Review Article | Palliative Medicine and Palliative Care for Incurable Cancer

End-of-life care for cancer patients with pre-existing severe mental disorders—a systematic review

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Background: Cancer patients with pre-existing severe mental disorders (SMDs) less frequently receive guideline recommended cancer treatment and have a higher cancer mortality. However, knowledge is needed concerning end-of-life care in this patient group. The aim of this systematic review was to provide an overview of the literature concerning end-of-life care in cancer patients with pre-existing SMD.

Methods: A systematic search was conducted in the following databases: PubMed, Embase and Science Direct and all results were downloaded to Endnote on 1st of September 2023. The review was registered on International Prospective Register of Systematic Reviews (PROSPERO) (ID: CRD42023468571). The quality of the studies was assessed according to the Newcastle-Ottawa Scale.

Results: Ten studies fulfilling the inclusion criteria were included. There was a recurring pattern indicating a difference between the end-of-life care received by cancer patients with SMD, compared to those without. Cancer patients with pre-existing SMD received more palliative end-of-life care but less high-intensive-end-of-life (HIEOL) care, e.g., less hospitalisations and chemotherapy at the end of life, and died less frequently at hospital.

Conclusions: The study indicates that patients with pre-existing SMD and cancer more often received palliative end-of-life care and less HIEOL care compared to controls. Further research regarding the difference in end-of-life care is lacking, including the consequences of less intense HIEOL care for this patient group. Thus, further studies are needed to identify reasons for less intense HIEOL among cancer patients with pre-existing SMD.

Keywords: Severe mental disorder (SMD); end-of-life care; cancer; high-intensive-end-of-life (HIEOL); palliative care

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Introduction

The end-of-life care of patients with cancer and pre-existing severe mental disorders (SMDs) may be a challenge for healthcare professionals and may not meet recognized standards for care (1). The terms severe mental illness (SMI) or SMD are synonyms and both refer to the diagnosis moderate to severe depression, bipolar disorder, and schizophrenia or psychotic disorders (2,3). The total prevalence of SMD in the general population is approximately 4.5% (2). The presence of SMD has been associated with various inequalities in health such as a higher tendency of multi-morbidity and higher mortality (4).

The literature has shown that cancer patients with a pre-existing SMD less frequently receive guideline recommended cancer treatment (5). Furthermore, these patients have been reported to have a lower cancer survival rate compared to controls. The barriers in cancer trajectories have been attributed to patients' characteristics, provider characteristics and the structural framework of a given healthcare system (6). According to Bentson *et al.* the main barriers within these categories include lack of patients' self-care and ability to identify symptoms and signs, negative stereotyping of healthcare professionals and the division of healthcare (5).

In the case of life-limiting diseases such as cancer, the patients should be offered palliative care if palliative care needs exist. Palliative care aims to alleviate disease manifestations and increase quality of life rather than eliminate a disease (7). Thus, palliative care can be offered to patients from the time of diagnosis of a life-limiting disease until death. End-of-life care is the health care offered patients with an expected lifetime of less than a year (8). The goal of palliative end-of-life care is to address the physical, emotional, social, and spiritual needs of both the patient and the patient's family in the last months of a patient's life (8). As end-of-life care is beyond curative treatment, the level of care should be in accordance with the medical guidelines, and refrain from life-saving interventions, or high-intensity care. Nonetheless, the level of inappropriate, intensive treatment in end-of-life has been observed to differ between patient groups (9). The following parameters have been used as markers indicating high-intensive-end-of-life (HIEOL) care (9):

- In the last month of life:
  - >1 hospital admission, >1 utilization of the emergency department (ED) or ≥1 admission to an intensive care unit (ICU).
  - Receive artificial nutrition, receive an intervention such as surgery, imaging endoscopies or blood transfusion.
- In the last 2 weeks of life: receive chemotherapy.
- Death in acute in-hospital care.

Research regarding cancer patients with SMD has been sparse up to this point, and the existing literature have mainly focused on the observed increase in mortality (10,11). Little is known about the differences in end-of-life trajectories between cancer patients with and without SMD (12). The aim of this systematic review was to produce an overview of the literature concerning end-of-life care and HIEOL care in cancer patients with pre-existing SMD. We present this article in accordance with the PRISMA reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-23-589/rc) (13).

Highlight box

Key findings

- Cancer patients with pre-existing severe mental disorder (SMD) receive more palliative end-of-life care and less high-intensive-end-of-life (HIEOL) care compared to cancer patients without SMD.

What is known and what is new?

- Patients with cancer and pre-existing SMD have a higher cancer mortality and cancer treatment does not meet recognized standards for care.
- According to this systematic review the inequality does not regard end-of-life care since cancer patients with pre-existing SMD receive more sufficient palliative end-of-life care than cancer patients without SMD.

What is the implication, and what should change now?

- Further studies are needed to identify at what level (patient, health care provider or health care system) and for what reason the decisions for less intense HIEOL care are being made.

Methods

We conducted a systematic review and reported to the International Prospective Register of Systematic Reviews (PROSPERO) with ID: CRD42023468571 (14).

Eligibility criteria

Studies were included if they met all of the following criteria: included original data and focused on experience with palliative care for adult patients with cancer and pre-

existing SMD or models for palliative care for adult patients with cancer and pre-existing SMD or palliative or end-of-life care for adult patients with cancer and pre-existing SMD.

Studies were excluded if the publication languages were not in English or if the publications had a focus on the following themes: cancer patients who did not have SMD prior to the cancer diagnosis, screening for SMD or cancer, specific symptom alleviation or drugs, support for relatives, pediatric patients, COVID-19 or euthanasia. Furthermore, publications were excluded if they were case reports or if they only concerned one of the subjects: palliative care, cancer or psychiatry.

Search strategy

The literature search was performed on the 1st of September 2023 in three databases: PubMed, Embase and Science Direct. Hand searching was done by going through the reference list on reports that were included in the study.

As an example, PubMed were searched using the search string: ("Neoplasms"[MeSH] OR "neoplasm"[Title/Abstract] OR cancer[Title/Abstract] OR onco*[Title/Abstract]) AND ("Bipolar Disorder"[Title/Abstract] OR "major depression"[Title/Abstract] OR "unipolar depression"[Title/Abstract] OR "Schizophrenia"[Title/Abstract] OR Mental[Title/Abstract] OR psychiatric[Title/Abstract]) AND ("Palliative Medicine"[Mesh] OR "Palliative Care"[Mesh] OR "Terminal Care"[Mesh] OR "Hospice Care"[Mesh] OR palliat*[Title] OR end-of-life[Title] OR terminal*[Title]) AND (2000:2023[pdat]) NOT ("meta-analysis"[Publication Type] OR "review"[Publication Type] OR "systematic review"[Filter]). See Appendix 1 for search strings for the other databases.

Study selection

All results from the databases were downloaded to the citation manager Endnote, and a function in Endnote was used to remove duplicates. First, titles and abstracts were screened by the first author. When in doubt, both the first and last author screened the records. Afterwards, relevant records were read in full text by the first and last author.

Data collection process and data quality assessment

Data was extracted from the included studies by the first author and collected according to the PROSPERO protocol, with the following headings: author, year of publication, country of origin, study design and focus, population, key findings (14). The studies were assessed according to the Newcastle-Ottawa Scale modified for non-randomised studies (15,16) (see Table S1).

Results

Inclusion of reports

In total, the original search included 643 records of which 27 duplicates were immediately removed. A PRISMA flow diagram of the process is seen in *Figure 1*.

The remaining 616 records were screened in Endnote and 603 records were excluded based on the predetermined inclusion and exclusion criteria. The full texts of the remaining 13 reports were then sought for retrieval, and all of them were assessed for eligibility according to the predetermined inclusion and exclusion criteria. Of the 13 reports, three reports were excluded, and 10 reports were included in the systematic review (17-26). Detailed information about the 10 included reports can be seen in *Table 1*.

The quality assessment using the Newcastle-Ottawa Scale (15,16) is seen in Table S1 and shows that the included studies were of good quality with a score of 8–9 stars out of a maximum of 10.

Characteristics of included studies

The 10 included studies were all retrospective cohort studies from three different countries/regions: USA (17-19,24), Taiwan (20) and France (21-23,25,26). There was a minimum of one publication for each pre-existing SMD: schizophrenia (17,20,21,26), depression (18,19,22) and bipolar disorder (23). The remaining studies had mixed SMD-diagnoses in their populations (24,25). In all 1,050,663 patients were included in the 10 studies with sample sizes between 256 and 226,547.

End-of-life and HIEOL care

Populations with cancer and mixed SMDs

Fond *et al.* found that patients with pre-existing SMDs received fewer interventions than patients without SMD such as chemotherapy, surgery, medical imaging and endoscopy in end-of-life in the last 14 days of life along with fewer admissions in EDs and ICUs in the last

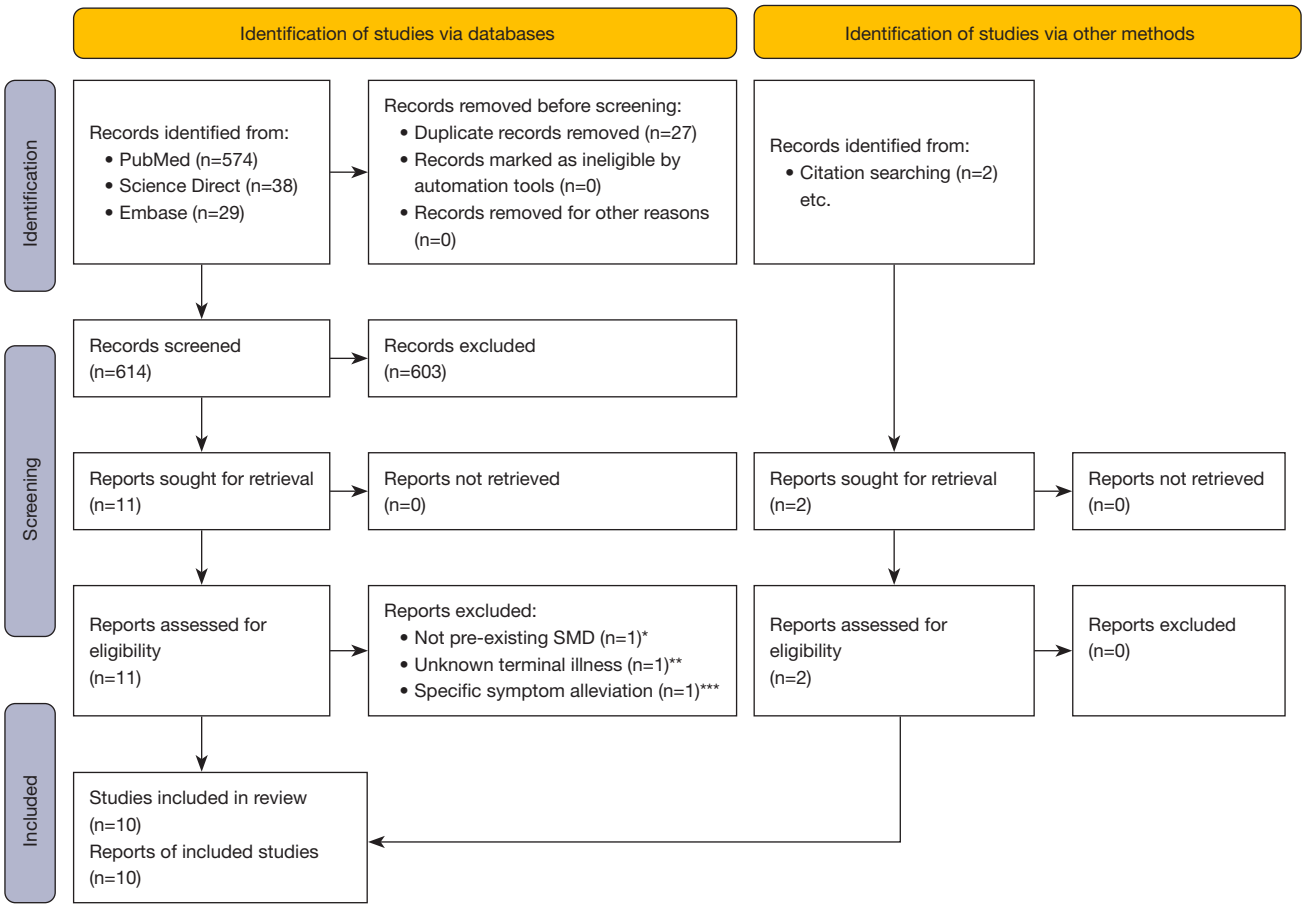

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Figure 1 The PRISMA flow-chart of the study. SMD, severe mental disorder.

31 days of life (25). However, they also found that patients with SMD also received specialized palliative care more frequently than patients without SMD [odds ratio (OR) =1.32; 95% confidence interval (CI): 1.15, 1.51] and had longer palliative care follow-up prior to death (25). On the contrary, Kashyap *et al.* found results indicating that elderly patients with pre-existing SMDs and cancer were more likely to have ED services in the last 30 days of life (OR =1.20; 95% CI: 1.16, 1.24) (24). However, looking at sub-groups of individual SMD diagnosis in the study, only patients with bipolar disorders were significantly more likely to have ED services in end-of-life (OR =1.12; 95% CI: 1.01, 1.24), whereas patients with depression (OR =0.97; 95% CI: 0.92, 1.03) and psychotic disorders (OR =0.98; 95% CI: 0.85, 1.12) did not.

Populations with cancer and pre-existing schizophrenia

Ganzini *et al.* found that veterans with schizophrenia were significantly less likely to receive chemotherapy in the trajectory (28% versus 43%, P=0.04). Furthermore, patients with schizophrenia received significantly higher quality of palliative end-of-life care on certain parameters, i.e., longer hospice stays (107 versus 63 days, P=0.05) and were more likely to have Physician orders for life-sustaining treatment

Table 1 An overview of the included studies and extracted data

Authors, year, country/region	Study design and focus	Population	Results	Quality assessment[†]
Ganzini *et al.*, 2010, USA (17)	Cross-sectional study. Cancer focus: no specific type. SMD focus: schizophrenia	256 veterans who died due to cancer, 60 (23.4%) patients had schizophrenia	Level of EOL was comparable between the groups. Patients with schizophrenia received a higher quality on the following measures: longer hospice stays (107 versus 63 days, P=0.05); more likely to have Physician orders for life-sustaining treatment documented (15% versus 5%, P=0.006); less likely to receive chemotherapy (28% versus 43%, P=0.04)	8/10
Doan, 2016, USA (18)	A retrospective cohort study. Cancer focus: no specific type. SMD focus: depression	84,947 patients, ≥66 years of age, were diagnosed with cancer from 2004–2011 and died within 3 years as a result of cancer, 5,072 (6.0%) patients had a pre-existing depression diagnosis	Patients with pre-existing depression received more quality EOL care: more likely use of hospice care (OR =1.20; 95% CI: 1.12, 1.28). Patients with pre-existing depression received less HIEOL care: less likely to have repeated hospitalizations (OR =0.91; 95% CI: 0.83, 0.99); ICU-visits (OR =0.89; 95% CI: 0.83, 0.94); in-hospital death (OR =0.83; 95% CI: 0.77, 0.89); receive ICU-service (OR =0.86; 95% CI: 0.79, 0.93) or chemotherapy late in the trajectory (OR =0.83; 95% CI: 0.70, 0.99)	8/10
McDermott *et al.*, 2018, USA (19)	A retrospective cohort study. Cancer focus: advanced NSCLC. SMD focus: depression	13,827 older adults (≥67 years of age) diagnosed with advanced NSCLC from 2009–2011, 1,485 (10.7%) patients had a pre-existing depression diagnosis	Patients with pre-existing depression received more quality EOL care: more often had more than 90 days of hospice care (OR =1.29; 95% CI: 1.06, 1.58). Patients with depression received less HIEOL care: lower odds of hospital admissions (OR =0.74; 95% CI: 0.62, 0.89); ICU admission (OR =0.78; 95% CI: 0.67, 0.90); in-hospital death (OR =0.75; 95% CI: 0.64, 0.87) and visits at ED visit in the last 30 days of life (OR =0.78; 95% CI: 0.62, 0.98)	8/10
Huang *et al.*, 2018, Taiwan (20)	A nationwide population-based cohort study. Cancer focus: colorectal cancer, liver cancer, lung cancer, breast cancer, oral cancer and prostate cancer. SMD focus: schizophrenia	9,555 patients >20 years of age who were newly diagnosed as having one of six common cancers between 2000 and 2012, 1,911 (20.0%) patients had schizophrenia	Patients with pre-existing schizophrenia received more HIEOL care: higher ICU utilization (OR =1.21; 95% CI: 1.07, 1.36) and more invasive interventions, such as cardiopulmonary resuscitation (OR =1.34; 95% CI: 1.15, 1.57); however, they received less chemotherapy (OR =0.60; 95% CI: 0.55, 0.66) and less often advanced diagnostic examinations, such as computed tomography/magnetic resonance imaging/sonography (OR =0.80; 95% CI: 0.71, 0.89)	8/10
Fond *et al.*, 2019, France (21)	Population-based cohort study. Cancer focus: brain cancer, liver cancer, or any metastatic solid cancer. SMD focus: schizophrenia	224,958 patients ≥15 years of age, with advanced cancer and had died in a hospital in France between Jan 1, 2013, and Dec 31, 2016, 2,481 (1.1%) individuals with pre-existing schizophrenia	Patients with pre-existing schizophrenia received more quality EOL care: more frequently admitted to palliative care units in the last 31 days of life (OR =1.61; 95% CI: 1.45, 1.80) and even more so in the last 3 days of life (OR =2.52; 95% CI: 2.25, 2.82) and had longer palliative care follow-up before death (β: 0.36; SD: 0.03). Patients with pre-existing schizophrenia received less HIEOL care: they received less chemotherapy, surgery, imaging, endoscopy, blood transfusions and acute care, and were less likely to die in ICU or ED (OR between 0.53–0.86)	9/10

Table 1 (*continued*)

Table 1 (*continued*)

Authors, year, country/region	Study design and focus	Population	Results	Quality assessment[†]
Fond *et al.*, 2020, France (22)	Nationwide cohort study. Cancer focus: brain cancer, liver cancer, or any metastatic solid cancer. SMD focus: recurrent major depressive disorder	226,547 patients aged ≥15 years of age who died from cancer in hospital in France, 4,070 (1.8%) individuals with depression	Patients with pre-existing depression received more quality EOL care: more frequently referred to palliative care in the last 31 days of life (OR =1.82; 95% CI: 1.66, 1.99) and in the last 3 days of life (OR =2.23; 95% CI: 2.05, 2.44). Patients with pre-existing depression received less HIEOL care in the last 31 days of life: less chemotherapy in the last 14 days of life (OR =0.70; 95% CI: 0.63, 0.79); less dialysis (OR =0.52; 95% CI: 0.33, 0.82); less blood transfusion (OR =0.82; 95% CI: 0.74, 0.91); less surgery (OR =0.82; 95% CI: 0.74, 0.91); less imaging (OR =0.69; 95% CI: 0.63, 0.74); less likely to be admitted to an acute care unit (OR =0.90; 95% CI: 0.84, 0.97); fewer deaths in the ICU/ED (OR =0.81; 95% CI: 0.73, 0.91). But more artificial nutrition (OR =1.37; 95% CI: 1.18, 1.58)	9/10
Fond *et al.*, 2020, France (23)	Nationwide cohort study. Cancer focus: brain cancer, liver cancer, or any metastatic solid cancer. SMD focus: bipolar disorder	224,492 patients ≥15 years of age, who died due to cancer in a France hospital between Jan 1, 2013, and Dec 31, 2016, 2,015 (0.9%) individuals with bipolar disorder	Patients with pre-existing bipolar disorder received more quality EOL care: higher chance of receiving palliative care in the last 31 days of life (OR =1.49; 95% CI: 1.32, 1.69) and in the last 3 days of life (OR =2.14; 95% CI: 1.89, 2.43). Patients with bipolar disorder received less HIEOL care: less chemotherapy (OR =0.77; 95% CI: 0.69, 0.86), less imaging (OR =0.76; 95% CI: 0.65, 0.90) and were less likely to die in the ICU/ED (OR =0.83; 95% CI: 0.70, 0.97)	9/10
Kashyap *et al.*, 2021, USA (24)	Population-based cohort study. Cancer focus: primary colorectal, pancreatic, gastric, hepatic, biliary, esophageal, small bowel, anal, and other (peritoneal, retroperitoneal, or unspecified) cancers. SMD focus: depression, bipolar disorder, psychotic disorders	160,367 patients ≥66 years of age at the time of diagnosis, that were diagnosed with gastrointestinal cancers between the years 2004 and 2013, 54,661 (34.1%) had a mental illness diagnosis and 15,647 (9.8%) had a SMD diagnosis	Patients with pre-existing mental illness diagnosis more frequently had >1 ED visit in the last 30 days of life (15.6% versus 13.3%, P<0.01). Of patients with pre-existing SMD the >1 ED use in the last 30 days of life was as follows: bipolar (16.5%; OR =1.21; 95% CI: 1.1, 1.34); psychotic disorders (15.6%; OR =1.12; 95% CI: 0.99, 1.28); depression (14.8%; OR =1.06; 95% CI: 1.01, 1.12)	9/10
Fond *et al.*, 2021, France (25)	Population-based cohort study. Cancer focus: breast cancer. SMD focus: no specific type	38,612 patients ≥15 years of age, who died due to breast cancer in a France hospital between Jan 1, 2014, and Dec 31, 2018, 1,742 (4.5%) women with SMD: 287 (0.7%) with bipolar disorder; 1,075 (2.8%) with depression; 380 (1.0%) with schizophrenia	Patients with pre-existing SMD received more quality EOL care: received more palliative care (OR =1.32; 95% CI: 1.15, 1.51) and extended palliative care follow-up prior to death. Patients with a SMD received less HIEOL care: less interventions such as chemotherapy, surgery, medical imaging and endoscopy in EOL along with less admissions in EDs and ICUs	9/10

Table 1 (*continued*)

Table 1 (*continued*)

Authors, year, country/region	Study design and focus	Population	Results	Quality assessment[†]
Viprey *et al.*, 2021, France (26)	Population-based cohort study. Cancer focus: lung cancer. SMD focus: schizophrenia	67,102 patients ≥15 years of age and had died from terminal lung cancer in a France hospital between Jan 1, 2014, and Dec 31, 2016, 633 (0.9%) individuals with schizophrenia	Patients with pre-existing SMD received more quality EOL care: started at an earlier point in palliative care and received more care compared to the controls (OR =1.27; 95% CI: 1.03, 1.56). Patients with pre-existing SMD received less HIEOL care: chemotherapy (OR =0.53; 95% CI: 0.41, 0.70) and surgery (OR =0.73; 95% CI: 0.59, 0.90)	9/10

[†], quality assessment was done according to the Newcastle-Ottawa Scale (15) modified for non-randomised studies (16). SMD, severe mental disorder; EOL, end-of-life; OR, odds ratio; CI, confidence interval; HIEOL, high-intensive-end-of-life; ICU, intensive care unit; NSCLC, non-small cell lung cancer; ED, emergency department; SD, standard deviation.

documented (15% versus 5%, P=0.006) (17). In accordance with these findings, Huang *et al.* found that patients with schizophrenia received less chemotherapy (OR =0.60; 95% CI: 0.55, 0.66) and less often received advanced diagnostic examinations, such as computed tomography/magnetic resonance imaging/sonography (OR =0.80; 95% CI: 0.71, 0.89) both when looking at 1 and 3 months prior to death compared to controls (20). On the other hand, Huang *et al.* demonstrated that patients with schizophrenia had a higher ICU utilization (OR =1.21; 95% CI: 1.07, 1.36) and more invasive interventions, such as cardiopulmonary resuscitation (OR =1.34; 95% CI: 1.15, 1.57). By comparison, Fond *et al.* found that patients with pre-existing schizophrenia less frequently received HIEOL care than patients without SMD (21). Patients with schizophrenia received less chemotherapy, surgery, imaging, endoscopy, blood transfusions and acute care in the last 31 days of life and were less likely to die in ICU or ED (OR between 0.53–0.86). Additionally, patients with schizophrenia were more frequently admitted to palliative care units in the last 31 days of life (OR =1.61; 95% CI: 1.45, 1.80), and even more so in the last three days of life (OR =2.52; 95% CI: 2.25, 2.82). Furthermore, they received a longer palliative care follow-up before death [β =0.36; standard deviation (SD): 0.03] (21). The results of Fond *et al.* were replicated in Viprey *et al.* where they found that patients with a pre-existing diagnosis of schizophrenia were observed to start at an earlier point in palliative care and receive more care compared to the controls (OR =1.27; 95% CI: 1.03, 1.56) (26). Furthermore, they received less HIEOL care than the controls (chemotherapy in the last 14 days of life (OR =0.53; 95% CI: 0.41, 0.70) and surgery in the last 31 days of life (OR =0.73; 95% CI: 0.59, 0.90).

Populations with cancer and pre-existing depression

Doan *et al.* demonstrated that pre-existing depression in cancer patients was associated with less HIEOL care intensity (18). Patients with depression were significantly less likely to have repeated hospitalizations (OR =0.91; 95% CI: 0.83, 0.99), ICU visits (OR =0.89; 95% CI: 0.83, 0.94), receive ICU service (OR =0.86; 95% CI: 0.79, 0.93) in-hospital death (OR =0.83; 95% CI: 0.77, 0.89), or receive chemotherapy 14 days before death (OR =0.83; 95% CI: 0.70, 0.99). Furthermore, patients with depression were more likely to utilise hospice care (OR =1.20; 95% CI: 1.12, 1.28) (18). Similar results are observed by McDermott *et al.*, as they found that patients with pre-existing depression were less likely to receive HIEOL care: lower odds of hospital admissions (OR =0.74; 95% CI: 0.62, 0.89), ICU admission (OR =0.78; 95% CI: 0.67, 0.90), in-hospital death (OR =0.75; 95% CI: 0.64, 0.87) and ED visits in the last 30 days of life (OR =0.78; 95% CI: 0.62, 0.98) (19). However, in their study they did not find a difference between the groups in receiving chemotherapy in the last 14 days of life. Additionally, patients with depression were significantly more likely to have more than 90 days of hospice care (OR =1.29; 95% CI: 1.06, 1.58). Comparably, Fond *et al.* demonstrated that patients with pre-existing depression less frequently received HIEOL care in end-of-life: less chemotherapy in the last 14 days of life (OR =0.70; 95% CI: 0.63, 0.79), less dialysis (OR =0.52; 95% CI: 0.33, 0.82), less blood transfusion (OR =0.82; 95% CI: 0.74, 0.91), less surgery (OR =0.82; 95% CI: 0.74, 0.91) and imaging (OR =0.69; 95% CI: 0.63, 0.74) (22). Furthermore, they were less likely to be admitted to an acute care unit (OR =0.90; 95% CI: 0.84, 0.97) and more seldomly died in the ICU or ED (OR =0.81; 95% CI: 0.73, 0.91). Albeit patients with pre-

existing depression received more artificial nutrition in the last 31 days of life (OR =1.37; 95% CI: 1.18, 1.58). Patients with depression also tended to be more frequently referred to palliative care in the last 31 days of life (OR =1.82; 95% CI: 1.66, 1.99) and in the last 3 days of life (OR =2.23; 95% CI: 2.05, 2.44) (22).

Populations with cancer and pre-existing bipolar disorder

Only one study specifically examined palliative end-of-life care among cancer patients with pre-existing bipolar disorder (23). Fond *et al.* found that patients with bipolar disorder had a lower chance of receiving HIEOL care apart from artificial nutrition. The patients also less frequently received chemotherapy in the last 14 days of life (OR =0.77; 95% CI: 0.69, 0.86), imaging examinations (OR =0.76; 95% CI: 0.65, 0.90) and had fewer deaths in the ICU or ED (OR =0.83; 95% CI: 0.70, 0.97). Moreover, patients with bipolar disorder had a higher chance of receiving palliative care in the last 31 days of life (OR =1.49; 95% CI: 1.32, 1.69) and in the last 3 days of life (OR =2.14; 95% CI: 1.89, 2.43).

Discussion

This systematic review demonstrated that a pre-existing diagnosis of SMD in cancer patients appears to affect patients' end-of-life care. This patient group received palliative care earlier, and more seldom received HIEOL care compared to controls. Although, to our knowledge, there are no specific clinical guidelines regarding end-of-life care for patients with cancer and pre-existing SMD, the different studies included in the review indicate that these patients seem to be receiving high-quality palliative end-of-life care.

Patients with cancer and pre-existing SMD

The two studies that included SMDs in their studies, Kashyap *et al.* and Fond *et al.* had conflicting results (24,25). Kashyap *et al.* only measured frequency of ED visits, and they reported that cancer patients with pre-existing different mental illnesses more frequently visited the ED in the last 30 days of life. This is compared to Fond *et al.* who measured their sample against the HIEOL markers defined by Earle *et al.* (9). Fond *et al.* reported that patients with pre-existing SMD diagnosis less seldom visited the ED in the last 30 days of life. The reason for difference between the two studies might be that Fond *et al.* examined women with breast cancer and Kashyap *et al.* focused exclusively on an older population with gastrointestinal cancers. Patients with gastrointestinal cancers are known to more frequently visit the ED as also described by Kashyap *et al.* (24). Also, the definition of mental illness differed between the studies since Kashyap *et al.* besides SMD also included patients with anxiety, dementia, and substance use disorders.

Patients with cancer and pre-existing schizophrenia

Overall, the studies in this review conclude that cancer patients with pre-existing schizophrenia receive less HIEOL (e.g., less chemotherapy and advanced diagnostic examinations in end-of-life) and the same or even more quality palliative end-of-life care (17,20,21,26). A factor that might influence the end-of-life care is that patients with a pre-existing schizophrenia have a higher frequency of multimorbidity besides cancer. It is plausible that the increased complexity of the patients' overall condition might reduce therapeutic options. Hence, we found that these patients have been reported to undergo fewer imaging examinations (20,21,26).

However, only one study, Huang *et al.*, found that patients with pre-existing schizophrenia were more likely to receive invasive measures such as having surgeries and being admitted into an ICU (20). These findings might be influenced by structural differences at patient, health care provider or health care system levels in Asia compared to western health care systems. Also, the results from Huang *et al.* should be interpreted with caution due to the relatively low sample size compared to Fond *et al.* and Viprey *et al.* (20,21,26).

Regarding social deprivation, Fond *et al.* and Viprey *et al.* reported that the patients with pre-existing schizophrenia were less socially deprived compared to their controls (21,26) which is surprising since schizophrenia has been found to be more frequent in low-income than non-low-income individuals (27). Hence, Ganzini *et al.* speculated whether the social deprivation of these patients might be limiting care (17). However, what most likely explains this disparity in social deprivation between groups, is that more socially deprived patients might have already died before entering cancer treatment (21).

Patients with cancer and pre-existing depression

Doan *et al.*, McDermott *et al.* and Fond *et al.* reported similar findings on cancer patients with a pre-existing

depression (18,19,22). Their results demonstrate an association between a pre-existing depression and less HIEOL care. In their studies, individuals with pre-existing depression were less likely to receive chemotherapy, and to die at a hospital (18,19,22). A discrepancy between the three publications was that as compared to Doan *et al.* and McDermott *et al.*, Fond *et al.* found that patients with pre-existing depression had a longer time between cancer diagnosis and death. Fond *et al.* speculated that their finding could be due to characteristics of depressed patients that they may be more anxious on their health which might lead them to seek help earlier. It remains important that individuals with depression are predisposed to suicidal thoughts and feelings of hopelessness. These characteristics of depressed individuals might well influence the patient's wishes of the intensity of their care. Additionally, the preconception regarding depressed individuals, and their perceived psychological complexity might lead to a bias towards end-of-life care referrals (22).

Patients with cancer and pre-existing bipolar disorder

Lastly, the only publication specifically focusing on patients with pre-existing bipolar disorder was Fond *et al.* and their results are in accordance with the above-mentioned studies (23). They found that patients with pre-existing bipolar disorder received more frequent palliative end-of-life care rather than HIEOL care, apart from more frequently receiving artificial nutrition than the control. Interestingly, in a sub-group analysis in the study by Kashyap *et al.* they found that patients with bipolar disorders were more likely to have more than one ED visit in the last 30 days of life (24). Even though the subgroups were small it shows the complexity of the topic.

Kashyap also showed that gender, age, ethnicity, income, and co-morbidity were factors that were significant for the HIEOL outcome and that outpatient mental health treatment in the trajectory were preventive for ED visits. Also, Fond *et al.* found that patients with pre-existing bipolar disorder in their study were less socially deprived compared to their controls (23). It seems that socio-economy may play a large role in this topic and that future studies should take that into consideration.

Clinical and research implications

It is important to note that the existing literature has not addressed what leads to the observed differences reported in end-of-life. The interpretation of the differences, especially in HIEOL care thus remains ambiguous. Various hypotheses for the differences exist (5). The differences may be due to the fact that current approaches to cancer care are not optimal to patients with SMD. Another reason may be the fact that cancer patients with pre-existing SMD are subjected to systemic stigma, which is affecting the intensive level in their end-of-life care and the efforts to save the life of the patient. The differences may also be due to the fact that current approaches are sufficient, and the differences reflect a positive tendency that patients with special needs actually get the best palliative care.

Although the interpretations of the data should be done with caution, it is safe to say that more awareness of the differences between patients with and without SMD is needed. Patients with pre-existing SMD and the healthcare workers around them need to be informed about the existence of the differences. Moreover, clinical guidelines need to make space for the added complexity of these patients. Lastly, policy makers have to be aware that there is a group of patients that are treated differently in end-of-life and the results call for focus and attention to potential equalities among patients with SMD, maybe not according to palliative services but to disease and life-saving treatments.

Strengths and weaknesses

Relatively few studies were included, and the fact that they only stem from three countries/regions, USA, France, and Taiwan is seen as a limitation. Hence, limited research on this topic should be taken into account. Also, five of the 10 included studies were conducted by the same research team with similar methodology which challenge the generalizability of the results. However, the homogeneity of their methodology can also be seen as a strength. Three of the included studies address depression (18,19,22). However, their results can be difficult to compare, as Doan *et al.* and McDermott *et al.* included confounding variables such as dementia, bipolar disorder, and psychotic depression (18,19). The lack of comparability between the three studies addressing depression is problematic. Furthermore, the precision of results regarding recurrent major depressive disorder and bipolar disorder was limited by the fact that only one paper focused on recurrent major depressive disorder (22) and only one paper specifically addressed bipolar disorder (23).

All studies were retrospective cohort studies and were

not able to identify at what level (patient, health care provider or health care system) and for what reason HIEOL care were less intense in the patient group.

Conclusions

This review shows that patients with cancer and pre-existing SMD in most studies receive more sufficient palliative end-of-life care and less HIEOL care compared to controls. The included studies had good research quality but only 10 studies were included. Research regarding the reason for this difference in end-of-life care is lacking, and the reasons for this less intense care in end-of-life is uncertain. Thus, further studies are needed to examine the reasons for these differences.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-23-589/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Appendix 1

Search strings

A literature search was done in the databases for studies that fulfilled the inclusion criteria on the 1st of September 2023.

PubMed—574 results

("Neoplasms"[MeSH] OR "neoplasm"[Title/Abstract] OR cancer[Title/Abstract] OR onco*[Title/Abstract]) AND ("Bipolar Disorder"[Title/Abstract] OR "major depression"[Title/Abstract] OR "unipolar depression"[Title/Abstract] OR "Schizophrenia"[Title/Abstract] OR Mental[Title/Abstract] OR psychiatric[Title/Abstract]) AND ("Palliative Medicine"[Mesh] OR "Palliative Care"[Mesh] OR "Terminal Care"[Mesh] OR "Hospice Care"[Mesh] OR palliat*[Title] OR end-of-life[Title] OR terminal*[Title]) AND (2000:2023[pdat]) NOT ("meta-analysis"[Publication Type] OR "review"[Publication Type] OR "systematic review"[Filter])

Embrace—29 results

('neoplasm'/de OR 'oncology':ti OR neoplasm:ti OR 'malignant neoplasm':ti) AND ('bipolar disorder':ti OR 'major depression':ti OR 'unipolar depression':ti OR 'schizophrenia':ti OR mental:ti OR psychiatric:ti) AND (palliat*:ti OR 'end of life':ti OR terminal*:ti OR hospice:ti OR eol*:ti) NOT ('meta analysis':it OR review:it OR 'systematic review':it) AND [2000-2023]/py

Science Direct—38 results

(neoplasm OR oncology OR malignant neoplasm) AND (Bipolar Disorder OR major depression OR unipolar depression OR Schizophrenia OR Mental OR psychiatric) AND (palliation OR end-of-life OR terminal)

Years: 2000–2023—All types of publications

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Table S1 Quality assessment of the included quantitative studies

Author, year, country/region	Selection				Comparability	Outcome		Total number of stars[†]
	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of exposure	Based on design and analysis	Assessment of outcome	Statistical test	
Ganzini *et al.*, 2010, USA (17)	*	None	*	**	*	**	*	8
Doan, 2016, USA (18)	*	None	*	**	*	**	*	8
McDermott *et al.*, 2018, USA (19)	*	None	*	**	*	**	*	8
Huang *et al.*, 2018, Taiwan (20)	*	None	*	**	*	**	*	8
Fond *et al.*, 2019, France (21)	*	None	*	**	**	**	*	9
Fond *et al.*, 2020, France (22)	*	None	*	**	**	**	*	9
Fond *et al.*, 2020, France (23)	*	None	*	**	**	**	*	9
Kashyap *et al.*, 2021, USA (24)	*	None	*	**	**	**	*	9
Fond *et al.*, 2021, France (25)	*	None	*	**	**	**	*	9
Viprey *et al.*, 2021, France (26)	*	None	*	**	**	**	*	9

Newcastle-Ottawa Scale (15) modified for cross-sectional studies according to Herzog *et al.* were used (16). [†], out of maximum 10 stars, since Ascertainment of the exposure, Comparability and Assessment of the outcome can provide two stars; *, indicate number of stars.

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