may r nent?	Are/Were you afraid that isolation/quarantine may reduce the effectiveness of your treatment?	tiveness
	It is worse than before the pandemic	han before Idemic	It is better than before the pandemic	ter than before pandemic	It is the same as before the pandemic	e as before demic	p value		Yes		No	Ihave	I have no opinion	p value
	د	[%]	د	[%]	۵	[%]		u	[%]	ے	[%]	ے	[%]	
Age														
< 50 years	20	54.4	4	4.3	38	41.3	0.86	88	73.9	15	16.3	6	8.6	0.89
≥ 50 years	32	51.6	2	3.2	28	45.2		4	71.0	12	19.3	9	2.6	
Education														
Secondary	34	50.0	-	1.5	33	48.5	0.23	47	69.1	14	20.6	7	10.3	99'0
High	47	55.3	гV	5.9	33	38.8		2	75.3	13	15.3	∞	9.4	
Place of residence														
Village	21	51.2	2	4.9	18	43.9	0.85	34	82.9	4	8.6	es es	7.3	0.004
City < 20 thousand residents	12	52.2	0	0.0	11	47.8		21	91.3	2	8.7	0	0.0	
City 20–100 thousand residents	23	60.5	-	2.6	14	36.9		27	71.1	4	10.5	7	18.4	
City > 100 thousand residents	26	50.0	23	5.8	23	44.2		30	57.7	17	32.7	5	9.6	





### Original article

Lung cancer

## Pattern of lung cancer recurrence after lung resection with bilateral lymph node dissection

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**Introduction.** Several studies have shown the survival benefit of bilateral lymph node dissection as part of curative-intent surgery for lung cancer. The pilot BML-1 study was the first randomized trial comparing bilateral with the standard (unilateral) systematic lymph node dissection.

**Material and methods.** Patients with non-small cell lung cancer stage I–IIIA, who underwent anatomical lung resection were randomised 1:1 to receive a bilateral or standard, unilateral lymphadenectomy. Data regarding the type of recurrence and time to recurrence were analysed.

**Results.** The rate of locoregional recurrence in the bilateral lymphadenectomy and the standard lymphadenectomy were 2.7% and 5.3% and those of distant relapse were 24.3% and 23.7% respectively (p = 0.99). The follow-up time was 87 months. The mean time from surgery to recurrence was 35.0 months and 22.8 months, respectively (p = 0.83). **Conclusions.** There is no firm evidence that bilateral mediastinal lymphadenectomy (BML) is associated with a recurrence pattern that is different than that following the systematic lymph node dissection (SLND). We found a trend towards lower incidence of local recurrence and longer time to recurrence in the BML group, but the differences were statistically not significant. A large randomised study is warranted to further analyse this matter.

Keywords: lung cancer, mediastinum, lymphadenectomy, recurrence

### Introduction

The rationale for bilateral lymph node dissection in patients with non-small cell lung cancer is the potential advantage of removal of contralateral mediastinal lymphatics harbouring metastatic deposits. Although it is not considered a standard, several studies have shown survival benefit [1–5]. The pilot BML-1 study was the first randomized trial comparing bilateral mediastinal lymphadenectomy (BML) with the standard systematic lymph

node dissection (SLND), and its results regarding the effect of BML on survival were published elsewhere [1]. However, the effect of BML on the pattern of recurrence was not studied.

### **Material and methods**

### **Clinical questions**

Is the BML associated with a different pattern of cancer recurrence as compared with SLND?

### How to cite:

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### Study design

Follow-up of patients participating in a randomized, clinical trial. Data regarding cancer recurrence were derived from the BML-1 study [1].

### Setting

Department of Thoracic Surgery, John Paul II Hospital, Cracow, Poland

### **Patients**

Following inclusion criteria were used:

- patients age 18–90, confirmed or suspected non-smallcell lung cancer (NSCLC) stage I–IIIA; accepted stage IIIA included only single-station, non-bulky N2 disease,
- preoperative staging included chest radiography, computed tomography, positron-emission tomography-computed tomography, abdominal ultrasonography, bronchoscopy, endobronchial ultrasonography, and endoscopic ultrasonography,
- general fitness enabling appropriate lung resection, assessed according to the European Respiratory Society and the European Society of Thoracic Surgery Guidelines [6].
   The exclusion criteria were as follows:
- history of other malignancy, with the exception of non--melanoma skin cancer,
- induction chemo- or chemoradiotherapy,
- pathological confirmation of tumour other than NSCLC,
- · ground-glass opacity lesions,
- lack of informed consent [1].

### Intervention

Randomization was performed by the study coordinator (JK) using a computer-based random-digit generator (LUCASC, version 1.0, Morawski, Poland), with a 1:1 allocation ratio. The technique of lymph node dissection was described in detail elsewhere [1].

Data regarding cancer recurrence were obtained from the hospital database. In patients lost to follow-up, survival data form the national vital records (PESEL database) was used.

### Endpoints

The primary endpoint was the recurrence type categorized as: no recurrence, locoregional and distant. The secondary endpoint was the time to recurrence.

### Statistical analysis

Analyses were performed using Stata 13.1, StataCorp LP, TX, USA. At first the groups were compared using baseline characteristics represented by a proportion (percentile) for categorical and a mean with standard deviation (SD) or a median with inter-quartile range (IQR) for continuous variables. To reveal significant differences between groups, a chi-squared test (or the Fisher exact test if the chi-squared test assumptions were not met) were run for categorical variables. The Shapiro-Wilk test was used to verify whether the assumption of normal

distribution was met. Next the t-test equal or unequal variance (depending on whether it was or was not confirmed by the F-test) was used if both groups met the assumption of normal distribution, otherwise the Mann-Whitney test was run. To answer a question on whether the type of recurrence was associated with the type of treatment, the multinomial logistic regression was used. Finally, as the sample size was small, to increase the precision of the assessment — especially for the impact of treatment on the risk of local recurrence — binomial logistic regression with bootstrap analysis was implemented. It was decided to use bootstrap as it leads to an increase in the precision of estimates, which was relatively low due to the sample size. The bootstrap model presents finally the point estimate [odds ratio (OR)] with normal-based 95% confidence interval (CI) for the OR, and the p value. There were some models with a different number of bootstrap repetitions run. It started with 10.000 and ended with 1.000.000 repetitions to observe the stability of estimates provided. Results with the p-value less than 0.05 were considered statistically significant.

### Results

The BML-1 study enrolled 102 patients. 13 patients met the exclusion criteria, so survival analysis data of 89 patients were available: 40 in the BML group and 49 in the SLND group [1]. Data regarding the type of recurrence in 14 patients were not available, so the recurrence pattern was analysed in 37 patients in the BML group and 38 in the SLND group.

Both groups were comparable regarding age, sex, location of the tumour, histology, clinical stage, type and side of resection and number of lymph nodes removed (Tab. I).

Survival analysis in the BML-1 study was reported elsewhere [1].

The 5-year recurrence-free survival was 64.9% in the BML group and 60.5% in the SLND group. The rate of locoregional recurrence in the BML and the SLND group were 2.7% and 5.3% and those of distant relapse were 24.3% and 23.7% respectively (Tab. II). Multinomial logistic regression did not show significant difference between the BML and the SLND group regarding the recurrence pattern (p = 0.99) (Tab. III). As the OR for observing local/regional recurrence in the BML was considerably lower, the binomial logistic regression with bootstrap analysis was additionally implemented to increase the precision of the estimate, however, no significant effect has been observed (Tab. IV). The follow-up time was 87 months. The mean time from surgery to recurrence was 35.0 months in the BML group vs. 22.8 months in the SLND group (p = 0.83).

### **Discussion**

As the BML study was the first randomised trial to compare BML with the standard systematic lymph node dissection, there is no literature data that could be used for comparison with our results. The published evidence pertains to recurrence in patients who underwent standard treatment, i.e., SLND.

**Table I.** Baseline characteristics of the study groups

Patients' characteristics	BML (n = 37)	SLND (n = 38)	p value
Age Mean (SD) Median (IQR)	61.5 (6.9) 61.0 (6.0)	62.1 (6.0) 62.5 (6.0)	0.678
Sex (M) — n (%)	26 (70.3)	27 (71.0)	0.941
Tumour location — n (%)			
RUL	10 (27.0)	8 (21.1)	
RML	0 (0.0)	1 (2.6)	
RLL	10 (27.0)	9 (23.7)	
CUL	5 (13.5)	9 (23.7)	
LUC	2 (5.4)	5 (13.2)	
LLL	8 (21.6)	5 (13.2)	
LC	2 (5.4)	1 (2.6)	
Histology — n (%)			
SCC	19 (51.4)	25 (65.8)	
ADC	16 (43.2)	9 (23.7)	
LCC	0 (0.0)	1 (2.6)	
ASC	2 (5.4)	2 (5.3)	
OTH	0 (0.0)	1 (2.6)	
cTNM — n (%)			
			0.925
T1aN0M0	4 (10.8)	3 (7.9)	
T1aN1M0	1 (2.7)	0 (0.0)	
T1bN0M0	3 (8.1)	4 (10.5)	
T1bN1M0	2 (5.4)	0 (0.0)	
T1bN2M0	1 (2.7)	2 (5.3)	
T2aN0M0	12 (32.4)	10 (26.3)	
T2aN1M0	1 (2.7)	1 (2.6)	
T2aN2M0	2 (5.4)	1 (2.6)	
T2bN0M0	4 (10.8)	8 (21.1)	
T2bN1M0	2 (5.4)	2 (5.3)	
T2bN2M0	2 (5.4)	2 (5.3)	
T2bN3M0	1 (2.7)	0 (0.0)	
T3N0M0	1 (2.7)	2 (5.3)	
T3N2M0	1 (2.7)	3 (7.9)	

Yamaouchi et al. [7] reported recurrence in 501 patients out of 1,374 operated on for lung cancer. Among them, 25% were local, 62.3% were distant and 11.2% of patients developed both local and distant recurrence at the same time. Similarly, in a large study published recently, the most common type of relapse was distant (56%), however this cohort included both small-cell and non-small cell lung cancer [8]. Jeong et al. [9] analysed recurrence patterns in 949 patients with early-stage lung cancer. As expected, the relapse rate was low (20.4%), but the distant recurrence rate was almost twice as high as the locoregional one (13.1% vs. 7.3%). These data are in line with our results, showing distant metastases to be the most

Patients' characteristics	BML	SLND	p value
	(n = 37)	(n = 38)	
Type of resection — n (%)			
			0.935
LBL	3 (8.1)	2 (5.3)	
UBL	1 (2.7)	1 (2.6)	
LLL	6 (16.2)	4 (10.5)	
RLL	6 (16.2)	5 (13.2)	
LUL	6 (16.2)	11 (28.9)	
RUL	9 (24.3)	7 (18.4)	
RML	0 (0.0)	1 (2.6)	
LPN	5 (13.5)	6 (15.8)	
RPN	1 (2.7)	1 (2.6)	
Extent of resection — n (%	b)		
Bilobectomy	4 (10.8)	3 (7.9)	
Lobectomy	27 (73.0)	28 (73.7)	
Pneumonectomy	6 (16.2)	7 (18.4)	
Side — n (%)			
Left	17 (45.9)	21 (55.3)	
Right	20 (54.1)	17 (44.7)	
Upper/lower lobes — n (%	o)		
			0.440
Upper*	16 (51.6)	20 (64.5)	
Lower	15 (48.4)	11 (35.5)	
N2 sum Mean (SD) Median (IQR)	24.9 (9.2) 24.0 (12.0)	14.7 (8.7) 14.0 (9.0)	< 0.001
N1 sum Mean (SD) Median (IQR)	10.1 (8.0) 7.0 (7.0)	8.7 (4.7) 8.0 (7.0)	0.865

\*Right middle lobe combined with right upper lobe; ADC — adenocarcinoma; ASC — adenosquamous carcinoma; BML — bilateral mediastinal lymphadenectomy; CUL — culmen/culmenectomy; IQR — inter-quartile range; LBL — lower bilobectomy; LCC — large cell carcinoma; LC — left central; LIN: lingula/lingulectomy; LLL — left lower lobe/lobectomy; LPN — left pneumonectomy; LUC — left upper central; LUL — left upper lobe/lobectomy; M — male; OTH — other; RLL — right lower lobe/lobectomy; RML — right middle lobe/lobectomy; RPN — right pneumonectomy; RUL — right upper lobe/lobectomy; SCC — squamous cell carcinoma; SD — standard deviation; SLND — systematic lymph node dissection; UBL — upper bilobectomy

Table II. Pattern of recurrence

Pattern of recurrence n (%)	BML	SLND	
No recurrence	24 (64.9)	23 (60.5)	0.999
Local/regional	1 (2.7)	2 (5.3)	
Distant	9 (24.3)	9 (23.7)	

 ${\rm BML}$  — bilateral mediastinal lymphadenectomy;  ${\rm SLND}$  — systematic lymph node dissection

common type of relapse. In our cohort, the rate of distant relapse was similar in the BML and the SLND group (24.3% and 23.7% respectively). On the other hand, the rate of locoregional

**Table III.** The risk estimate (odds ratio) of different recurrence types bilateral mediastinal lymphadenectomy (BML) vs. systematic lymph node dissection (SLND) groups (multinomial univariable logistic regression)

Pattern of recurrence	Odds ratio	95%	CI	p value
		LL	UP	
No recurrence	1 (ref.)			
Local/regional	0.48	0.04	5.65	0.559
Distant	0.96	0.32	2.84	0.939

CI — confidence interval; LL — lower limit for 95% CI; UP — upper limit for 95% CI

**Table IV.** Odds ratios (ORs) for observing local/regional recurrence in the bilateral mediastinal lymphadenectomy (BML) as compared to the systematic lymph node dissection (SLND) group in the bootstrap analyses (binomial univariable logistic regression)

Odds ratio	Normal based	l 95% CI	p value	No of bootstrap repetitions
	LL	UP		
0.48	0.11	2.12	0.333	10 000
0.48	0.11	2.13	0.334	100 000
0.48	0.11	2.13	0.334	300 000
0.48	0.11	2.13	0.333	1 000 000

CI — confidence interval; LL — lower limit for 95% CI; UP — upper limit for 95% CI

recurrence was two times lower in the BML group (2.7% vs. 5.3%), however the difference was statistically not significant. The lack of significance is probably due to the small number of patients available for analysis. The BML-1 trial was a pilot study, with one of its main weaknesses being the limited number of patients. It is also probably the reason for the lack of significance of difference in the time to relapse (35.0 months in the BML group vs. 22.8 months in the SLND group).

### **Conclusions**

There is no firm evidence that BML is associated with a recurrence pattern different than the SLND. We found a trend towards lower incidence of local recurrence and longer time to recurrence in the BML group, but the differences were statistically not significant. A large randomised study is warranted to further analyse this matter.

### **Article information and declarations**

### Data availability statement

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

### **Ethics statement**

The protocol of the BML-1 study has been approved by the Bioethical Committee of the Jagiellonian University (K/ZDS/002337.

### **Authors contributions**

Jakub Szadurski — project development, data collection, data analysis, manuscript editing.

Łukasz Trybalski — project development, data collection, data analysis, manuscript writing.

Jarosław Kużdżał — project development, data collection, data analysis, manuscript writing.

Aleksander Galas — data analysis, manuscript writing.

Janusz Warmus — data collection, manuscript writing.

Zbigniew Grochowski — data collection, manuscript writing.

Mirosław Janczura — data collection, manuscript writing. Katarzyna Żanowska — data collection, manuscript writing. Piotr Kocoń — project development, data analysis, manuscript writing.

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None.

### **Conflicts of interest**

None declared.

### Supplementary material

None.

### Jarosław Kużdżał

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### Original article

### Quality of life

# Quality of life components in women with cervical cancer post-diagnosis

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**Introduction.** A cervical cancer (CC) diagnosis can significantly impact an individual's quality of life (QoL) across many domains. This study aimed to identify QoL components\_in women diagnosed with CC post-diagnosis, and compare them to healthy controls.

**Material and methods.** QoL was assessed using the SF-36 survey and six-item Female Sexual Function Index in 60 women diagnosed with CC pre-treatment and 60 healthy women.

**Results.** The women with CC scored significantly lower on physical functioning (M = 53.56 vs. 69.69), psychological functioning (M = 35.33 vs. 85.67), and sexual functioning (M = 32.50 vs. 88.50) compared to controls (all p < 0.001).

**Conclusions.** A CC diagnosis was associated with markedly reduced QoL in physical, psychological, and sexual domains, even pre-treatment. Early screening and support for psychological and sexual wellbeing should be integral in CC patient care.

**Keywords:** cervical cancer, quality of life, sexual functioning

### Introduction

Cervical cancer (CC) is a frequently occurring cancer worldwide. In Poland, around 1.17 million people currently live with cancer. Due to medical advancements and improved treatment availability, cancer is becoming a chronic condition with decreasing mortality rates [1, 2]. However, CC diagnosis and treatment can still disrupt quality of life (QoL). Thus, research on the QoL of oncology patients is increasing.

The concept of QoL has evolved over the years. The definitions have changed to include various factors that contribute to a high QoL. The World Health Organization (WHO) defines QoL as "an individual's perception of their position in life in

the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [3]. However, the disease is understood as a disturbing event that can disrupt a person's functioning to varying degrees. It can significantly impact the fulfillment of previous social roles [4, 5], limit social interactions [6], and lead to a sense of insecurity, depression, or anxiety [5, 7]. The WHO recognizes sexual functioning as another vital QoL component [8]. However, sexuality is often overlooked as less important than other aspects of functioning. Importantly, sexual functioning includes self-image, relationships, and intimacy [9, 10], which change during illness and may become more important than

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previously. Moreover, as CC increasingly affects younger individuals [1], addressing sexuality is critical also because of fertility issues

Hence, the research on QoL involving psychosexual functioning has highlighted the need for a holistic, systematic approach to patient care. Gynecological cancers and treatments directly impact physical, emotional, and sexual wellbeing. Also, genital cancer localization may influence sexuality and body image perceptions [11]. Moreover, available studies have focused on QoL during/after treatment, which disrupts functioning [12]. However, the diagnosis itself could lower actual QoL [13], making assessment at different stages valuable.

This study aimed to identify QoL components in women diagnosed with CC post-diagnosis and compare them to healthy controls, as part of a broader effort exploring CC patients' psychosexual correlates of QoL. Based on the literature, QoL was conceptualized across three areas: physical, psychological, and sexual functioning. This study focused on CC patients due to CC's rising incidence, even among younger women [1], in the post-diagnosis, pre-treatment period.

### **Material and methods**

This study was conducted at the Radiotherapy and Clinical Brachytherapy departments, Oncology Center in Bydgoszcz, Poland. A bioethics committee approval and informed consent were obtained. The data were collected January 2022–October 2022.

### **Participants**

An experimental group was comprised of 60 women diagnosed with stage IIb–IIIa CC, pre-radiotherapy/brachytherapy. A control group included 60 healthy women, purposely selected to match the experimental group in gender, age, and education. The participants were recruited via snowball sampling. They were unpaid volunteers. The inclusion criteria were:

- participants aged 40–65, representing middle adulthood;
- participants diagnosed with CC in stages II to III according to the International Federation of Gynecology and Obstetrics (FIGO):
- participants undergoing radiotherapy or brachytherapy;
- participants without any medical and psychological conditions potentially affecting their sexual functioning.

### Study method

Quality of life was assessed using the 36-Item Short Form Survey (SF-36) that is a part of the Medical Outcomes Study (MOS). The SF-36 overall assesses two components (physical and mental functioning), and includes subscales addressing eight health concepts (physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional health problems, mental health) [14]. All necessary agreements

were obtained from the questionnaire's authors. The reliability in the study was  $\alpha = 0.93$ .

As the SF-36 does not include the sexual functioning component, the six-item Female Sexual Function Index (FSFI) was used. The survey measures five domains, including sexual desire arousal, lubrication, orgasm, satisfaction, and pain [15]. The reliability in the study was  $\alpha=0.87$ . Per the broader scope of the study, a more extensive set of questionnaires was employed, hence the authors opted to use the short version of the FSFI to prevent patient exhaustion.

### Statistical analysis

All analyses were performed using IBM's SPSS (Version 26). Descriptive statistics were employed to summarize the demographic and clinical characteristics of the patients. Reliability was assessed using Cronbach's  $\alpha$ . Bivariate analyses, including the Student's *t*-test and ANOVA, all were utilized depending on the distribution of the scales which was assessed using the Shapiro-Wilk test.

### Results

The sample comprised 120 women, with 60 women diagnosed with CC and 60 healthy controls. The average age in the CC group was 55.75 ( $\pm$  6.27) years, while in the control group it was 52.13 ( $\pm$  6.46) years. Approximately 63.33% of the women in both groups resided in urban areas. Most of the women reported being in a formal relationship (73% of the CC group; 70% of the controls). Educational backgrounds were equally distributed between the groups. In the CC group, 36.67% (n = 22) had vocational education, 30.00% (n = 18) had secondary education, and 33.33% (n = 20) had higher education, 33.33% (n = 20) had secondary education, and 41.67% (n = 25) had higher education.

Sixty percentage (n = 36) of the CC patients and 61.67% (n = 37) of the healthy controls reported coexisting medical conditions, most commonly hypertension, thyroid dysfunction, and diabetes. Among the CC group, the average time between diagnosis and examination was 4.06 ( $\pm$  1.91) weeks, and between hospital admission and examination was 2.13 ( $\pm$  1.23) days. In terms of treatment, 48.33% (n = 29) were undergoing radiation therapy and 51.67% (n = 31) were undergoing brachytherapy; 51.67% (n = 31) had stage II CC and 48.33% (n = 29) had stage III CC.

The CC patients scored significantly lower on all the QoL components. Their average physical functioning score was 53.56 ( $\pm$  2.92) vs. 69.69 ( $\pm$  10.45) in controls (p < 0.001). Their average psychological functioning score was 35.33 ( $\pm$  4.95) vs. 85.67 ( $\pm$  9.82) in the controls (p < 0.001). Their average sexual functioning score was 32.50 ( $\pm$  3.39) vs. 88.50 ( $\pm$  3.86) in the controls (p < 0.001).

Table I presents clinical data related to CC. The average time between diagnosis and examination was 4.06 weeks ( $\pm$  1.91). It

Table I. Clinical data related to cervical cancer

	М	SD
Time between diagnosis and examination [weeks]	4.06	± 1.91
Time between hospital admission and examination [days]	2.13	± 1.23
Treatment applied	n	[%]
Radiation therapy	29	48.33
Brachytherapy	31	51.67
Disease stage	n	[%]
T.	0	0.00
II	31	51.67
III	29	48.33
IV	0	0.00

SD — standard deviation

**Table II.** Quality of life components' descriptive statistics

	ССр	atients	Healthy i	individuals
Quality of life	M (± )	Range (min-max)	M (±)	Range (min–max)
Physical functioning	53.26 (± 2.92)	(45.14–58.40)	69.69 (± 10.45)	(40.50-91.00)
Psychological functioning	50.10 (± 4.95)	(37.52–57.16)	69.34 (± 9.82)	(46.50–89.50)
Sexual functioning	9.62 (± 3.39)	(5.00–16.00)	18.65 (± 3.86)	(12.00-28.00)

CC — cervical cancer

is important to note that the assessment was conducted prior to the initiation of appropriate treatments to minimize the potential side effects' impact on QoL. The average time between hospital admission and examination was 2.13 days ( $\pm$  1.23); 48.33% (n = 29) of the patients underwent radiation therapy, and 51.67% (n = 31) underwent brachytherapy; 51.67% (n = 31) were diagnosed with stage II CC and 48.33% (n = 29) were diagnosed with stage III CC according to the FIGO criteria. Table II refers to the QoL components' descriptive statistics. The lowest levels of QoL were reported by the group with CC. The QoL components are compared in Table III.

### **Discussion**

This study aimed to gather information about the QoL of women diagnosed with CC after their diagnosis and compare it with that of healthy women. In the study, both the psychological and physical aspects of QoL were found to be significantly lower in CC patients than in healthy controls, which is consistent with previous reports. In other studies using the SF-36, the average score for physical functioning was 50.99, and for psychological functioning it was 53.17 [16–18]. Summarized norms for the SF-36 show that the average score for women aged 35–64 is 80.33 for physical functioning and 78.55 for psychological functioning [19]. This suggests a significantly

**Table III.** Comparison of quality of life components

	CC patients	Healthy individuals
Physical functioning	Mean: 53.56	Mean: 69.69
	t value: -10.81	
	df: 118	
	p value: < 0.001	
Psychological functioning	Mean rank: 35.33	Mean rank: 85.67
	U: 290.00	
	Z: -7.926	
	p value: < 0.001	
Sexual functioning	Mean rank: 32.50	Mean rank: 88.50
	U: 120.00	
	Z: -8.832	
	p value: < 0.001	

CC — cervical cancer; df — degrees of freedom; U — U statistic; Z — Z-scored

lower QoL in the CC group, not only in the present study but also when compared to the general population. Furthermore, the average score for sexual functioning was 9.62, significantly

lower than the cutoff point for possible sexual dysfunction (a score of 19 or less) [15].

This study's findings can be interpreted considering the distinction between objective and subjective QoL [20]. In its early stages, CC is often asymptomatic [21]; thus, objective QoL indicators related to daily functioning may not yet deteriorate. However, a patient's subjective appraisal of life and wellbeing seems relevant. A cancer diagnosis and the associated stress can disrupt psycho-physical functioning, even pre-treatment [13]. Prolonged tension may lead to somatic issues like fatigue, sleep disruption, decreased energy, and limited daily activity [22]. Additionally, having to organize life around cancer treatment (e.g., involving work absences and delegation of duties) negatively impacts social and emotional functioning. Also, fear about one's health and life, exacerbated by cognitive distortions, may intensify depression and anxiety symptoms. According to previous research, oncology patients often exhibit cognitive errors such as discounting positives, fortune telling, catastrophizing, or overgeneralizing. Expecting both the situation and the future to be worse than reality may lead to a significant decline in the emotional component of QoL before treatment even begins. Additionally, it is essential to note that the patients studied were diagnosed with advanced cervical cancer, which could also contribute to increased stress and fear, potentially affecting their subjective quality of life [23].

The observed decrease in sexual functioning at the post--diagnostic stage is also concerning. When analyzing the results obtained, it is crucial to consider specific questions from the tool used. The tool assesses sensations and sexual responses over the 4 weeks previously, so for the patients it was a period shortly after their diagnosis. Moreover, an analysis of individual questions revealed that none of the patients had engaged in vaginal intercourse. That said, most of them indicated that they had engaged in various sexual activities during this time, such as kissing or caressing. The results obtained are consistent with previous studies in which sexual functioning was significantly lower in CC patients. However, these studies focused on periods during or after treatment, when significant changes may be caused by the treatment, such as vaginal dryness, anatomical alternations in vaginal structure, or dyspareunia [24, 25]. Changes in sexual functioning can result from subjective changes in the perception and attitude towards one's own sexuality [26]. Sexual activity is crucial for fulfilling physical needs, but it also aims to create and maintain intimacy between partners or to confirm one's attractiveness [27, 28]. A stressful event, such as a cancer diagnosis, can lead to a decrease in sexual needs and a perception that sexual activity is less important. However, engaging in sexual activity — understood as a form of closeness and intimacy with a partner — could be helpful in maintaining wellbeing and reducing stress. Nho [29] and Jang [30] created two separate training programs aimed at educating gynecological cancer patients and their partners about sexual health. They found that couples who participated in these programs showed significantly higher sexual functioning compared to couples who did not participate. These findings highlight the importance of addressing the sexual well-being of cancer patients as a part of their overall care and support.

The present findings highlight an urgent need to provide women with CC comprehensive, interdisciplinary care encompassing psychological and sexual aspects that starts immediately after diagnosis. Further research into psychose-xual functioning changes at different cancer stages is warranted to optimize therapeutic strategies. Ultimately, the results demonstrate that a CC diagnosis itself exerts a profoundly detrimental impact on women's QoL across physical, mental, and sexual domains. This underscores the necessity of implementing comprehensive psychological and sexual support as the standard of care for female cancer patients from the earliest possible stage.

The study has several limitations. The study's relatively small sample size and the selection of the sample (snowball sampling) limit the generalizability of the results. The study's cross-sectional design limited the ability to observe changes during treatment. A longitudinal strategy would yield more information about general quality of life over the period. Furthermore, the study focused on specific aspects of sexual functioning related to the sexual response cycle. Assessing sexual distress could have added a new dimension to the study's findings. Future research might consider including patients with various stages of the disease, including those undergoing surgical and palliative treatments. It would also be valuable to investigate the experiences of cancer patients with different types of cancer, as well as younger individuals, to understand how their sexuality evolves.

### Clinical implications

Despite several limitations, assessing pre-treatment QoL was a strength of this study, demonstrating the need for early psychological interventions as standard care to improve patient experiences. Our results also highlight the importance of incorporating sexual functioning within the broader QoL framework and addressing patient sexual wellbeing proactively from diagnosis, ensuring comprehensive, holistic care from the outset, and providing insights into the multifaceted issues patients encounter throughout their cancer journey.

Additionally, by addressing psychological and sexual well-being right from diagnosis, healthcare professionals can better understand and handle the myriad concerns that arise from patients during treatment and beyond. A proactive approach would help patients receive well-rounded care from the start, thereby enhancing the overall patient experience.

### **Conclusions**

Overall, this study found significantly poorer physical, psychological, and sexual QoL ratings of women diagnosed with CC

starting immediately after receiving the diagnosis even before the initiation of treatment. Our findings emphasize the need for early intervention and holistic care that addresses patients' psychological and sexual wellbeing as an integral component of care to improve cancer patients' overall QoL.

### **Article information and declarations**

### Data availability statement

Data will be made available by the authors upon reasonable request.

### **Ethics statement**

Bioethics Committee approval and informed consent were obtained.

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None.

### **Conflict of interest**

None declared.

### Supplementary material

None.

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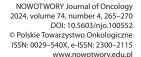
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### Original article

### Cancer epidemiology

### The relationship between bone sarcoma incidence/ /mortality rate in Poland and Internet searches — Google Trends Analysis

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**Introduction.** Internet searches reflect public awareness, which may be influenced by cancer epidemiology. The aim was to characterize the relationship between the occurrence of bone cancer and the number of Internet searches in Poland. A secondary goal was to assess the relationship between awareness campaigns and online searches. The last goal was to assess the incidence and mortality rate of bone sarcoma in Poland over 10 years.

**Material and methods.** The epidemiology data of bone cancer in 2010-2020 were analyzed in relation to search volume index (SVI) in Google Trends for terms — 'osteosarcoma', 'chondrosarcoma', 'Ewing sarcoma', 'bone cancer', 'bone tumor'. **Results.** On average, 317.6 ( $\pm$  29.8) new cases of bone cancer were diagnosed annually, and 272.2 ( $\pm$  43.3) patients died annually. Correlations between incidence rates and SVI for terms: osteosarcoma (r = 0.17; p = 0.035), chondrosarcoma (r = 0.36; p < 0.001) and Ewing sarcoma (r = 0.21; p = 0.008), and between mortality rate and SVI for terms: chondrosarcoma (r = 0.42; p < 0.001) and bone cancer (r = 0.20; p = 0.012) were noted. There was no increase in interest in the topic of bone cancer in July (Sarcoma Awareness Month) in Poland and worldwide.

**Conclusions.** The incident and mortality rate of bone sarcomas is correlated with the number of online searches for individual phrases. Awareness campaigns do not significantly increase interest in the topic of bone sarcomas on the Internet. Epidemiological data on bone cancer in Poland are comparable to worldwide data.

Keywords: bone sarcoma, google trend, epidemiology, bone cancer, incidence, mortality

### Introduction

Primary malignant bone cancers (bone sarcomas) are a group of rare tumors of mesenchymal origin, the incidence of which is estimated at 0.5–1% of all adult oncological patients and 5–7% in children [1]. The most common types of primary bone cancer are osteosarcoma, chondrosarcoma and Ewing sarcoma [2]. The first one affects about 1–2 people per million per year, while the second one occurs with a frequency of about 0.5 people per million per year and the third type mainly affects

patients under 18 years of age and is estimated to affect 2.93 children per million worldwide [3]. The risk of developing primary malignant bone tumors has a bimodal distribution, with the first peak in the  $2^{\text{nd}}$ - $3^{\text{rd}}$  decade of life (osteosarcoma) and the second peak in the  $6^{\text{th}}$ - $7^{\text{th}}$  decade of life (chondrosarcoma) [1]. The Internet has become a significant source of information in the field of health and medicine for both health care professionals and patients. According to available data, currently up to half of cancer patients search for information

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about the disease on the Internet [4,5]. In addition, information from the Internet has been considered a surrogate tool for estimating epidemiology and collecting data on disease patterns and population behavior [5]. Google Trends, a recent technological advance in data acquisition, was used to examine many topics related to oncology, including the seasonality of interest in cancer or the effectiveness of awareness campaigns [6,7]. Moreover, a relationship between media reports, such as the death or cancer of a famous people, and subsequent public interest on the Internet, were reported [8–10].

Oncological disease registries are a valuable source of information. However, rigorous data from nationwide registries are often unavailable, especially for rare cancers such as bone sarcoma. Moreover, as in most registries, epidemiological data in the National Cancer Registry in Poland are delayed on average by 2 to 3 years until the incidence data are made public. Therefore, Internet search data may be a new and promising tool for estimating the number of new cases. We hypothesized that the number of Internet searches would be positively correlated with the registry-recorded incidence and mortality of bone sarcoma. To test this hypothesis, we conducted a study comparing the number of Internet searches for bone cancer, normalized to the total number of searches, with published bone cancer incidence and mortality rates in Poland. Additionally, we checked whether Sarcoma and Bone Cancer Awareness Month, which takes place in July, increases the number of online searches.

### **Material and methods**

We used Google search volume data collected via Google Trends (https://trends.google.com/trends/) to estimate the relative volume of searches for primary bone sarcoma by specific provinces (voivodeships) in Poland. The Google Trends application is a free and public analytical tool started in 2004. It provides data with the option to provide search information for specific geographic regions such as countries, regions or cities. Data from the application are provided as the "search volume index" (SVI) or "relative search volume" (RSV), which shows the number of searches for a specific term per time point in relation to the total number of searches on the Google search engine during that time period. This is scaled from 0 to 100, 100 signifying the peak search volume for the search term during the time period. For example, the province with the most searches for the term, Osteosarcoma, relative to the total number of searches, would be assigned an SVI = 100, while other provinces that have a lower relative search volume for this phrase would have a lower SVI compared to this value.

In the study, we analyzed 5 search terms (topics) in Google Trends, namely: 1) osteosarcoma; 2) chondrosarcoma; 3) Ewing sarcoma; 4) bone tumor; 5) bone cancer, within 10 years (from January 1, 2010 to December 31, 2020) for all provinces in Poland. The above phrases are related to primary bone neoplasms and more than one phrase has been selected to

determine which phrases are most searched for in the field of primary bone sarcoma. The term 'Bone sarcoma' was not used due to the very low number of Google searches in Poland and worldwide. The application was accessed for the current study on September 15, 2023. Next, we used data from the National Cancer Registry [pol. Krajowy Rejestr Nowotworów (KRN); https://onkologia.org.pl/pl] website to obtain epidemiological data on primary bone sarcoma new cases and deaths. We used the age-adjusted incidence and mortality rates by province for bone sarcoma for the period from 2010 to 2020. Incidence and mortality included both genders.

We used Pearson correlation coefficients to evaluate the relationship between bone sarcoma incidence and mortality rates and Google SVIs by voivodeships in Poland. Each relationship was checked visually for outliers, and if outliers were present, the Pearson correlation coefficient and p value were compared with a Spearman rank-order correlation coefficient and p value for concordance. Statistical significance was defined as p value < 0.05. All analyses were performed using the Statistica 13.0.2 program (StatSoft Polska Co. Ltd., Kraków. Poland).

### **Results**

The most frequently searched phrase related to bone sarcoma in Poland was 'Bone tumor', followed by 'Osteosarcoma' and 'Bone cancer'. The above trend is also confirmed by the results obtained in worldwide searching. However, worldwide searches for the term 'osteosarcoma' peaked in 2019, when the 9-year-old daughter of Spain's national football team coach, Luis Enrique, died from bone cancer (Fig. 1). However, this peak was not so clear in the Google search in Poland. Over a period of 10 years, there was no significant increase in interest in the topic of bone cancer in July (Sarcoma Cancer Awareness Month) worldwide and in Poland (Tab. I).

We found statistically significant correlations between incidence rates and relative Google search volume (SVI) in Poland from 2010 to 2020 for the terms: osteosarcoma (r = 0.17; p = 0.035), chondrosarcoma (r = 0.36; p < 0.001) and Ewing sarcoma (r = 0.21; p = 0.008). When examining cancer mortality, we noted statistically significant correlations between the mortality rate of bone neoplasms and relative Google search volume for terms: chondrosarcoma (r = 0.42; p < 0.001) and bone cancer (r = 0.20; p = 0.012). The rest of the terms relating to bone neoplasms did not have statistically significant correlations with incidence or mortality rates. The Table shows the correlation coefficients between actual incidence rates and relative Google search volume for bone neoplasms in Poland (Tab. II). We did not observe a statistically significant relationship between the number of cases and deaths by voivodeship (regions) and SVI.

Over 10 years, 3494 new cases of bone cancer were diagnosed in Poland and 2994 people died from this disease. For compression, on average, 317.6 (± 29.8) new cases of primary

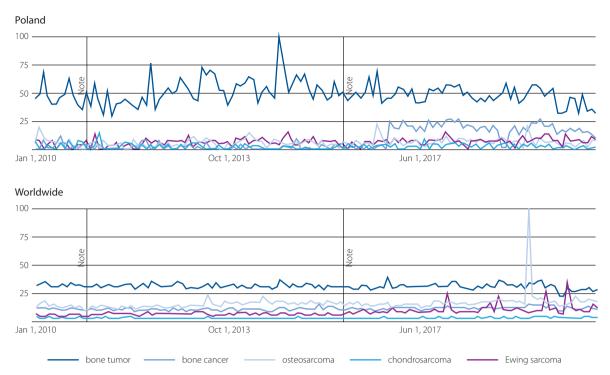


Figure 1. The chart shows the search volume index (SVI) for five phrases from 2010 to 2020. The top figure represent data from Poland, while the bottom figure shows worldwide searches. Topics: bone tumor (yellow), bone cancer (green), osteosarcoma (blue), chondrosarcoma (red), Ewing sarcoma (purple)

Table I. Comparison of the search volume index (SVI) from worldwide data in July (sarcoma cancer awareness month) and in other months of the year

Торіс	Average SVI	in July (SD)	Average SVI in o	ther months (SD)	pν	alue alue
	World	Poland	World	Poland	World	Poland
Bone tumor	30.36 (± 2.1)	49.36 (± 10.4)	31.29 (± 2.3)	49.64 (± 10.6)	0.195	0.947
Bone cancer	11.00 (± 0.7)	8.09 (± 9.1)	11.26 (± 1.2)	7.88 (± 9.0)	0.509	0.827
Osteosarcoma	14.82 (± 3.2)	10.40 (± 12.9)	16.04 (± 8.1)	11.76 (± 11.2)	0.622	0.110
Chondrosarcoma	3.18 (± 0.4)	1.84 (± 1.01)	3.20 (± 0.4)	2.18 (± 2.3)	0.896	0.072
Ewing sarcoma	7.36 (± 1.5)	6.01 (± 2.6)	8.36 (± 4.0)	6.24 (± 3.4)	0.410	0.489

SD — standard deviation

malignant bone tumors were diagnosed per year in Poland and 272.2 ( $\pm$  43.3) patients died per year (Fig. 2).

### **Discussion**

Our study is the first to show a relationship between the number of new cases of bone sarcoma and the number of searches for phrases related to bone sarcoma in Google. However, this only applies to specific phrases, like 'osteosarcoma', 'chondrosarcoma', and 'Ewing sarcoma', as more general phrases such as 'bone cancer' and 'bone tumor' do not correlate with the number of new cases. There may be several reasons for this result. First of all, the phrases 'bone cancer' and 'bone tumor' are the most frequently used phrases in Google regarding the topic, however, they can also be used to search for information about bone metastases or benign lesions, which occur

much more often than bone sarcomas. Second, the most common bone sarcomas in the adult and pediatric population are osteosarcoma, chondrosarcoma, and Ewing sarcoma, and therefore use of these phrases in Google may correlate with the overall number of bone sarcomas in the population. The situation is different with the mortality rate, which is correlated only with the phrases 'bone cancer' and 'chondrosarcoma'. In another study, Wehner et al. [11] noted that online searches are corelated with cancer incidences. They observed that the relative search volume was highly related to the level of cancer incidence rates in 5 of the 8 most commonly diagnosed cancers in the United States: colon cancer, lung cancer, lymphoma, melanoma and thyroid cancer. However, the correlation for mortality rates was statistically significant only for the 4 most common cancers: colon cancer, lung cancer,

Table II. Correlation coefficients between bone cancer incidence and mortality rates and relative google search volume index (SVI), 2010 to 2020

	Incidence		Mortality	
Торіс	r (correlation coefficient)	p value	r (correlation coefficient)	p value
Osteosarcoma	0.17	0.035	0.03	0.712
Chondrosarcoma	0.36	< 0.001	0.42	< 0.001
Ewing sarcoma	0.21	0.008	0.12	0.123
Bone cancer	0.05	0.490	0.20	0.012
Bone tumor	0.04	0.626	0.03	0.733

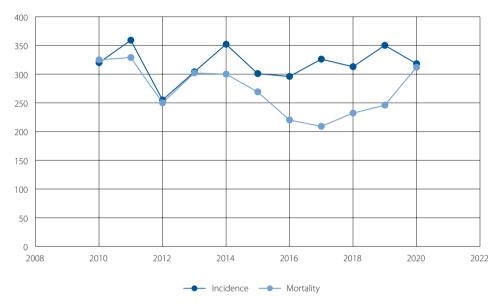


Figure 2. The graph shows the trend of incidence and mortality rate due to bone neoplasms in the period 2010–2020 in Poland

melanoma, lymphoma [11]. Phillips et al. [12] noted in their study, relative search volume was highly related to the level of cancer incidence for breast, prostate, lung, uterine cancers and leukemia in the USA. The above studies indicate that in the case of common cancers, Google Trends can be used as a tool for estimating the number of new cases. However, in our study we show that such a relationship also occurs in rare types of cancer such as bone sarcoma. Wehner et. al also noted in their study the relationship between the cancer incidence rate in the United States and SVI depending on the state [11]. However, in another study conducted in Peru, Luna-Abanto et al. [13] did not note such a relationship when correlating the SVI with the incidence by province, for breast, cervical and colorectal cancer. Also in our study, the incidence rate of bone sarcomas divided into provinces did not show any correlation with searches in Google Trends.

Some studies observed the significant impact of social campaigns and awareness months on the increase in interest in specific cancer topics in Google searches [6–8]. Nishimura et al. [6] in their study showed that breast cancer awareness

month had significant impacts on U.S. public interest in breast cancer from 2012 to 2021, with peaks in the RSVs from 21.9% to 46.7%, while lung cancer and prostate cancer awareness months did little to affect the public interest in lung or prostate cancer. Also, Cohen et al. [8] showed that public interest in 6 out of 13 cancers (cervical cancer, colorectal cancer, skin cancer, ovarian cancer, breast cancer and lung cancer) was significantly higher in their respective awareness months when compared to the rest of the year. However, this correlation was not observed in less common cancers in the population, such as esophageal cancer, pancreatic cancer, testicular cancer, brain cancer, blood cancer and thyroid cancer [8]. Demirici et al. [14] found that the bladder cancer awareness month did not cause an increase in online interest in Google. In our study, we also did not observe an increase in public interest in the topic of bone sarcomas during Sarcoma Cancer Awareness Month in July — both in Poland and worldwide. However, during data collection, we observed that global searches for the term 'osteosarcoma' peaked in 2019, when the 9-year-old daughter of the coach of the Spanish national football team

— Luis Enrique — died of bone sarcoma. A similar trend was observed by Gianfredi et al. [9] in their study, where they noted increased interest in online searches in the terms 'neuroendocrine tumor' and 'pancreatic cancer' after the famous Italian rapper Fedez, revealed that he had undergone surgery due to pancreatic cancer in March 2022. Also, Kamiński et al. [10] describe that most disease search peaks are related to date of diagnosis or death from dissease of famous people. They give the following examples: Selena Gomez with lupus, Ashton Kutcher with vasculitis or Lady Gaga with fibromyalgia. Kaleem et al. [15] showed a significant increase in public interest in Google searches for lung cancer, pancreatic cancer, endometrial cancer, cervical cancer, brain cancer, and glioblastoma after a celebrity-related event covered in the media. In our study, the increase in interest in the topic of osteosarcoma on Google increased more than 6 fold in August 2019. No social campaign or event has been able to increase public interest in the topic of bone cancer to such a significant extent. This shows what a significant impact the topics discussed by celebrities have on society's awareness, especially in the case of rare diseases.

There is an unchanging trend in the last 10 years of new cases of bone sarcoma in Poland, which is on average 318 (between 250–350) cases per year, and in line with the literature. It is estimated that primary malignant bone tumors constitute approximately 0.2% of all malignant tumors. In Poland, on average, approximately 170 000 new cases are diagnosed each year, which means that the estimated number of new cases of bone sarcomas should be approximately 340. Also, if we take into account that the incidence of bone sarcomas is 0.9 per 100 000 people, in relation to the average Polish population over the last 10 years (approximately 38 million), we obtain a similar result — 340 new cases per year [16]. Since 2014, a decrease in the number of deaths due to bone sarcomas has been observed, from approximately 300 per year to approximately 235. However, this trend changed in 2020, when the mortality rate was again above 300 cases per year. The reason for this could be the COVID-19 pandemic, which significantly limited access to medical care and specialists. A multicenter study showed that SARS-CoV-2 virus infection is one of the risk factors for death in pediatric oncology patients [17]. Moreover, it was shown that the delay in diagnosis increased during the pandemic, which influenced the later detection of the disease in bone sarcoma patients [18, 19]. Moreover, Kamiński et al. [20] showed that public opinion interest, represented by online searches in Google in many cancers during the COVID-19 pandemic, was significantly lower than in the prepandemic period. Consequently, a loss of interest in cancer may delay the diagnosis of malignancies and worsen the long-term outcomes, which may result in an increase in mortality.

This study has many limitations. Using Google search data to estimate disease rates may not be fully generalizable because the data is limited to people who have access to the Internet and use Google. However, currently in Poland the majority

of the population has permanent access to the Internet. We can therefore assume that even if the oncological patient was not able to use the Google search tool, closest family could indeed do so. Moreover, in the study we only used phrases related to the three most common types of bone sarcomas, without taking into account other rare types that were included in the incidence and mortality rate statistics. However, the aim of our study was to determine whether there is a correlation between the number of patients with a rare cancer such as bone sarcomas and public interest estimated based on online searches — not an accurate estimate of the number of patients with a given type of cancer based on Google searches. Another limitation is the reliability of data from the national cancer registry. Data comes from reports by physicians. For this reason, some patients may not be reported. However, the KRN currently provides the most reliable and easily accessible data on the number of malignant neoplasms cases in Poland.

### **Conclusions**

Bone sarcoma incidence is correlated with online search volume. For the potential estimation of the number of patients based on Google searches, the most appropriate phrases are: 'Osteosarcoma', 'Chondrosarcoma' and 'Ewing sarcoma'. However, this tool cannot be used to estimate the incidence rate divided into regions in Poland. Furthermore, there was no increase in public interest in the topic of bone sarcoma during the awareness campaign in July (Sarcoma Cancer Awareness Month). However, there was a significant increase in public interest in the topic of osteosarcoma related to famous people activity. The additional use of stories from celebrities with bone sarcoma may help increase public interest during awareness campaigns. Epidemiological data on bone cancer in Poland are comparable to worldwide data.

### Article information and declarations Data availability statement

Data available on request.

### **Ethics statement**

The Institutional Review Board was permitted to perform the present study without full review, which is necessary for interventional studies on humans, according to national regulations.

### **Authors contributions**

Dawid Ciechanowicz — conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, visualization, writing — original draft preparation.

Maria Wójtowicz — investigation, writing — original draft preparation.

Andrzej Bohatyrewicz — supervision, validation, writing — review & editing.

Daniel Kotrych — supervision, writing — review & editing.

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None.

### Conflict of interest

The authors declare no conflict of interest.

### Supplementary material

None.

### **Dawid Ciechanowicz**

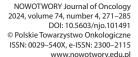
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## Original article

## Cancer epidemiology

## Cancer-dedicated infrastructures (CDIs) and associated risks for its user — the link between architecture and cancer

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**Introduction.** In recent decades, significant advancements in oncological treatments, technology, survivorship rates, screening behaviors, and healthcare support services have occurred. Yet, there has been minimal research on the architectural design of spaces where these processes occur, their characteristics, evolution, and adaptation; this makes it difficult to understand how it impacts healthcare provision and reception. This systematic review aims to explore the impact of cancer-dedicated infrastructure (CDI) on user outcomes, identify key variables, and emphasize the importance of the care environment.

**Material and methods.** Our literature review on this association identified 13 relevant articles. However, increasing interest suggests opportunities for exploration.

**Results.** Findings indicate that architectural characteristics, spatial features, and physical elements influence patient health outcomes and users' performance.

**Conclusions.** However, generalizability is constrained by the early stage of spatial analysis and sparse evidence. This review underscores the untapped potential of studying CDI architecture and integrating it as a variable to enhance the overall healthcare experience.

**Keywords:** cancer, architecture, cancer-dedicated Infrastructures

## Introduction

The precise origins of cancer-dedicated infrastructures can vary depending on the region and healthcare advancements, but the historical data of the establishment of the first CDI is associated with the foundation of The Royal Marsden as the first hospital in the world dedicated to the study and treatment of cancer. This institution was founded as the Free Cancer Hospital in 1851 [1]. However, CDIs gained significant momentum during the latter half of the 20<sup>th</sup> century and continue to evolve with advancements in cancer treatment and research.

The CDI construction program represents a pivotal, once--in-a-lifetime design project. In Europe, this undertaking is guided by several key entities: the European Society for Medical Oncology (ESMO), which sets standards for the quality of cancer care and treatment facilities; the European Organization for Research and Treatment of Cancer (EORTC), providing recommendations on research facilities; and European Union Directives and Regulations, including those concerning radiation protection (e.g., Council Directive 2013/59/Euratom), as well as the impact of constructing and operating radiotherapy facilities. Additionally, depending on the CDI's location, specific building codes and health regulations for healthcare facilities may vary across different countries within Europe.

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However, due to the continuous evolution and increasing demand for cancer care [2], as well as advancements in treatments, these infrastructures may have been initially constructed with standards that no longer fully reflect the current state of cancer care and might have several implications. In similar contexts, researchers have been studying what the implications are of hospital characteristics to either increasing or decreasing the risk of medical errors and the overall quality of healthcare, finding spatial layout and ergonomics as crucial contributors for cancer care [3–5]. These findings raise the question of whether a spatial layout designed for current processes is adaptable to future needs.

This discussion points to an interdisciplinary collaboration that pushes the research field to embrace evidence-based design principles in order to ensure that architectural layout choices, such as those in the construction or renovation of CDIs, are informed by rigorous research and aligned with evolving healthcare practices (Hamilton, D. K., 2003). By integrating empirical evidence into design decisions, healthcare facilities can not only better support efficient workflows, enhance patient safety, and improve overall healthcare delivery in the rapidly advancing field of cancer care [5], but also enable us to assess the under/over architectural performance of a space. This impacts not only the quality of care and patient experiences, but the conditions, comfort, and quality of work for medical staff that might be related with certain outcomes. Additionally, it could also impact the efficiency of the investment in CDI construction and renovation.

So far, CDIs'closest variables identified in scientific literature fit more on the spectrum of variables related to organizational performance of the institution such as levels of cancer care, hospital volume, population, racial composition, and availability of treatment [6] and patient physiotherapy [7]. However, spatial and architectural variables have still not yet been defined to

be able to have a standard for the analysis of spaces and to understand the risks or benefits that it represents for diverse CDI users, such as patients or medical staff.

As early as the 1990s, research began exploring the link between architectural features, care quality, and patient wellbeing [8, 9] This research so far has focused on how improving design makes hospitals less risky and stressful and, while promoting more healing for patients, their families, and staff. However, judging how scientifically credible the evidence is that design affects clinical outcomes and staff effectiveness in delivering care is still not defined [10]. To our knowledge, this is the first review addressing the impact of CDI on its users.

#### **Material and methods**

We prepared systematically review the scientific literature to examine the relationship between architecture and spatial features of cancer-dedicated infrastructures (CDIs) and users' health/wellbeing-related outcomes. The study was performed in phases, with partial results reported in accordance with the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) checklist, updated in 2020 [11].

## Search strategy

A systematic search of relevant papers was carried out in the following databases: PubMed, Science Direct, Scopus, and on the Health Environments Research & Design Journal from SAGE publications. The query was built to find original articles published between the years 2000 and 2023 and include the words "cancer facility" OR "cancer center" OR "oncology center" OR "hospital characteristics" AND "impact" OR "risk" OR "effect" in their title, abstract or keywords. The search strategy words organization varies in each database. For more detailed information refer to Table I.

Table I. Search strategies. Source: original. Elaboration: author

Source	Quantity	Query
PubMed	346	((((IMPACT[Title/Abstract]) OR (RISK[Title/Abstract])) OR (EFFECT[Title/Abstract]) AND ((ffrft[Filter]) AND (excludepreprints [Filter]) AND (fft[Filter]) AND (2000/1/1:2023/12/31[pdat]))) AND ((((HOSPITAL CHARACTERISTICS[Title/Abstract])) OR (CANCER CENTER[Title/Abstract])) OR (ONCOLOGY CENTER[Title/Abstract])) OR (CANCER FACILITY[Title/Abstract]) AND ((ffrft[Filter]) AND (excludepreprints[Filter]) AND (fft[Filter]) AND (2000/1/1:2023/12/31[pdat])))) AND (CANCER CARE[Title/Abstract] AND ((ffrft[Filter]) AND (excludepreprints[Filter]) AND (fft[Filter]) AND (2000/1/1:2023/12/31[pdat]))) Filters: Free full text, Full text, Exclude preprints, from 2000/1/1-2023/12/31
Elsevier	50	TITLE-ABS-KEY("cancer facility" OR "hospital characteristics" OR "cancer center" OR "oncology center") AND TITLE-ABS-KEY("impact" OR "risk" OR "effect")
Scopus	2074	TITLE-ABS-KEY("cancer+facility" OR "hospital+characteristics" OR "cancer+center" OR "oncology+center") AND TITLE-ABS-KEY("CANCER CARE") AND TITLE-ABS-KEY("impact" OR "risk" OR "effect") AND PUBYEAR > 1999 AND PUBYEAR > 2024 AND (EXCLUDE (DOCTYPE,"cb") OR EXCLUDE (DOCTYPE,"cr") OR EXCLUDE (DOCTYPE,"dp") OR EXCLUDE (DOCTYPE,"tb") OR EXCLUDE (DOCTYPE,"er") OR EXCLUDE (DOCTYPE,"sh") OR EXCLUDE (DOCTYPE,"ed") OR EXCLUDE (DOCTYPE,"ed") OR EXCLUDE (DOCTYPE,"no"))
SAGE (HERD: Health Environments Research & Design Journal)	93	CANCER (2007–2023)
Total	2563	

#### Inclusion criteria

A decision was made to include only original articles that investigate the relationship between the selected topics, regardless of the type of cancer-dedicated infrastructures (CDIs) or their location. The target population of the selected studies were non-permanent users of CDIs (patients or visitors), and the outcomes of interest were those directly related to their health or well-being implications. To complement the definition and enhance the purpose of the research, we decided to include case-study articles that run qualitative architectural analyses of any area of the CDI. Article variables included architectural or spatial characteristics, and physical elements present in the space. Conversely, articles that focused on the CDIs' geographic distribution, capacity/volume, facility type, or oncology services' performance were not considered.

Additionally, all non-original studies (such as abstracts, brief notes, commentaries, conference proceedings, reviews, and correspondence) were excluded from the analysis. No geographic restrictions were applied. A detailed description of the inclusion criteria is provided in Table II.

## Study selection

As the first step, all the identified records were integrated and deduplicated using EndNote Web. After deduplication, we performed a two-phase screening procedure, the first for titles and abstracts and the second for full texts, as is usually done in this kind of work.

The screening of titles and abstracts was conducted using the machine-learning-powered tool ASReview (v1.0rc0) [12]. ASReview is a "free open-source machine learning tool for screening and systematically labeling a large collection of textual data" [13]. It utilizes natural language processing and active learning to identify the features of articles that meet the inclusion criteria of a review. Based on the inclusions and exclusions made by the reviewers, it iteratively suggests

Table II. Inclusion criteria. Source: original. Elaboration: author

Inclusion criteria	
Publication year	2000–2023
Country of publication	Any
Population type	Oncology infrastructure users (patients, visitors/families, or medical staff)
Population size	Any
Population age	18 years old or more
Type of cancer	Any
Type of article	Original articles only
Infrastructure definition	Cancer center private or public oncology ward

the next article. This approach ensures that the most relevant papers are identified early in the screening process, significantly saving time. The full-text screening involved evaluating all articles deemed potentially relevant based on their titles and abstracts to make the final decision regarding their inclusion in the review.

In both phases, authors of this article collaborated to label each record as relevant or irrelevant based on the inclusion criteria. Any disagreements were resolved through a secondary analysis discussion, which included a third-party researcher from the institution.

#### **Data extraction**

A pre-defined, customized, and original spreadsheet was utilized to extract and collect useful data from the selected papers [14]. The data encompassed both qualitative and quantitative aspects. Qualitative data recorded included: source, name of the first author, journal's name, title, year of publication, country, study design, cancer facility type, population type of cancer, study aim, space focus, space variables, type of architectural analysis, main variable analyzed, outcome measure, and results. Quantitative data extracted included sample size, scope, and other significant results quantifying the studied association.

Moreover, the articles were grouped based on the type of space under analysis: indoor spaces, outdoor spaces, and analysis not focused on a single space. In addition, the architectural variables were divided into three categories: architectural characteristics, spatial features, and physical elements present in the area under analysis.

## Risk of bias assessment

The risk of bias due to sample selection, robustness of comparability, and ascertainment of exposure for all included articles was assessed jointly by authors of this article using the Cochrane Risk of Bias assessment tool and represented using the Risk of Bias Assessment tool (RobVis).

## Results

## Included studies

The search of the repositories yielded 2563 articles. After removing duplicates (n = 282), 2281 articles were loaded into ASReview for screening. Out of these, 2149 articles were categorized as irrelevant based on a review of their titles. The remaining 87 articles underwent abstract screening, during which 74 articles were considered potentially eligible for review. However, 63 of these were excluded after the full-text screening. Ultimately, 11 articles met all the inclusion criteria. Additionally, 2 more articles were identified through snowballing and reference list, bringing the total to 13 articles, all of which were included in the review. The PRISMA flowchart in Figure 1 summarizes the selection process.

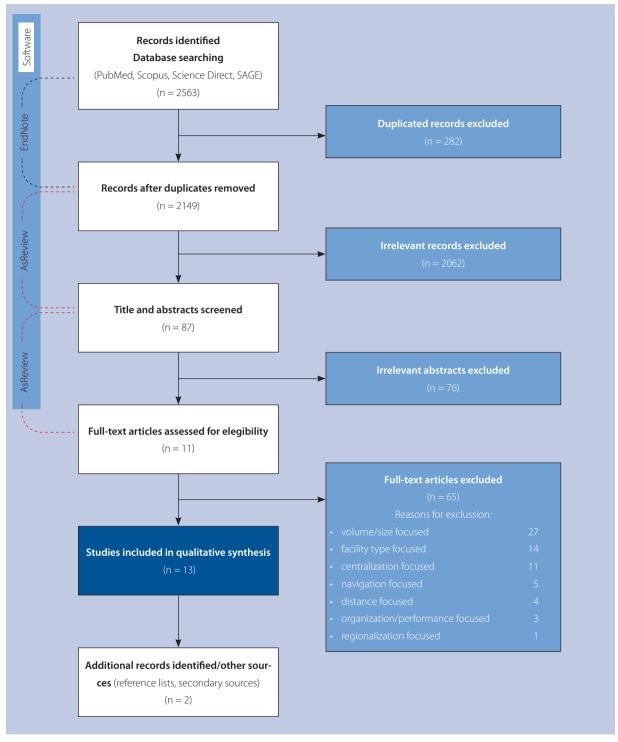


Figure 1. Systematic review process. Author: Rafael J. Salas Carretero. Source: own study

## **Characteristics of included studies**

The relevance of the topic is highlighted by the fact that most of the articles (11/13, 85%), were published in the last 9 years (2014–2023). The geographic distribution of the articles shows a North American predominance, with 5 articles written in the USA and 1 in Canada (6/13, 46%). Four studies were written in Europe: one each Belgium, Italy, Poland,

and The United Kingdom (4/13, 31%). South America is represented in two articles written in Brazil (2/13, 15%). Lastly, one article was written in Australia (1/13, 8%), representing Oceania.

Regarding the facility type, 5 studies were conducted in oncological academic hospitals (5/13, 38%), 3 were conducted in oncological centers but did not have precise details (3/13,

23%), 2 were conducted in non-academic oncological centers (2/13, 15%). Additionally, 1 study was conducted in a breast center, 1 in a cancer-related non-medical facility, and 1 did not focus on any specific institution. Regarding the specific spaces inside the infrastructures, 6 studies analyzed indoor spaces, 1 study analyzed an outdoor space, and the remaining 6 did not focus on any single space.

Ten articles (10/13%, 77%) focused on analyzing the three types of variables identified by the authors simultaneously: architectural characteristics, spatial features, and physical elements. Of the remaining studies, two focused on spatial features and one on the physical elements present in the space.

As for the study population, 4 studies focused solely on cancer patients (4/13, 31%), and 3 studies focused on both patients and staff members (3/13, 23%). Furthermore, 1 study collected data from staff and family members, another collected data from patients, staff, and family members; and 1 study collected data only from staff members. Three studies did not have a specific study population due to their study design, as they are case-study designs (3/13, 23%).

Finally, the remaining studies' study designs were as follows: 4 were qualitative (4/13, 31%), 3 used a multi-design approach (3/13, 23%), and the last three were cross-sectional, retrospective, and comparative observational studies, respectively. For more detailed information, refer to Table III.

## Observed results of included studies

For better identification, the authors categorized the observed results into three distinct categories based on the spatial focus analyzed in the articles: indoor spaces, outdoor spaces, and articles not specifically focused on a particular space.

## Indoor spaces

## Infusion room

The article by Wang and co-authors examines how different spatial arrangements — private rooms, semi-open areas, or open areas in chemotherapy care units — affect the experiences of cancer patients, their families, and nursing staff. Private rooms offer maximum privacy and are quiet but limit social interaction and are more costly. Semi-open areas provide a balance of privacy and social interaction, allowing for some patient interaction while maintaining personal space. Open areas facilitate easy monitoring by staff and social interaction among patients but offer the least privacy [15]. Another study, focusing on the same space with an emphasis on identifying the impact of the architectural layout of infusion rooms on nurse activities, nurse and patient satisfaction, patient privacy, and clinical collaboration, also highlighted the importance of balancing privacy and social interaction needs for both patients and staff [16]. Both studies stated the need for further research to determine the best design solutions to optimize these spaces, highlighting the need for spatial optimization and balanced environments.

#### ICU units

The article written by Matos and co-authors explores whether the design of ICU rooms, specifically single bed versus multibed layouts, has an impact on the stress levels and burnout rates of ICU staff and on the satisfaction levels of patients' families. The findings reveal that while room design significantly affects ICU staff stress and family satisfaction, it does not have a discernible influence on the burnout rates among ICU staff. However, it provides valuable insights into the considerations for ICU room design to optimize staff well-being and family experience [17]. On the other hand, the article of Caruso and co-authors compares the prevalence of delirium in patients admitted to single-bed rooms versus those in multibed rooms. The findings suggest that the architectural design of ICU rooms plays a significant role in influencing delirium rates, with notable differences observed between the two room types. This research highlights the importance of ICU design considerations in patient outcomes, particularly regarding the mental health and cognitive function of critically ill patients [18].

#### Palliative care ward

The article by Rowlands J. and co-author [19] focuses on studying how the environment of the palliative ward and its design impacts the quality of life of advanced cancer patients. As a result of this study, four themes emerged as impactful: staff behavior, the immediate environment, single vs. multi-bedded rooms, and contact with the outside environment. Findings show that the attitude, competence, and helpfulness of the staff create the atmosphere of the ward — regardless of layout, furnishings, equipment and décor; however, most of the patients in this study expressed a strong preference for a multi-bedded room when they were well enough to interact and a single cubicle when they were very ill or dying, which is contrary to the current advice for building new hospitals with all single rooms [19].

## Waiting room

The article from Blaschke and co-authors [20] explores the impact of incorporating artificial greenery into the waiting room of an oncology clinic. The study investigates how the presence of artificial plants and green decor affects patient well-being, anxiety levels, and overall satisfaction with the clinical environment. Despite the use of non-natural elements, the findings indicate that the introduction of artificial greenery can significantly enhance the perceived quality of the space, providing psychological benefits to patients during their waiting periods. This research underscores the potential value of environmental enhancements in healthcare settings, even when natural elements are not feasible [20].

## **Outdoor spaces**

## Healing gardens

The article by Valente and Cooper Marcus [21] explores the concept of healing gardens and their role in promoting health and well-being for cancer patients. It delves into the design

Table III. Characteristics of included studies. Main elements of the included studies for the systematic review on cancer-dedicated infrastructures (CD) and user's outcomes (n = 13)

ID Author									
	or	Title	Year	Source/Journal	Country	Cancer facility type	Cancer type	Population	Study Design
De M	De Matos et al.	Single-Bed or Multi-bed Room Designs Influence ICU Staff Stress and Family Satisfaction, But Do Not Influence ICU Staff Burnout	2020	Review/Health Environments Research and Design Journal	Brazil	480-bed teaching oncology hospitals with 45 ICU beds	Not specified	156 ICU staff, 176 family members	Comparative observational study. Cross-sectional data collection
Carus	Caruso et al.	ICU architectural design affects the delirium prevalence: A comparison between single-bed and multi-bed rooms	2014	Critical Care Medicine	Brazil	290-bed teaching oncology hospital with 31 ICU beds	Notspecified	1253 patients	Retrospective observational study
Blasch	Blaschke et al.	Artificial but better than nothing: The greening of an oncology clinic waiting room	2017	Review/Health Environments Research and Design Journal	Australia	Metropolitan comprehensive cancer center	Not specified	72 patients, 13 staff, 52 careers, 5"other"	Cross-sectional survey study
Tinner	Jo	Perceived Importance of Wellness Features at a Cancer Center: Patient and Staff Perspectives	2018	Review/Health Environments Research and Design Journal	USA	Cancer center, details nor provided (90000 square foot)	Not specified	52 patients, 59 staff	Qualitative. Post-occupancy evaluation study
Gronos Czajka	Gronostajska & Czajka	Architecture therapy: principles of designing and shaping space in centers for cancer patients, based on the architecture of Maggie's Centers	2021	Review/Builder Science	Poland	Maggie's center: independent building with recreational and facilities without accommodation	Not applicable	Not applicable	Case-study. Analysis of literature on elementary design principles; architectural analysis of plans; and a critical analysis
Bloom	Bloom et al.	Ten trends transforming cancer care and their effects on space planning for academic medical centers	2015	Review/Health Environments Research and Design Journal	USA	Academic Medical Center (AMC) cancer center	Not applicable	Not applicable	Case-study. Review of the implication of the cancer care trends
Wang	Wang & Pukszta	Private Rooms, Semi-Open Areas, or Open Areas for Chemotherapy Care: Perspectives of Cancer Patients, Families, and Nursing Staff	2018	Review/Health Environments Research and Design Journal	USA	Academic Medical Center	Not specified	171 patients, 145 family member, and 16 staff	Mixed method designquantitative and qualitative with open-ended questions

**Table III cont.** Characteristics of included studies. Main elements of the included studies for the systematic review on cancer-dedicated infrastructures (CDI) and user's outcomes (n = 13)

	Study Design	Multi-design. Comprehensive review of literature; photographic analysis, and a field evaluation	Mixed method design. Nurse shadowing and survey	Qualitative-in-depth interviews	Qualitative — analysis of the narratives	Case-study	Qualitative — phenomenological
esign	Population	19 staff 1 Center coordinator	19 staff, 22 patients	14 patients	7 patients	Not applicable	12 patients
Study design	Cancer type	Breast cancer	Not specified	Breast cancer	Not specified	Not applicable	Type not specified
	Cancer facility type	Breast Cancer center	2 Medical Campus Cancer centers	Not focus on a single institution	Several Cancer Hospital, not details provided	Rocky Mountain Cancer Center Hospital (270 000 square foot)	Cancer Hospital, not details provided
	Country	USA	USA	Canada	Belgium	Italy	United Kingdom
	Source/Journal	Review/Health Environments Research and Design Journal	Review/Health Environments Research and Design Journal	Review/Social science and Medicine	Review/European Journal of cancer care	Literature quote/ /Research and experimentation	Literature quote/ /Palliative medicine
Study information	Year	2021	2019	2008	2019	2015	2008
Stu	Title	Specialty Space: Breast Care Centers	The Impact of Infusion Center Layout on Workflow and Satisfactions in Two Cancer Infusion Centers: A Case Study on Staffand Patients	Health, healing and recovery: Therapeutic landscapes and the everyday lives of breast cancer survivors	Foregrounding the built environment in the experience of cancer care: A qualitative study of autobiographical cancer narratives	Giardini che guariscono: processi progettuali e realizzazioni di ambienti benefici	How does the environment impact on the quality of life of advanced cancer patients? A qualitative study with implications for ward design
	Author	Guevara	Jalalianhosseini et al.	English et al.	Jellema et al.	Valente & Marcus	Rowlands & Noble
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**Table III cont.** Characteristics of included studies. Main elements of the included studies for the systematic review on cancer-dedicated infrastructures (CDI) and user's outcomes (n = 13)

В.		Study info			Arch	Architectural analysis		Outcome
QI	Author	Study aim	Type of space	Space focus	Type of variable	Specific Variables	Outcome Measure	Results
<b>≓</b>	De Matos et al.	Compare the impact of single-bed vs. multi-bed room intensive care units (ICU) architectural designs on the stress and burnout of ICU staff and, on the stress and satisfaction of family visitors	Indoor space	ICU Unit	Architectural characteristics, spatial features and physical elements	Multi-bed room: Larger size, Window, view, shared toilet, furniture (chair), temperature, bed, space curtain, reading light Single room: bed, furniture (chair), tv, temperature, natural light, window, windows cover, view, artificial light controllable, reading light, dedicated toilet, sliding door	Maslach Burnout Inventory for Human Services Survey (MBHSS; Maslach, Schaufeli, & Leiter, 2001) for burnout and psychological stress,ISSL for Adults (Lipp & Guevara, 1994), and a modified version of Molter's Critical Care Family Needs Inventory (Johnson et al., 1998), respectively for psychological stress and satisfaction	Single-bed ICU design was associated with greater satisfaction of family visitors yet with higher levels of stress for ICU staff.  Meanwhile, similar burnout levels were observed for ICU staff who worked in single-bed or multi-bed rooms
.2	Caruso et al.	Compare the ICU delirum prevalence and characteristics (coma//delirum-free days, first day in delirum, and delirum motor subtypes) of critically ill patients admitted in single or multibed rooms	Indoor space	ICU Unit	Architectural characteristics, spatial features and physical elements.	Multi-bed rooms: Bed, Furniture (chair), temperature, natural light, curtains, reading light Single rooms: Bed, Natural light, toilet, furniture (2 chairs), temperature, windows cover, sliding door, room light controllable	Level of consciousness using the Richmond Agitation Sedation Scale or Glasgow Coma Scale, as appropriate. Delirium using the Confusion Assessment Method for ICU (CAM-ICU) and its motoric subtype is classified as hypoactive, hyperactive, or mixed	Prevalence was significantly lower for patients in single-bed rooms, and the admitted due to a medical or postoperative reason. However, once the delirium occurred, the coma//delirium-free days, the firstday in delirium, and the delirium motoric subtypes were not different from patients in single or multi-bed rooms.
ന്	Blaschke et al.	Investigate patient, staff, and carer responses to an environmental intervention in an oncology clinic waiting room and evaluate the acceptability of artificial plants	Indoor space	Oncology outpatient clinic waiting room	Physical elements	Artificial plants divided in: two movable green walls covered in plants, six hanging plant displays, one movable rock garden and 12 tabletop plant arrangements. Mostly green foliage and few colored flowers	Questionnaire. Topic times of visit to the place, notice-ability, type of plant preference (natural or artificial), and nature preferences and effects (effect on the aesthetics of the place and sensation self-effect, how does it make them feel)	The environmental intervention positively impacted patients', staff, and carers' perceptions of the oncology waiting room environment. Patients, staff, and carers mostly accepted artificial plants as an alternative design solution to real plants

 Table III cont.
 Characteristics of included studies. Main elements of the included studies for the systematic review on cancer-dedicated infrastructures (CDI) and user's outcomes (n = 13)

e e		Study info			Arci	Architectural analysis		Outcome
QI	Author	Study aim	Type of space	Space focus	Type of variable	Specific Variables	Outcome Measure	Results
4	Tinner	Determine the hierarchical importance of wellness building features for both patients and staff at a healthcare facility using targeted post-occupancy evaluations and, second, to determine whether patients who are ill and caregivers who are well have different needs concerning the design, layout, and implementation of wellness features	Not focus on a single space	Not focus on a single space	Architectural characteristics, spatial features and physical elements	Views of nature; access to the roof garden; plants inside the building; pictures and artwork representing nature; daylight; the lack of visible medical equipment; ease of movement through the center; access to privacy; and access to privacy; and access to spaces that promote social interaction, thermal comfort, and acoustic tranquility	2 different questionnaires, one addressed to the patients (building feature rating outcomes, patient confidence in care and building features, and patient preferred treatment areas) and one addressed to the staff workers (building feature rating outcomes and staff break area preferences)	Access to private and quiet spaces is the top need for caregivers. For patients, the top are ease of movement, thermal comfort, and natural light. Features with high common values between patients and staff include thermal comfort, views of nature, and natural light. In contrast, there are significant differences regarding art and murals and indoor plants
·S.	Gronostajska & Czajka	The goal of the study is to aid in humanizing the built environment and medical and healthcare settings by presenting a case study of good practice in design solution focused on architecture that supports CDI users	Not focus on a single space	Not focus on a single space	Architectural characteristics, spatial features and physical elements	Public (entrance zone, kitchen, dining room, large rest zone, group space, administrative spaces, and garden) semi-private (group space, and small rest zone) and private (therapy room, and toilets)	Architectural analysis based on the concise Maggie's architecture and landscape brief	Applying a hierarchy analysis of functional zones so as to gradually ease guest emotions; ensure a triple center functioning scheme
ú	Bloom et al.	Understand the spatial implication of the ten trends transforming cancer care and their effects on space planning for academic medical centers	Not focus on a single space	Not focus on a single space	Spatial features	Flexibility of the space, collaboration, treatment requirement space, technology requirement space and correspondence with the processes done in the space	Analysis of the new models expanding and emerging in health reform specifically in AMC cancer care	There is a direct relation between alignment of processes, technology and treatment updates, and space requirements. Planning of new spaces in CDI should aim to multipurpose function, conversion between uses, and planning for future steps. Working spaces, strategies should emphasize opportunities for sharing and collaboration

Table III cont. Characteristics of included studies. Main elements of the included studies for the systematic review on cancer-dedicated infrastructures (CDI) and user's outcomes (n = 13)

B.		Study info			Arc	Architectural analysis		Outcome
	Author	Study aim	Type of space	Space focus	Type of variable	Specific Variables	Outcome Measure	Results
	Wang & Pukszta	Analyze what type of treatment environments (private, semiopen, or open) do most chemotherapy patients, patient's families, and nursing staff preferand the environmental needs during chemotherapy treatment	Indoor space	/Infusion room	Architectural characteristics, spatial features	Preferred environments (private, semi-open, and open), Privacy/ /openness of the space, socialization opportunity within/ beyond family, patient-nurse access, window views/daylight, sound/ noise, bathroom availability	Three different questionnaires with same research focus for patients, families, and staff participants about preferred environment and appropriate number of patients with a section of qualitative analyzed through keyword and content analysis on patients' statements	Semi-open areas were preferred by the staff, whereas the three types of treatment environments were equally popular among both patients and families. Female patients and patients receiving longer periods of treatment per occurrence were more likely to prefer private rooms. Three common reasons were needs for privacy, social interaction, and patient—nurse access. Additional reasons included needs for sleep, openness, and access to nature. A shared environment of chemotherapy care was suggested to be appropriate for four to seven patients to occupy
	Guevara	The objective of this study was to support future evidence based design and universal design guidelines use in the development of patient areas by presenting case studies of good practice in design solutions.	Not focus on a single space	Not focused on a single space	Architectural characteristics, spatial features and physical elements.	Design factors (support to variety of users, seating choices, and wheelchair maneuverability chance), lighting and views (artificial light, indirect light, natural light, and views of nature), privacy (auditory and visus), and webbased patient intake tool), and aesthetics (spa-like atmosphere, monochromatic choice of colors, and wood and plants presence)	Multi-design. First a comprehensive review of literature; then an photographic analysis of best practices on worldwide cancer centers and finally, a field evaluation including an interview with the coordinator, a survey to collect data from nine staff members and architectural surveillance and analysis of the interior space characteristics	Recommended guidelines in breast care center should target the following features: robes (vs. hospital gowns), spa-like atmosphere, mono-chromatic color scheme, use of wood and stone, private checkin areas, way-finding, room temperature comfort, seating comfort, seating style choice, personal items storage, access to natural light, indirect artificial lighting, living plants, views of nature, flooring comfort, and wheelchair accessibility

Table III cont. Characteristics of included studies. Main elements of the included studies for the systematic review on cancer-dedicated infrastructures (CDI) and user's outcomes (n = 13)

Outcome	Results	Comparison of shadowing data indicated that although the infusion centers have different layouts, there are no significant differences in the activities or time spent by nurses in different areas among the centers. However, staff have different satisfaction levels with visual and speech privacy, ability to concentrate, collaboration, and the process of medication delivery. Patients also had slightly different satisfaction levels with their ability to communicate with staff and design of bays	Extraordinary therapeutic landscapes and the broader community and nature are important for healing. Landscapes with which women interact on an everyday basis are most important for physical and psychological healing. In addition, the research suggests a strong interplay between emotions and place, which appear to be embedded within places of healing, and play an important role in shaping and maintaining therapeutic landscapes	Architecture impacts the experiences of cancer patients as the exposure to buildings where formal cancer care takes place is intense and meaningful. Additionally, the buildings around them offer metaphors that help patients rethink their experiences of illness and care and can be used on identification of variables for future research.
	Outcome Measure	"Mixed-method approach. Shadowing nurses to capture time spent in different areas of the cancer treatment center, travel patterns, activities performed, frequency and duration of nurse–patient//family member interactions, medication delivery, and workflow processes. Online survey for a staff and paper-based questionnaire using a 5-point Likert-type scale."	Qualitative semi-structured interviews	Autobiographies about the experience of people undergoing cancer treatment
Architectural analysis	Specific Variables	"Open bay design: infusion chair, curtains, guest chair, semi-private design: infusion chair, television, guest chair, and hand sanitizer. inclusion of embedded pharmacy."	Exposure to dangerous materials, individual space, emotional, social, and informational needs spaces	Facility's physical features, Furniture, Accessibility and Psycho-spiritual perception
Arc	Type of variable	Architectural characterístics, spatial features and physical elements	Spatial features	Architectural characteristics, spatial features and physical elements
	Space focus	Infusion room	Not a single space	Not a single space
	Type of space	Indoor space	Not focus on a single space	Not focus on a single space
Study info	Study aim	Compare nurses' operational workflow and nurses' and patients' satisfactions of two different infusion center design. Identify the impact of the layout of infusion rooms on nurse activities, nurse and patient satisfaction, patient privacy, and clinical collaboration	Examine the importance of the place for shaping health and healing among breast cancer survivor. Understand how different landscapes are conductive to healing and recovery process for woman who have experienced breast cancer	The role of built environment in the experience of cancer care.
	Author	Jalalianhosseini et al.	English et al.	Jellema et al.
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Table III cont. Characteristics of included studies. Main elements of the included studies for the systematic review on cancer-dedicated infrastructures (CDI) and user's outcomes (n = 13)

Outcome	Results	Positive results frequently encountered in patients' health and in the cost benefits for medical facilities encourage further studies of healing gardens as therapeutic tools for various diseases	Four main themes emerged: staff behaviors, the immediate environment, single vs. multibedded rooms and contact with the outside environment. The attitude, competence and helpfulness of the staff creates the atmosphere of the ward regardless of layout, furnishings, equipment and decor. The majority of the patients in this study expressed a strong preference for a multi-bedded room when they were well enough to interact and a single cubicle when they were very ill or dying, which opposes the current advice for building new hospitals with all single rooms
	Outcome Measure	Qualitative analysis of the functioning of the spaces	Semi-structured qualitative interviews
Architectural analysis	Specific Variables	Garden 1: location, visibility, seating (orientation, availability, design), tables, cushions, plants, light stanchions, greening/paving ratio, furniture material Garden 2: location, visibility, feature availability (playground), seating availability (orientation, plants (color, type) Garden 3: size, shape, feature availability (fountain), seating, plants (color, odor)	Cleanliness, light and a view outside, possibility of interaction, layout ofroom, privacy, natural light, pictures, & colors
Arc	Type of variable	Architectural characteristics, spatial features and physical elements	Architectural characteristics, spatial features and physical elements
	Space focus	Garden	Palliative care ward
	Type of space	Outdoor space	Indoor space
Study info	Study aim	Identify the main characteristics of therapeutic gardens, analyze them and understand what is the opportunity that they provide for cancer infrastructure's patients, staff and relatives	Analyze the environment from the patient's perspective and understand the effect it may have on them
	Author	Valente & Marcus	Rowlands & Noble
B.	Q	.2.	13.

ICU — intensive care unit; CDI — cancer dedicated infratructure; AMC — academic medical center

processes and practical implementations of these therapeutic spaces, outlining the design principles and processes involved in creating healing gardens, including user-centered design, natural elements, and accessibility. The article states that healing gardens are effective in promoting well-being and recovery, suggesting that incorporating therapeutic gardens into health-care can significantly enhance the quality of life for users and offer cost benefits for medical facilities. Further research and interdisciplinary collaboration are recommended to continue the development of these beneficial environments [21].

## Not linked to specific spaces

## Space characteristics

In the article by Tinner and co-authors [22], which aims to determine the importance of wellness-building features and their design, layout, and implementation on the satisfaction of patients and caregivers' needs, it is shown that caregivers' top need is access to private and quiet spaces. This contrasts with patients' needs, who prioritize ease of movement, thermal comfort, and natural light. Additionally, spatial features with high common values between patients and staff include thermal comfort, views of nature, and natural light. In contrast, there are significant differences regarding the importance of art, murals, and indoor plants [22].

Regarding the article by Gronostajska and Czajka [23], which analyzed architectural characteristics, the spatial features and physical elements of a non-medical oncological infrastructure that supports cancer patients and their relatives during the journey in the CDI showed that the application of a hierarchy of functional zones allowing for a mix of spaces accessible to all patients and accompanies at the same time, spaces accessible to few patients at the same time and spaces accessible only to a single patient (or plus 1) that ensure too little natural light, spatial openness, ease of movement, mobility adaptation, application of colors, and contrasts, produce positive emotions and reduce the treatment burden [23].

The article from Guevara ran an analysis [24] of the architectural design of a breast center's interior based on the evidence-based design (EBD) process and the Universal Design (UD) guidelines standards available. The study of layout-design factors, lighting and views, privacy, and the aesthetics of the space along with the mixed-method approach of the research of the study produced recommended design guidelines, enhancing CDIs design to target the following features: robes (vs. hospital gowns), spa-like atmosphere, monochromatic color scheme, use of wood and stone, private check-in areas, wayfinding, room temperature comfort, seating comfort, seating style choices including bariatric, personal item storage, access to natural light, indirect artificial lighting, living plants, views of nature, flooring comfort, and wheelchair accessibility [24].

Finally, the article by Jellema and co-authors [25] analyzed the narratives of cancer patients to understand the role of the built environment (such as place of residence,

ease of commuting) in their experience of cancer care. The article found out that the facility's architectural characteristics, spatial features, and physical elements impact the experience of cancer patients as the exposure to buildings becomes intense and meaningful. Results show that furnishings, distance to the center, technology availability, physical limitations, odour control, temperature, and noise all impact the experience in the cancer center [25].

## Space needs

The article by Bloom and co-authors [26], which studied the trends transforming cancer care and effects on space planning for academic medical centers, showed that as treatment advances, there is a current spatial need for new and improved health services as the translational research, clinical trials, and supportive & complementary care. This article emphasized the direct relation between the alignment of processes, technology, and treatment updates with the space requirements, enhancing the multipurpose design of new spaces in order to be able to implement future changes in oncological treatment and care [26].

The article by English and co-authors [27] focused on studying the importance of the place in shaping health and healing among breast cancer survivors. For them, understanding how different landscapes contribute to healing and aid the recovery process of women who have experienced breast cancer is key to identifying therapeutic spaces for better health outcomes. Results from this study show that it is important to consider individual space availability, as well as emotional, social, and informational spaces that fulfill the needs of the patient [27].

## **Discussion**

The findings of this systematic review underscore the importance and significance of the architectural design of CDIs in the experience of cancer care. It has been identified that architectural design can impact patient outcomes, family and visitors' experiences, and medical staff's performance in delivering care, while also minimizing their work-related risks such as burnout. The study and evaluation of CDIs offering a good balance between spaces that provide well-being to the patients and families while also allowing medical staff perform efficiently has not been deeply explored in the literature despite the potential impact of its benefits.

From this, it is evident that more qualitative research is needed to promote the building of evidence-based design spaces that might impact health and well-being-related outcomes for all users of CDIs. This kind of research is essential to identify the main variables of these spaces. Results from our review have identified beneficial architectural characteristics such as indoor greenery, access to green areas, contrast-color walls, and natural light; spatial features such as adaptability, ease of movement, and privacy/social interaction opportunities;

and physical elements such as privacy screens, support tools, and diverse seating options which might play a positive role during the cancer care journey for patients and visitors/ /families. Meanwhile, room visibility, working space size, layout distribution, and green area accessibility play a significant role in the performance and well-being of medical staff.

These findings align with previous research on different populations [28, 29], in which new health infrastructure has been built or renovated. The design of this health infrastructure has been guided by qualitative research using a user-centered approach to understand the behavior and needs of the patients.

However, with the continuous evolution of treatments, technological developments, the increasing number of survivors, screening behaviors, and healthcare support services, the needs of CDI users are in constant evolution. Despite the need for more space being consistently supported by the sustainable growth of infrastructures worldwide [30–33], this alone does not seem to be the solution. Infrastructure's role remains primarily as a support for medical services, with the possibility of it becoming a significant factor in treatment outcomes still not enough explored.

Other facts identified in this review, such as the different denominations given to CDIs according to their capacity, volume, teaching activity, or location; along with the non-definition of a standard categorization of architectural variables; and the lack of data about the architectural layout of CDIs in medical databases, challenge the progression of research in analyzing how they are linked to patients' health outcomes. At the same time, it complicates the possibility of evaluating the performance of spaces in adapting to new current improvements in oncology care delivery and treatments.

Finally, from the analysis, it has been noted that due to the intrinsic characteristics of CDI architecture, such as form, structure, and materiality, along with the high levels of hygiene and infection guidelines for health infrastructure, a high level of maintenance is needed. At the same time, there is no evidence in research about the maintenance of CDIs on their spatial adaptation to the actual processes, and the populations treated inside them.

## **Conclusions**

The results of this systematic review show a scarcity of research on the impact of oncology CDI related variables on patients, family, and medical staff outcomes. However, the increasing appearance of the topic in recent years suggests growing interest in this interdisciplinary relationship. The results of the reviewed literature support the hypothesis that CDI variables such as architectural characteristics, spatial features, and physical elements are associated with specific patient health outcomes, visitor/family well-being, and staff performance levels. More specifically, the results demonstrate that CDI variables can significantly contribute to improving certain aspects of the lives of cancer patients, their families, and medical staff. In fact, the results show that places designed with a user-centered

approach, especially those based on evidence-based design research, are currently contributing positively to cancer patient's treatment journey.

So far, the investigation is still in its early stages, and the results are quite inconsistent, so the possibility of a comparison between them still represents a high risk of bias as they have not taken into consideration the same variables. Consequently, it seems that the need to identify these variables and promote an international standard of categorization for them, becomes more relevant for their inclusion in epidemiological studies. Finally, as physical spaces are undeniably necessary for the delivery of healthcare, especially in oncological care where procedures involve a diverse range of professionals and processes, future directions for the inclusion of architectural layout are needed as it implies potential improvements for all users.

## **Future directions**

This systematic review explored the current knowledge about the relationship between the architectural layout and its variables and the diverse health-related, well-being, and performance outcomes of CDIs' range of users. Including this type of interdisciplinary research underscores the importance of considering architectural design as a significant factor in healthcare delivery, and some considerations must be made.

- The cancer journey is a long process encompassing prevention, diagnosis, treatment, and survivorship stages. Users are exposed to infrastructure at different levels in each stage.
- Cancer-dedicated infrastructure combines multiple users.
   User-centered design research is encouraged, but it must encompass the diversity of oncology infrastructure users.
- Space division in oncological infrastructure must be developed, with a categorization based on collaboration between both disciplines.

## **Article information and declarations**

## **Authors contributions**

Rafael Jamie Salas Carretero — conceptualization, data curation, formal analysis, investigation, methodology, visualization, writing — original draft preparation, writing — review and editing.

Mariola W. Borowska — data curation, project administration, writing — original draft preparation, writing — review and editing.

## **Conflict of interest**

None declared.

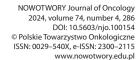
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## Pictures in oncology



## Multiple non-melanoma skin cancers during 43-years long therapy with azathioprine in renal transplant recipient

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**Figure 1A–C.** A 75-year-old patient presented with numerous skin lesions on the limbs and trunk morphologically consistent with SCC and BCC

Non-melanoma skin cancers (NMSC), mainly squamous cell carcinoma (SCC) and basal cell carcinoma (BCC), account for over 90% of all skin cancers in solid organ transplant recipients. NMSC incidence steadily increases over time following transplantation, mainly due to exposure to long-term immunosuppression and additional factors such as ultraviolet radiation, ionizing radiation and human papillomavirus (HPV) infection [1–2]. A 75-year-old patient presented with numerous skin lesions on the limbs and trunk morphologically consistent with SCC and BCC (Fig. 1A–C). In the 1970s he was diagnosed with end-stage renal failure, likely due to chronic glomerulonephritis. After months of dialysis, a kidney transplant from a deceased donor was performed in 1980. Since the transplantation he has been on continuous immunosuppressive

therapy (azathioprine 50 mg once daily and prednisone 5 mg once daily). This regime is currently known to have strong carcinogenic effects with long-term use [3]. The most suspicious skin lesions on his right thigh, left arm, and left submandibular area were removed with a few millimeters margins and were histologically confirmed as SCC in situ (right thigh) and BCC (left arm and left submandibular area). Apart from these three lesions, patient had multiple SCCs and BCCs removed over past decades. Ongoing immunosuppression, coupled with the current condition of his skin (Fig. 1A-C), suggests that new foci of NMSC are expected to develop in the near future. This case clearly emphasizes the urgent need for strict and systematic skin monitoring of organ transplant recipients on long-term immunosuppressive therapy, considering the increased risk of developing NMSC. Awareness of this risk, along with early detection and intervention, significantly improves the general prognosis and quality of life for these patients.

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# Management of renal cell cancer bone metastasis — a case report on embolization and orthopaedic intervention

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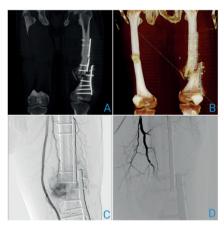
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**Figure 1.** Computed tomography — pathological fracture and a broken stabilizing plate; **A.** 3D multiplanar reconstruction; **B.** 3D volumetric reconstruction. Digital subtraction arteriography; **C.** Metastatic tumour. Vascular supply from the deep femoral artery; **D.** Shadow of the embolization coil and effective occlusion of the tumour blood supply. Absence of flow in the distal segment of the deep femoral artery

We present the case of a 63-year-old man diagnosed with clear cell renal cell cancer (RCC) with multiple osteolytic bone metastases who was treated at our hospital. The patient underwent a pathological fracture of the left femur, surgically stabilized with a titanium plate in August of 2023. Due to the risk of spinal compression syndrome and pain, the pa-

tient underwent a palliative sacrum and Th8 radiotherapy. In October 2023, due to the destabilization of a surgical anastomosis of the femur, the patient was qualified for embolization, followed by orthopaedic surgery (Fig. 1A, B). The procedure involved puncturing the right femoral artery under local anaesthesia using the Seldinger method. A guidewire catheter was inserted on the left side. Pathological vessels supplying the richly vascularized tumour of the left thigh from the deep femoral artery were visualized. Embolization was performed using Embozene 700 µm microspheres for small pathological vessels (Fig. 1C). In the end, coils were used to close the bigger vessels. Control arteriography showed effective devascularization of the tumour (Fig. 1D). After two days, the patient underwent the removal of destabilized material from the femur with internal repositioning and stabilization with an intramedullary nail. No intraoperative complications occurred. Post-surgery, the patient was qualified for systemic therapy with ipilimumab and nivolumab as he belongs to the intermediate-risk group, according to the International Metastatic RCC Database Consortium [1].

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