# **Original Article**



# Psychiatric Diagnoses and Their Treatment in Women With Breast Cancer: A Latent Class Analysis of 1062 Inpatients

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## **Abstract**

This retrospective study involving 1062 breast cancer patients from a Comprehensive Cancer Center between 2012 and 2019 highlights a high prevalence of psychiatric disorders in this population. While psychooncological support (POS) and psychopharmacological interventions are effective, a substantial proportion of patients with psychiatric diagnoses remained untreated. Latent class analysis identified three patient subgroups, suggesting a need for more tailored treatments to address the unmet needs of this vulnerable population.

Introduction: Psycho-oncological support (POS) and psychopharmacological interventions are effective in treating psychiatric symptoms in patients with breast cancer. However, despite high prevalences of psychiatric disorders in patients with breast cancer, a significant proportion remains untreated. Methods: Data from 1062 breast cancer patients who had been diagnosed and treated at a Comprehensive Cancer Center between 2012 and 2019 were analyzed retrospectively. We descriptively evaluated the number of patients with a psychiatric diagnosis, POS and psychiatric medication. Latent class analysis was used to examine the relationship between ICD-10 coded psychiatric diagnoses, POS, psychiatric medication, and, as important prognostic factors, tumor stage and somatic comorbidity. **Results:** 31.5% of all patients had a psychiatric diagnosis, 20% received POS and up to 60% received psychiatric medication. Latent class analysis revealed three subgroups: 1) patients with a low cancer stage, low somatic comorbidity, no psychiatric diagnosis, no POS and no psychiatric medication; 2) patients with a low cancer stage, low somatic comorbidity, a psychiatric diagnosis, and a higher probability of POS and psychiatric medication than class 1 and class 3; 3) patients with advanced cancer stage, high somatic comorbidity, a higher probability of a psychiatric diagnosis and POS than class 1, and no psychiatric medication. Conclusion: This study indicated a high prevalence of psychiatric disorders among patients with breast cancer and a discrepancy between the number of patients having a psychiatric disorder and those receiving psychiatric medication. The identification of subgroups might contribute to better tailored treatment for those patients whose needs are insufficiently met.

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Keywords: Psycho-oncology, Psychiatric treatment, Breast cancer, Psychiatric medication, Psychiatric comorbidity

## Introduction

Breast cancer is the most common cancer and the leading cause of cancer deaths in women.<sup>1,2</sup> Globally, 2.1 million women are diagnosed with breast cancer every year, and the highest incident

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rates can be found in Northern and Western Europe, North America, Australia and New Zealand.<sup>3</sup> Major risk factors for breast cancer include female sex, age, family history, early menarche, late menopause, obesity in postmenopausal women, nulliparity, and first childbirth after age 30.<sup>1,3</sup>

A breast cancer diagnosis and the associated therapy can be extremely stressful. It poses a threat to an organ that symbolizes femininity and sexuality and may greatly affect the patients' self-representation of their body and identity. Between 15% and 54% of breast cancer patients suffer from distress caused by the disease itself or the treatment in terms of both physical and psychological aspects, such as pain, fatigue, feelings of fear, hopelessness and desperation. In some cases, distress can escalate to the magni-

tude of a psychiatric disorder. In fact, a breast cancer diagnosis is associated with a considerably high probability of occurrence of psychiatric disorders. <sup>10</sup> Previous studies indicated that the prevalence of psychiatric disorders in patients with breast cancer ranges from nine to 55%, particularly depression, anxiety, and adjustment disorders. <sup>11-19</sup> These statistics imply that, in comparison with the general population, breast cancer patients exhibit a higher prevalence of psychiatric disorders. <sup>4</sup> Furthermore, many patients with breast cancer suffer from multiple psychiatric disorders simultaneously, and these disorders are present in both early- and late-stage disease. <sup>15,20</sup> Breast cancer patients who develop a psychiatric disorder often struggle with impaired adaptive capacities and diminished coping skills. <sup>4</sup> Consequently, adherence to therapy decreases, symptom load increases, and quality of life (QoL) deteriorates, which finally impact the course of the disease. <sup>15,19-22</sup>

Thus, it is important to identify and treat psychiatric comorbidities in patients with breast cancer to improve treatment adherence and QoL. For instance, psycho-oncological support (POS) is an effective measure to improve QoL and to reduce distress and psychiatric symptoms. <sup>23-26</sup> On the other hand, psychiatric medication is commonly used in the treatment of psychiatric disorders in cancer patients. <sup>27</sup> Although both approaches have demonstrated to be effective in the treatment of psychiatric symptoms in patients with breast cancer, a significant proportion remains untreated. <sup>25,27</sup>

Our exploratory study aimed (1) to evaluate the proportion of breast cancer patients with a psychiatric diagnosis, POS and psychiatric medication in a sample of a Comprehensive Cancer Center. As a novelty, we also aimed (2) to investigate the association between psychiatric diagnoses, POS, psychiatric medication, and, as important prognostic factors, tumor stage and somatic comorbidity,<sup>28</sup> using latent class analysis (LCA). Our goal was to distinguish specific subgroups of patients with different psychiatric profiles to

contribute to a more tailored treatment approach of patients with breast cancer.<sup>29</sup>

### **Methods**

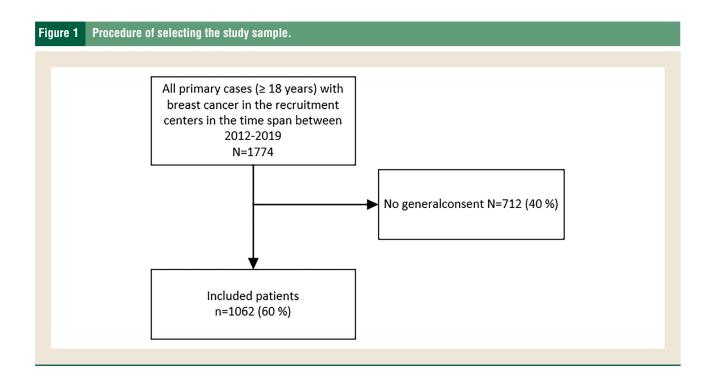
## Subjects and Data Collection

For this study, we retrosprectively included 1062 inpatients with an initial diagnosis of breast cancer who were diagnosed and treated at the Comprehensive Cancer Center Zurich (CCCZ), University Hospital Zurich, between 2012 and 2019 (see Figure 1). We excluded patients who received their diagnosis prior to 2012, those who did not sign a general consent for research at the beginning of their treatment, those below the age of 18, and men with a breat cancer diagnosis. The data were retrieved from the electronic case files via the hospital information system (KISIM, Cistec AG) and the institutional cancer register of the CCCZ (Oncostar, IT-Choice). The study was approved by the Ethics Committee of the State of Zurich, Switzerland (BASEC No. 2020-00977; June 2020).

#### Measurements

The distress thermomenter is a commonly used screening tool for distress. <sup>30</sup> In the CCCZ, it is administered by nurses to patients during inpatient treatment and combined with the question, whether POS is requested. Patients with a score above the cut-off and/ or a wish for POS are referred to internal POS services of the cancer center by the treating physician. The POS staff consists of psychiatrists and clinical psychologists who provide supportive interventions (eg, regular visits including psychoeducation and conversational therapy) to help patients to cope with their disease and prescribe psychiatric medication based on common guidelines.

Psychiatric medication was divided into five classes, applying the Anatomical Therapeutic Chemical (ATC) codes: antidepressants (N06A), antipsychotics (N05A), antiepileptics (N03), benzodi-



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azepines and other sedatives (N05B and N05C), and opioids (N02A and N07B). We defined opioid treatment as psychiatric medication according to 31 and 32 Psychiatric diagnoses were classified according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10), including F00-F99. The psychiatric diagnoses were extracted from the hospital's clinical information system by a psychiatrist. The diagnoses were already encoded as ICD-10 diagnoses. No mental symptoms or syndromes that were described were transcribed into diagnoses. Patients received their psychiatric diagnoses from psychiatric inpatient and outpatient treatment and primary care settings.

The stage of cancer was classified according to the Union for International Cancer Control (UICC).<sup>33</sup> Additionally, we analyzed the age-adjusted Charlson comorbidity index (CCI). The CCI was developed to predict the contribution of chronic comorbid diseases to mortality.<sup>34-36</sup>

#### Statistical Procedures

For statistical analysis, we used IBM SPSS Statistics, version 29 (Armonk, NY: IBM Corp). In a first step, different calculations, such as mean scores, standard deviations and relative and absolute distributions were performed to describe various patient characteristics, such as age, civil status, nationality, stage of cancer, CCI, cancer therapy (surgery, radiotherapy, systemic therapy), POS and psychiatric medication. To compare characteristics between patients diagnosed with versus without a psychiatric diagnosis, we used an unpaired t-test for continuous and a chi-square test for categorical variables. Significance level (two-sided p-value) was set at p < 0.05.

The LCA was performed using the R program for Statistical Computing (version 1.2.1578)<sup>37</sup> with poLCA packages.<sup>38</sup> LCA is a statistical model to identify subtypes of related cases (latent classes) from multivariate categorical data and distinguishing each cluster.<sup>39</sup> Compared to other statistical approaches, which analyze classes or clusters, it has several advantages.<sup>29</sup> An LCA is an exploratory technique to detect groups of patients with comparable symptom experiences. 40,41 In this way, distinct symptom profiles and symptom subgroups can be identified and clinicians are enabled to target support toward specific subgroups of patients.<sup>39,42,43</sup> The appropriate number of classes was identified using the Akaike information criterion (AIC), the Bayesian information criterion (BIC), the sample size-adjusted BIC (SSABIC), the Lo-Mendell-Rubin likelihood-ratio test and entropy. 42 Usually, the class solution with the lowest AIC, BIC, SSABIC and entropy values represents the best LCA model.

## **Results**

Sociodemographic and clinical variables are depicted in Table 1. The average age (standard deviation) was  $58.1 \pm 14.3$  years. All examined variables except for age did not differ significantly between patients with a psychiatric diagnosis and those without. In this study, 109 patients received both POS and psychiatric medication, 104 patients received only POS, and 527 (including opioids), respectively, 142 (excluding opioids) patients were exclusively treated with psychiatric medication. Total 322 patients did not receive any psychiatric treatment.

Table 2 illustrates all psychiatric diagnoses that were present in the study sample. One third of all breast cancer patients were diagnosed with a psychiatric disorder. Most patients suffered from anxiety, stress-related or somatoform disorders, followed by patients with an affective disorder and those with psychoactive substance use.

The 3-class solution demonstrates the best LCA model quality (see Table 3). In the 3-class solution of the LCA, conditional item response probabilities show how classes differentiate (see Table 4 and Figure 2). In class 1 (63% estimated population share), patients seem to be most probable to have a low cancer stage, low somatic comorbidity, no psychiatric diagnosis, no psychiatric medication and no POS. Class 2 (27% estimated population share) also indicates a low cancer stage and low somatic comorbidity. However, in this class, more than three-fourths of all patients had a psychiatric diagnosis, almost half of the patients received POS, one third received antidepressants, and one fourth benzodiazepines. In Class 3 (9% estimated population share), patients seem to be most probable to have an advanced cancer stage (III or IV) and high somatic comorbidity. One-quarter had a psychiatric diagnosis and received POS, while the probability of receiving psychiatric medication was relatively low.

## **Discussion**

This study investigated the proportion of female patients with breast cancer who had a psychiatric diagnosis, received POS and psychiatric medication in a naturalistic setting of a comprehensive cancer center. As a novelty, this study further explored the association between psychiatric diagnoses, POS, psychiatric medication, tumor stage and somatic comorbidity in patients with breast cancer. Using an LCA approach, we identified specific subgroups of patients with different profiles, potentially providing data for the development of tailored treatment approaches.

In this study, 31.5% of all breast cancer patients had a psychiatric diagnosis. The most prevalent psychiatric diagnoses were anxiety, stress-related and somatoform disorders (F4 group of ICD-10 classification), followed by affective disorders (F3 group). A recent metaanalysis<sup>44</sup> explored the prevalence of depression, anxiety and adjustment disorders in patients with cancer. Adjustment disorders were the most prevalent among these psychiatric disorders observed in patients with cancer. Adjustment dsiorders belong to the F4 group of the ICD-10 classification, alongside anxiety disorders, and are primarily characterized by symptoms related to anxiety and depression. Although we did not differentiate between ICD-10 subgroup diagnoses, our findings mainly align with prior studies that explored prevalences of psychiatric disorders in patients with cancer. 11-19,45-47 It is not surprising that these psychiatric disorders are the most prevalent in breast cancer patients, since anxiety is a natural response of the body to unfamiliar and stressful situations. Having breast cancer is a life-changing situation and a threat of vital significance, which also often causes a feeling of sadness, a lack of interest in previously enjoyable activities and depression.<sup>47</sup> In line with prior studies, 15,20 psychiatric diagnoses were present throughout the course of the disease, regardless of cancer stage or somatic comorbidity.

Given the considerable prevalence of psychiatric diagnoses, the identification and treatment of patients in need becomes even more

Table 1	Study Sample Characteristics
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		Total (N = 1062)	Psychiatric Diagnosis $(n=334)$	No Psychiatric Diagnosis (N = 728)	
		n (%)	n (%)	n (%)	<i>P</i> -value
Age, mean (SD)		58.1 (14.3)	56.8 (14.5)	58.7 (14.1)	.046
Civil status	single	511 (48.1)	171 (51.2)	380 (52.2)	.762
	Not single	551 (51.9)	163 (48.8)	348 (47.8)	
Nationality	Swiss	774 (72.9)	223 (66.8)	551 (75.7)	.601
	European (non-Swiss)	206 (19.4)	79 (23.7)	127 (17.4)	
	non-European	82 (7.7)	32 (9.6)	50 (6.9)	
Stage of cancer					
	0	118 (11.1)	33 (9.9)	85 (11.7)	.601
	I	385 (36.3)	133 (39.8)	252 (34.6)	
	II	374 (35.2)	113 (33.8)	261 (35.9)	
	III	122 (11.5)	30 (9.0)	92 (12.6)	
	IV	63 (5.9)	25 (7.5)	38 (5.2)	
CCI	CCI<5	847 (79.8)	264 (79.0)	583 (80.1)	.695
	CCI≥5	215 (20.2)	70 (21.0)	145 (19.9)	
Therapy	Surgery	1009 (95%)	317 (94.9)	692 (95.1)	.92
	Radiotherapy	610 (57.4)	190 (56.9)	420 (57.7)	.805
	Systemic Therapy	858 (80.8)	275 (82.3)	583 (80.1)	.388
POS	yes	213 (20.1)	70 (21.0)	143 (19.6)	.623
	no	849 (79.9)	264 (79.0)	585 (80.1)	
Psychiatric medication	All	636 (59.9)	200 (59.9)	436 (59.9)	.998
	All, excluding opioids	251 (23.6)	67 (20.1)	184 (25.3)	.331
	Antidepressants	131 (12.3)	41 (12.3)	90 (12.4)	.968
	Antipsychotics	63 (5.9)	25 (7.5)	38 (5.2)	.147
	Antiepileptics	32 (3)	6 (1.8)	26 (3.6)	.116
	Benzodiazepines & other sedatives	122 (11.5)	30 (9)	92 (12.6)	.083
	Opioids	385 (36.3)	133 (39.8)	252 (34.6)	.101

Significant *P*-values are marked bold.

We used an unpaired t-test for continuous, and a chi-square test for categorical variables.

Abbreviations: n = number; SD = standard deviation; CCI = age-adjusted Charlson comorbidity index; POS = psycho-oncological support.

Table 2 Psychiatric Diagnoses of the Study Sam	ple
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		Frequency	Percent
No psychiatric diagnosis		728	68.55
psychiatric diagnosis		334	31.45
	Organic, including symptomatic, mental disorders	0	0.00
	Mental and behavioural disorders due to psychoactive substance use	88	8.29
	Schizophrenia, schizotypal and delusional disorders	8	0.75
	Mood [affective] disorders	89	8.38
	Neurotic, stress-related and somatoform disorders	143	13.47
	Behavioural syndromes associated with physiological disturbances and physical factors	3	0.28
	Disorders of adult personality and behaviour	3	0.28
	Mental retardation	0	0.00
	Disorders of psychological development	0	0.00
	Behavioural and emotional disorders with onset usually occurring in childhood and adolescence	0	0.00
	Unspecified mental disorder	0	0.00

Psychiatric diagnoses according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10).

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Table 3 Latent Class Model Solutions and Fit Indices for 2-Class Through 4-Class Solutions							
Model S	Solution	Number of Estimated Parameters	Residual Degrees of Freedom	LL	AIC	BIC	Entropy
2-class		19	492	-3605.368	7248.736	7343.126	3.396008
3-class		29	482	-3558.076	7174.152	7318.221	3.354211
4-class		39	472	-3525.633	7129.266	7323.014	3.325023

The 3-class solution was selected because the BIC for that solution (bold) was lower than the BIC for both the 2-class and 4-class solutions. Abbreviations: AIC = Akaike information criterion; BIC = Bayesian information criterion; LL = log likelihood.

Table 4 Conditional Iter	n Response Probabili	ties of a Patient Withi	n a Particular Class to	Provide a Specific Item Response
Item	Class 1	Class 2	Class 3	Max. Difference/Within Category
Estimated class size % (n)	0.63 (n = 668)	0.27 (n = 291)	0.09 (n = 103)	
Stage of cancer				
0,1,11	0.9232	0.8784	0.0446	88%
III, IV	0.0768	0.1216	0.9554	
CCI				
<5	0.8423	0.8779	0.2795	83%
≥5	0.1577	0.1221	0.7205	
FDX				
No	0.8762	0.2337	0.7268	64%
Yes	0.1238	0.7663	0.2732	
POS				
No	0.9313	0.515	0.7489	42%
Yes	0.0687	0.485	0.2511	
AD				
No	0.9664	0.6609	0.9052	30%
Yes	0.0336	0.3391	0.0948	
AP				
No	0.9998	0.9115	0.9118	9%
Yes	0.0002	0.0885	0.0882	
AE				
No	0.9917	0.9312	0.9379	6%
Yes	0.0083	0.0688	0.0621	
BZD				
No	0.8119	0.7399	0.8483	11%
Yes	0.1881	0.2601	0.1517	
OPI				
No	0.9658	0.8828	0.8344	13%
Yes	0.0342	0.1172	0.1656	

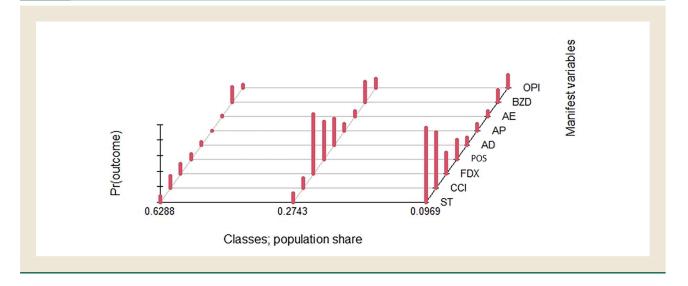
Conditional item response probabilities above 0.80 are in bold.

Abbreviations: AD=antidepressant medication; AP = antipsychotic medication; AE = antiepileptic medication; BZD = benzodiazepines (and other sedatives) medication; FDX= psychiatric diagnosis; OPI=opioid medication.

important. The large discrepancy between the number of patients with a psychiatric diagnosis and received POS is striking. Specifically, only 21.0% of cancer patients with a psychiatric diagnosis received POS, and 60%(including opioids) or 20% (excluding opioids) received psychiatric medication. However, this observation is supported by previous studies, indicating that the number of psychiatric or psychological interventions in patients with cancer is rather low.<sup>48</sup> There are many reasons possibly explaining this observation. Some patients decline these interventions to sustain a sense of normality in everyday life, which is called the "normality paradox." Other patients are not convinced that their psychiatric

symptoms are severe enough for treatment.<sup>50</sup> Moreover, perceived stigma in older patients and cultural views might be a barrier to psychiatric or psychological treatment.<sup>51-53</sup> On the other hand, there may also be insitutional barriers to appropriate treatment, such as lack of staff, lack of time and lack of training.<sup>54,55</sup> Some studies pointed out that cancer patients with a psychiatric disorder are less likely to receive psychiatric or psychological care than those without a psychiatric disorder,<sup>56,57</sup> although other studies found depressive mood and high levels of anxiety to be predictive of expressing the wish for POS.<sup>58,59</sup> Oncologists, who skillfully recommend psychiatric interventions and destigmatization of psychosocial problems

Figure 2 Graphical representation of conditional item response probablilities. Abrreviations: ST = stage of cancer; CCI = age-adjusted Charlson comorbidity index; FDX = psychiatric diagnosis; POS = psycho-oncological support; AD = antidepressant medication; AP = antipsychotic medication; AE = antiepileptic medication; BZD = benzodiazepines (and derivatives) medication; OPI = opioid medication.



could increase patients' request of those services. <sup>58,60</sup> Furthermore, the discrepancy between the number of patients with a psychiatric diagnosis and received psychiatric medication could possibly hint at a positive effect of POS for some patients, who may not need further psychiatric medication. Moreover, patients' fears of potential side effects might prevent them from taking any psychiatric medication.

Interestingly, 25% of patients without a psychiatric diagnosis received psychiatric medication (excluding opioids). This raises the question whether some medication might be given without necessary indication. Alternatively, this could be explained by a potential high prevalence of anxiety symptoms and the application of benzo-diazepines and other sedatives in breast cancer patients without a psychiatric diagnosis (see Table 1).

Additionally, the identification of subgroups of cancer patients with different psychiatric profiles might be an effective approach to improve psychiatric care in patients with breast cancer. In our study, we identified three different patient classes. Patients in class 1 are most probable to have a low cancer stage, low somatic comorbidity, no psychiatric diagnosis, no psychiatric medication and to not receive POS. Patients in class 2 are also likely to have a low cancer stage and low somatic comorbidity. However, most patients in class 2 are likely to have a psychiatric disorder, with almost half receiving POS and a quarter to a third likely to receive benzodiazepines or antidepressants. Patients in class 3 have advanced cancer and high somatic comorbidity, with one quarter having a psychiatric diagnosis and receiving POS. Psychiatric medication is given only in rare cases, mainly opioids and benzodiazepines, probably because of increased pain levels and agitation. Taken together, these results suggest that patients in class 1 may be able to cope with their mostly low stage breast cancer adequately and are not primarily affected by psychiatric disorders, and thus may not necessarily need POS or psychiatric medication. On the other hand, patients in class 2 may have more difficulties coping with their disease and

seem to struggle with psychiatric disorders. Although some of these patients are receiving POS or psychiatric medication, future research might focus on why this is not the case for every cancer patient with a psychiatric disorder. Finally, those patients in class 3, who have a psychiatric diagnosis also seem to receive POS, which is an encouraging finding of our study. Still, it is not obvious why those patients are less likely to receive psychiatric medication, and why patients with advanced cancer and high somatic comorbidity are less likely to be diagnosed with a psychiatric disorder than those with a low cancer stage and low somatic comorbidity. Perhaps, in such instances, the treatment team might prioritize addressing somatic complications and the cancer therapy itself. The recognition and treatment of psychiatric disorders might be neglected at these stages. In clinical practice, oncological treatment teams should be sensitized for recognizing patients with psychiatric problems or diagnoses, because these patients have an increased need for psychiatric care and an unfavourable disease course. 15,19-22 Indeed, previous studies indicated that psychiatric and psychological treatments, such as POS and psychiatric medication, may increase survival rates of breast cancer patients with and without a psychiatric disorder. 61,62 Our findings suggest that specific subgroups of breast cancer patients should receive more tailored treatment, such as POS, psychiatric medication, or even cognitive behavioral therapy or problem-solving therapy, as was previously suggested.<sup>63</sup>

Our study has several strengths, such as the large sample, including patients with various cancer stages and treatments, and the advanced statistical approach. However, there are also notable limitations. Generalizability is limited, because the study was conducted in a single Comprehensive Cancer Center in Switzerland. Our study sample includes only initial diagnoses of breast cancer of inpatients, who were diagnosed and treated at the CCCZ. Therefore, our findings may not reflect the real world scenario including outpatients as well. Retrospective file analysis is prone to

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human errors in documentation, and cultural aspects and treatment guidelines may change over time, which might have an impact on patients' perception of or suffering from psychiatric symptoms, as well as physicians' sensitivity in diagnosing such disorders. Furthermore, patients with substance use, such as smoking, were defined as having a psychiatric disorder. This classification is correct by definition of the ICD-10, but smoking does not necessarily indicate the need for POS or psychiatric medication. Therefore, we focused on the two other main categories of psychiatric disorders (adjustment and anxiety or affective disorders) in the interpretation of the results. We defined opioid treatment as psychiatric medication, which is debatable. However, it is a psychoactive substance, which is often used in the treatment of breast cancer and its associated symptoms, such as pain, and these symptoms might eventually lead to depression and anxiety. Additionally, our LCA approach examines each variable separately (such as opioids, benzodiazepines, antiepileptics, antipsychotics, antidepressants), which might reduce the possibility of biased results. We also did not investigate whether our patients developed a psychiatric disorder after the breast cancer diagnosis or before.

### **Conclusions**

The present study highlights a high prevalence of psychiatric disorders among patients with breast cancer and showed a discrepancy between the number of patients having a psychiatric disorder and those receiving POS and/ or psychiatric medication. Given the results of our study, we recommend that healthcare providers pay more attention to the psychiatric aspects of those patients, since those patients are at greater risk of having an unfavourable disease course and might benefit the most from psychiatric and psychological treatment. Psychiatric interventions have proven to successfully increase survival rates and reduce psychiatric symptoms in breast cancer patients.<sup>61,62</sup> Since such interventions require patient motivation, proper information about services and motivational interviewing could increase uptake in those who are hesitant.<sup>58,60</sup>

## Clinical Practice Points

- · Regular Mental Health Screening: Incorporate regular mental health assessments as an integral part of breast cancer patient care to identify psychiatric disorders at an early stage.
- Emphasis on the Importance of Psycho-oncological Support (POS): Recognize that providing psycho-oncological support can significantly contribute to addressing the mental health needs of breast cancer patients and should be integrated into the treatment
- Individualized Treatment Approaches: Tailor treatment plans to meet the specific needs of patients, considering factors such as cancer stage, existing comorbidities, and diagnosed psychiatric conditions.
- Closing Care Gaps: Develop and implement strategies to reduce the gap between the number of breast cancer patients with psychiatric diagnoses and those receiving psychopharmacological treatment, ensuring that all eligible patients receive appropriate care.
- Promoting Interdisciplinary Collaboration: Encourage collaboration among healthcare professionals, including oncologists, psychiatrists, and psycho-oncologists, to ensure comprehensive

care that addresses both physical and mental aspects of breast cancer treatment, thereby improving patient health and wellbeing.

## **Declarations**

Ethics approval and consent to participate: The study was reviewed and approved by the Ethics Committee of the State of Zurich, Switzerland (Ref.-No. BASEC-NR. 2020-00977). This is a retrospective study. For this type of study formal consent is not required. Informed consent was waived by the same Ethics Committee that approved the study (Ethics Committee of the State of Zurich, Switzerland, BASEC NR. 2020-00977; June 2020).

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

## Availability of data and materials

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

### **Disclosure**

The authors have no conflicts of interests that are directly or indirectly related to the research.

## **CRediT** authorship contribution statement

Jan Ben Schulze: Writing – review & editing, Writing – original draft, Supervision, Software, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. Marc Dörner: Writing - review & editing, Writing - original draft, Conceptualization. Mona Huber: Writing - original draft, Formal analysis, Conceptualization. Katja-Daniela Jordan: Writing – review & editing. Roland von Känel: Writing - review & editing. Sebastian **Euler:** Writing – review & editing.

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## References

- 1. Key TJ, Verkasalo PK, Banks E. Epidemiology of breast cancer. Lancet Oncol. 2001:2(3):133-140.
- Katsura C, Ogunmwonyi I, Kankam HK, Saha S. Breast cancer: presentation, investigation and management. Br J Hosp Med (Lond). 2022;83(2):1–7.

  3. Ginsburg O, Bray F, Coleman MP, et al. The global burden of women's cancers:
- an unmet grand challenge in global health. *Lancet*. 2017;389(10071):847–860.

  4. Izci F, Ilgün AS, Findikli E, Özmen V. Psychiatric symptoms and psychosocial problems in patients with breast cancer. *J Bresat Health*. 2016;12(3):94–101.
- 5. Gagnon P, Massie MJ, Holland JC. The woman with breast cancer: psychosocial considerations. Cancer Bulletin. 1993;45:538-542.
- 6. Baider L, Andritsch E, Uziely B, et al. Do different cultural settings affect the psychological distress of women with breast cancer? a randomized study. Eur J Cancer Care. 2003;12:263-273.
- 7. Sebri V, Mazzoni D, Triberti S, Pravettoni G. The impact of unsupportive social support on the injured self in breast cancer patients. Front Psychol.
- 8. Sebri V, Triberti S, Pravettoni G. Injured self: autobiographical memory, selfconcept, and mental health risk in breast cancer survivors. Front Psychol. 2020:11:607514.

- An Y, Fu G, Yuan G. Quality of life in patients with breast cancer: the influence of family caregiver's burden and the mediation of patient's anxiety and depression. J Nerv Ment Dis. 2019;207(11):921–926.
- Berard RM. Depression and anxiety in oncology: the psychiatrist's perspective. J Clin Psychiatry. 2001;6:58–61.
- Lueboonthavatchai P. Prevalence and psychosocial factors of anxiety and depression in breast cancer patients. J Med Assoc Thai. 2007;90:2164–2174.
- Pasacreta JV. Depressive phenomena, physical symptom distress and functional status among women with breast cancer. Nursing Research. 1997;4:214–221 46.
- Gallagher J, Parle M, Cairns D. Appraisal and psychological distress six months after diagnosis of breast cancer. Br J Health Psychol. 2002;7:365–376.
- Ramirez AJ, Richards MA, Jarrett SR. Fentiman IS. Can mood disorder in women with breast cancer be identified preoperatively? Br J Cancer. 1995;72:1509–1512.
- Kissane DW, Grabsch B, Love A, Clarke DM, Bloch S, Smith GC. Psychiatric disorders in women with early stage and advanced breast cancer: a comparative analysis. Aust N Z J Psychiatry. 2004;38:320–326.
- Mehnert A, Koch U. Psychological comorbidity and health-related quality of life and its association with awareness, utilization, and need for psychosocial support in a cancer register-based sample of long-term breast cancer survivors. J Psychosom Res. 2008;64:383–391.
- Christensen S, Zachariae R, Jensen AB, et al. Prevalence and risk of depressive symptoms 3–4 months post-surgery in a nationwide cohort study of Danish women treated for early stage breast-cancer. *Breast Cancer Res Treat*. 2009;113:339–355.
- Hopwood P, Howell A, Maguire P. Psychiatric morbidity in patients with advanced cancer of the breast: prevalence measured by two self-rating questionnaires. Br J Cancer. 1991;64:349–352.
- Karakoyun-Celik O, Gorken I, Sahin S, Orcin E, Alanyali H, Kinay M. Depression and anxiety levels in woman under follow-up for breast cancer: relationship to coping with cancer and quality of life. *Med Oncol*. 2010;27:108–113.
- Kadan-Lottick NS, Vanderwerker LC, Bkock SD, Zhang B, Prigerson HG. Psychiatric disorders and mental health service use in patients with advanced cancer. Cancer. 2005;104:2872–2881.
- Fann JR, Thomas-Rich AM, Katon WJ, et al. Major depression after breast cancer: a review of epidemiology and treatment. Gen Hosp Psychiatry. 2008;30:112–126.
- Montazeri A. Health-related quality of life in breast cancer patients: a bibliographic review of the literature from 1974 to 2007. J Exp Clin Cancer Res. 2008;27:32.
- Schiel RO, Brechtel A, Hartmann M, et al. Multidisciplinary health care needs of psychologically distressed cancer patients in a comprehensive cancer center. Dtsch Med Wochenschr. 2014;139:587–591.
- Mitchell AJ. Screening for cancer-related distress: when is implementation successful and when is it unsuccessful? Acta Oncol. 2013;52:216–224.
- Hart SL, Hoyt MA, Diefenbach M, et al. Meta-analysis of efficacy of interventions for elevated depressive symptoms in adults diagnosed with cancer. J Natl Cancer Inst. 2012;104:990–1004.
- Faller H, Schuler M, Richard M, Heckl U, Weis J, Küffner R. Effects of psycho-oncologic interventions on emotional distress and quality of life in adult patients with cancer: systematic review and meta-analysis. *J Clin Oncol.* 2013;31:782–793.
- Lee SA, Nam CM, Kim YH, Kim TH, Jang S-I, Park E-C. Impact of onset of psychiatric disorders and psychiatric treatment on mortality among patients with cancer. Oncologist. 2020;25(4):e733–e742.
- Land LL, Dalton SO, Jorgensen TL, Ewertz M. Comorbidity and survival after early breast cancer. A review. Crit Rev Oncol Hematol. 2012;81(2):196–205.
- Schulze JB, Günther MP, Riemenschnitter C, Wicki A, von Känel R, Euler S. Distinct psycho-oncological support incliniations and needs in patients with cancer: a large sample latent class analysis approach. *Gen Hosp Psychiatry*. 2022;75:17–22.
- Ownby KK. Use of the distress thermometer in clinical practice. J Adv Pract Oncol. 2019;10:175–179.
- Tenore PL. Psychotherapeutic benefits of opioid agonist therapy. J Addict Dis. 2008;27(3):49–65.
- Janakiram C, Okunev I, Tranby EP, Fontelo P, Iafolla TJ, Dye BA. Opioids for acute and chronic pain when receving psychaitric medications. PLOS OONE. 2023;18(9):e0286179.
- Bertero L, Massa F, Metovic J, et al. Eighth edition of the UICC classification of malignant tumours: an overview of the changes in the pathological TNM classification criteria—what has changed and why? Virchows Arch. 2018;472:519–531.
- Charlson ME, pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–383.
- Quan H, Li B, Couris CM, et al. Updating and validating the charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol. 2011;173:676–682.
- Kim DH, Park HC, Cho A, et al. Age-adjusted Charlson comorbidity index score is the best predictor for severe clinical outcome in the hospitalized patients with COVID-19 infection. *Medicine*. 2021;100:e25900.
- Team RC. R: a language and environment for statistical computing. Version 3.1.2 [computer program]. Vienna, Austria: R foundation for Statistical Computing; 2014.

- 38. Linzer D, Lewis J. poLCA: polytomous variable latent class analysis. R package (version 1.4) [computer program]. 2013.
- Wong E, Zhang L, Kerba M, et al. Analysis of symptom clusters in patients with brain metastases with three different statistical methods. J Pain Manag. 2015;8(2):133.
- Barsevick AM, Whitmer K, Nail LM, Beck SL, Dudley WN. Symptom cluster research: conceptual, design, measurement, and analysis issues. J Pain Symptom Manag. 2006;31(1):85–95.
- Chen E, Khan L, Zhang L, et al. Symptom clusters in patients with brain metastases – a reanalysis comparing different statistical methods. J Radiat Oncol. 2013;2(1):95–102.
- Scotto Rosato N, Baer JC. Latent class analysis: a method for capturing heterogeneity. Soc Work Res. 2012;36(1):61–69.
- Nylund KL, Asparouhov T, Muthen BO. Deciding on the number of classes in latent class analysis and growth mixture modeling: a Monte Carlo simulation study. Struct Equ Model Multidiscip J. 2007;14(4):535–569.
- Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a metaanalysis of 94 interview-based studies. *Lancet Oncol.* 2011;12(2):160–174.
- Tsaras K, et al. Assessment of depression and anxiety in breast cancer patients: prevalence and associated factors. Asian Pac J Cancer Prev. 2018;19(6):1661–1669.
- AyalewPrevalence of depression and anxiety symptoms and their determinant factors among patients with cancer in southern Ethiopia: a cross-sectional study. BMJ Open. 2022;12(1):e051317.
- Soqia J, Al-shafie Agha LY, Alameer MB, Alhomsi D, Saadoun R, Saifo M. Depression, anxiety and related factors among Syrian breast cancer patients: a cross-sectional study. BMC Psychiatry. 2022;22:796.
- Schulze JB, Dörner M, Usas H, Günther MP, von Känel R, Euler S. Reading wishes from the lips: cancer patients' need for psycho-oncological support during inpatient and outpatient treatment. *Diagnostics*. 2022;12:2440.
- Carolan C, Smith A, Davies G, Forbat L. Seeking, accepting and declining help for emotional distress in cancer: a systematic review and thematic synthesis of qualitative evidence. *Eur J Cancer Care*. 2017;27:e12720.
- Clover KA, Mitchell AJ, Britton B, Carter G. Why do oncology outpatients who report emotional distress decline help? *Psycho-Oncology*. 2015;24:812–818.
- Kacel EL, Pereira DB, Estores IM. Advancing supportive oncology care via collaboration between psycho-oncology and integrative medicine. Support Care Cancer. 2019;27:3175–3178.
- Stark A, Kaduszkiewicz H, Stein J, et al. A qualitative study on older primary care patients' perspectives on depression and its treatments—potential barriers to and opportunities for managing depression. BMC Fam Pract. 2018;19:2.
- Bracke P, Delaruelle K, Verhaeghe M. Dominant cultural and personal stigma beliefs and the utilization of mental health services: a cross-national comparison. *Front Sociol.* 2019;4:40.
- Knies AK, Jutagir DR, Ercolano E, Pasacreta N, Lazenby M, McCorkle R. Barriers and facilitators to implementing the commission on cancer's distress screening program standard. *Palliat Support Care*. 2019;17:253.
- Fradgley EA, Byrnes E, McCarter K, et al. A cross-sectional audit of current practices and areas for improvement of distress screening and management in Australian cancer services: is there a will and a way to improve? Support Care Cancer. 2020;28:249–259.
- Günther MP, Kirchebner J, Ben Schulze J, Götz A, von Känel R, Euler S. Uncovering barriers to screening for distress in patients with cancer via machine learning. J Acad Consult Psychiatry. 2022;63:163–169.
- Günther MP, Schulze JB, Jellestad L, Mehnert-Theuerkauf A, von Känel R, Euler S. Mental disorders, length of hospitalization, and psychopharmacy—New approaches to identify barriers to psychological support for patients with cancer. *Psycho-Oncology*. 2021;30:1773–1781.
- Loth FL, Meraner V, Holzner B, Singer S, Virgolini I, Gamper EM. Following patient pathways to psycho-oncological care: Identification of treatment needs by clinical staff and electronic screening. *Psycho-Oncology*, 2018;27:1312–1319.
- clinical staff and electronic screening. Psycho-Oncology. 2018;27:1312–1319.
   59. Schweer C, Doering S, Haier J, et al. Psychooncological interventions—what do cancer patients aged 60 years or older wish for? Z Psychosom Med Psychother. 2011;57:223–232.
- Frey Nascimento A, Tondorf T, Rothschild SI, et al. Oncologist recommendation matters—predictors of psycho-oncological service uptake in oncology outpatients. *Psycho-Oncology*. 2019;28:351–357.
- Giese-Davis J, et al. Decrease in depression symptoms is associated with longer survival in patients with metastatic breast cancer: a secondary analysis. J Clin Oncol. 2011;29(4):413

  –420.
- **62.** Andersen BL, et al. Psychologic intervention improves survival for breast cancer patients: a randomized clinical trial. *Cancer*. 2008;113(12):3450–3458.
- Hart SL, Hoyt MA, Diefenbach M, et al. Meta-analysis of efficacy of interventions for elevated depressive symptoms in adults diagnosed with cancer. J Natl Cancer Inst. 2012;104(13):990–1004.