

# End-of-life care among patients with schizophrenia and cancer: a population-based cohort study from the French national hospital database



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## Summary

**Background** Patients with schizophrenia represent a vulnerable, underserved, and undertreated population who have been neglected in health disparities work. Understanding of end-of-life care in patients with schizophrenia and cancer is poor. We aimed to establish whether end-of-life care delivered to patients with schizophrenia and cancer differed from that delivered to patients with cancer who do not have diagnosed mental illness.

**Methods** We did a population-based cohort study of all patients older than 15 years who had a diagnosis of advanced cancer and who died in hospital in France between Jan 1, 2013, and Dec 31, 2016. We divided this population into cases (ie, patients with schizophrenia) and controls (ie, patients without a diagnosis of mental illness) and compared access to palliative care and indicators of high-intensity end-of-life care between groups. In addition to unmatched analyses, we also did matched analyses (matched in terms of age at death, sex, and site of primary cancer) between patients with schizophrenia and matched controls (1:4). Multivariable generalised linear models were done with adjustment for social deprivation, year of death, time from cancer diagnosis to death, metastases, comorbidity, and hospital type (ie, specialist cancer centre *vs* non-specialist centre).

**Findings** The main analysis included 2481 patients with schizophrenia and 222 477 controls. The matched analyses included 2477 patients with schizophrenia and 9896 controls. Patients with schizophrenia were more likely to receive palliative care in the last 31 days of life (adjusted odds ratio 1.61 [95% CI 1.45–1.80];  $p < 0.0001$ ) and less likely to receive high-intensity end-of-life care—such as chemotherapy and surgery—than were matched controls without a diagnosis of mental illness. Patients with schizophrenia were also more likely to die younger, had a shorter duration between cancer diagnosis and death, and were more likely to have thoracic cancers and comorbidities than were controls.

**Interpretation** Our findings suggest the existence of disparities in health and health care between patients with schizophrenia and patients without a diagnosis of mental illness. These findings underscore the need for better understanding of health inequalities so that effective interventions can be developed for this vulnerable population.

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## Introduction

Survival and quality of life have improved greatly in people with cancer as a result of earlier detection and substantial advances in treatments and supportive care. However, not all patients benefit equally from this progress. Race, socioeconomic status, medical insurance coverage, area, age, and mental illness are all factors that can affect cancer treatment, survival, and care quality.<sup>1</sup> Among patients with mental illnesses, those with schizophrenia are one of the most vulnerable, underserved, and undertreated populations,<sup>2,3</sup> and have been neglected in health disparities work and cancer health services research.<sup>4</sup> Schizophrenia is associated with a substantial decrease in life expectancy of roughly 14 years as a result of accidents, suicide, and physical illnesses, including cancer.<sup>5</sup> Compared with people without a diagnosis of mental illness, patients with schizophrenia experience increased delays in cancer

diagnoses and less frequent adapted care as a result of both physician-related<sup>6,7</sup> (eg, stigma, diagnostic overshadowing) and patient-related (eg, poor insight into potential symptoms, reduced likelihood to seek help) factors—observations that are being reported around the world.<sup>5–7</sup> Mortality from cancer in patients with schizophrenia is between 1.5 and four times higher than that in people without a diagnosis of mental illness,<sup>4,8–10</sup> and patients with schizophrenia are less likely to undergo cancer screening examinations.<sup>11</sup>

Although many studies have focused on whether the risk of cancer is increased or decreased in patients with schizophrenia, only a few have investigated end-of-life care in patients with schizophrenia who are diagnosed with terminal cancer. Palliative care specialists improve the quality of life of patients with life-threatening illnesses<sup>12</sup> by preventing, assessing, and treating pain

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### Research in context

#### Evidence before this study

We searched MEDLINE, Web of Science, and Google with the medical subject headings “end-of-life” AND “cancer” AND “schizophrenia” for articles published in any language from inception to March 1, 2019. Previous work on end-of-life care in patients with schizophrenia diagnosed with terminal cancer is rare. Some qualitative studies suggested that patients with schizophrenia are at risk of receiving poor-quality end-of-life care, but small sample sizes limit the generalisability of these findings. The three quantitative studies that have been done were based on data from before 2012, and had contradictory findings. We did not find any more recent quantitative studies of end-of-life care in patients with schizophrenia and cancer.

#### Added value of this study

Our study of a national database of cancer deaths in hospitals in France between 2013 and 2016 provides new data for end-of-life care in a large population of patients with schizophrenia and cancer (n=2481). Compared with patients without a diagnosis of mental illness, patients

with schizophrenia died younger and sooner after cancer was diagnosed; were more likely to have comorbidities, to have thoracic cancer, and to receive care at a specialist cancer centre; and were less likely to have metastatic disease and to be socioeconomically deprived. In adjusted analyses, patients with schizophrenia were more likely to receive palliative care but less likely to receive high-intensity end-of-life care than matched controls.

#### Implications of all the available evidence

Patients with schizophrenia might receive more palliative care but less high-intensity care than matched controls without a diagnosis of mental illness. Our findings suggest disparities in health and health care between patients with schizophrenia and those without a diagnosis of mental illness. Caring for an individual with schizophrenia and cancer requires knowledge and expertise in both oncology and psychiatry, which might necessitate improved training of health-care professionals and coordination and integration of care.

and other symptoms, and by providing psychological, emotional, and spiritual support. Palliative care is both patient centred and family centred, and emphasises patient autonomy and advance planning for care.<sup>13</sup> Patients are usually referred to palliative care delivered by a hospice organisation when they are expected to have less than 6 months to live and when a cure for their illness is no longer being pursued. Most previous research<sup>13–16</sup> into end-of-life care and cancer was done in general populations in which the mental health status of participants was not specified, and focused on two aspects of poor-quality end-of-life care: late referral or not being referred to a palliative care unit, and high-intensity end-of-life care resulting in a high frequency of emergency department visits and admission to intensive care units, and overuse of chemotherapy and other potentially life-prolonging interventions near death. In addition to well known barriers to optimal end-of-life care (eg, inadequate advance planning of care, poor communication between professionals and patients and caregivers, poor health literacy, and uncertainty about imminence of death),<sup>15,17,18</sup> barriers such as stigma, stereotypes about mental illnesses, and personal factors (eg, persecutory delusion, attribution bias, memory and attention impairments, lack of motivation, hostility, impaired autonomy, social withdrawal and increased isolation or poor social support) could specifically affect patients with schizophrenia.<sup>3,6</sup> End-of-life care works best when patients and their families participate in establishing the goals of care, but half of patients with schizophrenia have impairments in decision-making capacity and, when incapacitated, often do not have surrogate decision makers.<sup>19</sup>

Some studies<sup>20–22</sup> have suggested that patients with schizophrenia are at risk of receiving poor-quality

end-of-life care, but these studies had small sample sizes, which limits the generalisability of their findings. The only quantitative studies that have been done were based on data from before 2012 and had contradictory findings, showing a lack of palliative care,<sup>21</sup> similar or better-quality end-of-life care,<sup>19</sup> and similar access to palliative care with more frequent invasive treatments but less frequent chemotherapy and fewer examinations<sup>22</sup> for patients with schizophrenia compared with those without a diagnosis of mental illness. No more recent quantitative studies of end-of-life care in patients with schizophrenia and cancer have been done. Such studies are needed to provide objective data for end-of-life care in this population. We aimed to establish whether the end-of-life care delivered to patients with schizophrenia and cancer differed from that delivered to patients with cancer who did not have a diagnosis of mental illness.

## Methods

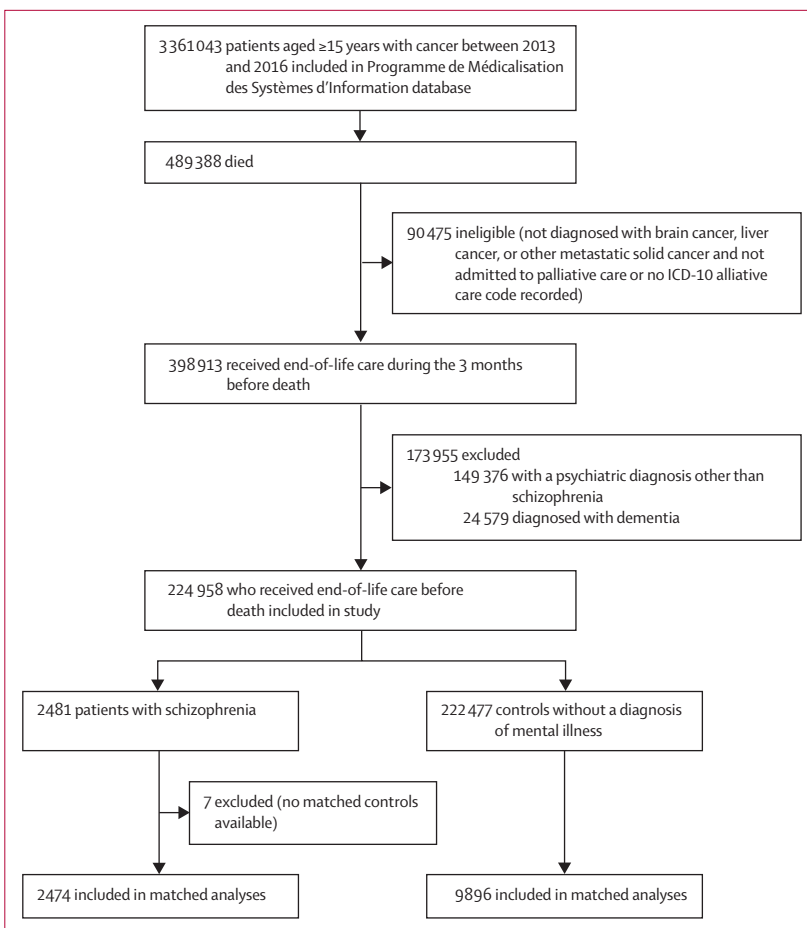
### Study design and data sources

In this population-based cohort study, we used data from Programme de Médicalisation des Systèmes d'Information, the French national hospital database in which administrative and medical data are systematically collected for acute and psychiatric care. The database is based on diagnosis-related groups, with all diagnoses coded according to the 10th revision of the International Classification of Diseases (ICD-10), and includes data for all hospitalised people in France diagnosed with cancer. In our study, we included all hospitalised patients aged 15 years or older with a diagnosis of brain cancer, liver cancer, or any metastatic solid cancer, for whom admission to palliative care was authorised or the ICD-10 code for palliative care (Z515) was recorded, and

Period of study	
<b>Palliative care</b>	
Access to palliative care	Last 31 days of life and last 3 days of life
Time between first interaction with palliative care and death	Last 3 months of life
<b>High-intensity end-of-life care*</b>	
In-hospital chemotherapy	Last 14 days of life
Artificial nutrition (ie, enteral or parenteral nutrition)	Last 31 days of life
Tracheal intubation	Last 31 days of life
Mechanical ventilation	Last 31 days of life
Gastrostomy (or change in gastrostomy status)	Last 31 days of life
Cardiopulmonary resuscitation	Last 31 days of life
Dialysis	Last 31 days of life
Blood transfusion	Last 31 days of life
Surgery	Last 31 days of life
Imaging	Last 31 days of life
Endoscopy	Last 31 days of life
At least one emergency department admission	Last 31 days of life
At least one ICU admission	Last 31 days of life
At least one air extraction chamber (ie, sterile chamber) admission	Last 31 days of life
More than one admission to acute care unit	Last 31 days of life
Length of stay in acute care unit	Last 31 days of life
Death in emergency department ICU	Last day of life

All variables were binary (ie, yes or no), except for the time between first interaction with palliative care and death, which was a continuous variable. ICU=intensive care unit. \*High-intensity end-of-life care based on previously defined criteria (Earle and colleagues, 2003, 2004, 2005, and 2008).<sup>13,18,23,24</sup>

**Table 1: Outcome measures**



**Figure: Flow chart**  
ICD-10=10th revision of the International Classification of Diseases.

who died from cancer in hospital between Jan 1, 2013, and Dec 31, 2016. We excluded patients with a diagnosis of dementia (ICD-10 codes F00\*, F01\*, F02\*, F03\*, F051\*, G30\*, and G31\*) and patients with a psychiatric diagnosis other than schizophrenia (ie, those with ICD-10 chapter F codes other than those for schizophrenia [ie, F20\*, F22\*, and F25\*] or those included in the psychiatric care database for diagnoses other than schizophrenia codes).

Data in the Programme de Médicalisation des Systèmes d'Information are anonymised and can be reused for research purposes.<sup>16</sup> Under French law, no ethics approval is necessary for analyses of national databases. No informed consent was necessary because all data were anonymous.

**Procedures**

For the purposes of our study, we defined three populations. Cases were patients who had a diagnosis of schizophrenia according to specific ICD-10 codes (ie, F20\*, F22\*, or F25\*) in either the acute care or psychiatric Programme de Médicalisation des Systèmes

d'Information database. Controls were patients who did not have a diagnosis of mental illness according to specific ICD-10 codes in the acute care database and who were not listed in the psychiatry databases. Finally, we defined a matched control population, who were matched to cases in a 4:1 ratio according to three criteria: age at death ( $\pm 2$  years), sex, and primary cancer location (15 modalities).

The outcomes we used were based on previously defined criteria (table 1).<sup>13,18</sup> The specific codes used for each outcome are listed in the appendix (pp 1–2). We gathered data for six sociodemographic, clinical, and hospital characteristics that could potentially affect the quality of end-of-life care: social deprivation, year of death (because practice could have evolved with time), time from cancer diagnosis to death, comorbidities, metastasis (ICD-10 codes C78 and C79, because metastasis might accelerate initiation of palliative care), and hospital category at the last admission before death (ie, specialist cancer centre vs non-specialist centre). Social deprivation was assessed with the FDep09, an index that has been previously validated with French data and that is based on the residential code of the person's

See Online for appendix

	Controls (n=222 477)	Patients with schizophrenia (n=2481)	p value
Age at death, years*			<0.0001
15–62	49 438 (22.2%)	1205 (48.6%)	..
63–71	53 515 (24.1%)	614 (24.7%)	..
72–81	63 224 (28.4%)	430 (17.3%)	..
≥82	56 300 (25.3%)	232 (9.4%)	..
Sex			0.061
Male	129 517 (58.2%)	1398 (56.3%)	..
Female	92 960 (41.8%)	1083 (43.7%)	..
Social deprivation index*			<0.0001
More favoured	54 484 (24.5%)	721 (29.1%)	..
Favoured	35 913 (16.1%)	403 (16.2%)	..
Deprived	74 284 (33.4%)	725 (29.2%)	..
More deprived	54 406 (24.5%)	571 (23.0%)	..
Missing	3390 (1.5%)	61 (2.5%)	..
Year of death			0.32
2013	56 120 (25.2%)	589 (23.7%)	..
2014	55 904 (25.1%)	620 (25.0%)	..
2015	55 443 (24.9%)	640 (25.8%)	..
2016	55 010 (24.7%)	632 (25.5%)	..
Median time from cancer diagnosis to death, days (IQR)	327 (70–780)	290 (70–714)	<0.0001
Primary cancer site			<0.0001
Digestive tract	79 035 (35.5%)	645 (26.0%)	<0.0001
Thorax	44 706 (20.1%)	733 (29.5%)	<0.0001
Endocrine system	916 (0.4%)	12 (0.5%)	0.99
Haematological site	16 611 (7.5%)	167 (6.7%)	0.99
Female genitalia	11 880 (5.3%)	149 (6.0%)	0.99
Male genitalia	12 054 (5.4%)	74 (3.0%)	<0.0001
Bone	643 (0.3%)	12 (0.5%)	0.99
Skin	4782 (2.1%)	42 (1.7%)	0.99
Breast	18 774 (8.4%)	236 (9.5%)	0.99
CNS	5055 (2.3%)	88 (3.5%)	0.0004
Connective tissue	1161 (0.5%)	20 (0.8%)	0.77
Respiratory system	6000 (2.7%)	92 (3.7%)	0.030
Urinary tract	14 169 (6.4%)	140 (5.6%)	0.99
Eye	275 (0.1%)	3 (0.1%)	0.99
Unspecified	6416 (2.9%)	68 (2.7%)	0.99
Metastasis	146 852 (66.0%)	1604 (64.7%)	0.16
Charlson modified Comorbidity Index score			<0.0001
0	103 316 (46.4%)	1006 (40.5%)	..
1–2	74 570 (33.5%)	914 (36.8%)	..
≥3	44 591 (20.0%)	561 (22.6%)	..
Comorbidities			
Renal disease	22 966 (10.3%)	239 (9.6%)	0.26
Rheumatological disease	1911 (0.9%)	21 (0.8%)	0.94
Peripheral vascular disease	13 901 (6.2%)	194 (7.8%)	0.0013
Peptic ulcer disease	5340 (2.4%)	70 (2.8%)	0.17
Hemiplegia or paraplegia	15 246 (6.9%)	237 (9.6%)	<0.0001
Mild liver disease	12 132 (5.5%)	229 (9.2%)	<0.0001
Moderate or severe liver disease	11 060 (5.0%)	143 (5.8%)	0.071

(Table 2 continues on next page)

address.<sup>25</sup> The FDep09 index involves four socioeconomic ecological variables: the proportion of residents who graduated from high school, median household income, the percentage of residents who are blue-collar workers, and the unemployment rate. We classified these area data according to quartiles, from least deprived (Q1) to most deprived (Q4). Comorbidities were assessed with the Charlson modified Comorbidity Index,<sup>26</sup> which was computed from ICD-10 codes recorded as primary or secondary diagnoses during the last 3 months of life (excluding dementia and the two items referring to cancer—ie, metastatic solid tumour and malignancy).

### Statistical analysis

Analyses were done in two steps. First, we used either the  $\chi^2$  test or the Student's *t* test to compare sociodemographic, clinical, and hospital data between cases and unmatched controls. Second, we used univariate conditional logistic regressions and univariate generalised mixed models with log normal distribution to compare binary outcomes and quantitative outcomes, respectively, between cases and matched controls. Then, we did as many multivariate analyses as there were outcomes to analyse the association between cases and matched controls for each outcome. Six confounding factors were included: social deprivation (Q1 vs Q2 vs Q3 vs Q4), year of death (2013 vs 2014 vs 2015 vs 2016), time from cancer diagnosis to death, metastasis (yes vs no), Charlson modified Comorbidity Index (no comorbidities vs 1 or 2 comorbidities vs ≥3 comorbidities) and hospital category (specialist vs non-specialist cancer centre). These analyses were done with a multivariable generalised linear model with the matched cluster as a random intercept with PROC GLIMMIX. For quantitative data, the response distribution was log normal, and the identify link function was used. For binary data, the response distribution was binomial, and the logit link function was used. To assess the goodness-of-fit of the models, we reported the ratio between the Pearson  $\chi^2$  statistic and its degrees of freedom. Multiple comparison corrections (ie, to measure the false discovery rate) were done. A significance of  $p < 0.05$  was used. All analyses were done in SAS (version 9.4).

### Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and final responsibility for the decision to submit for publication.

### Results

Overall, 3 361 043 people with cancer, 398 913 (11.9%) of whom died, were recorded in the Programme de Médicalisation des Systèmes d'Information database between 2013 and 2016. 224 958 (6.7%) people who received end-of-life care before dying were included in our study (figure). 2481 patients with schizophrenia were

classified as cases and 222 477 patients without a diagnosis of mental illness were classed as controls. 2474 patients with schizophrenia were then matched with 9896 controls (table 2). Seven patients with schizophrenia were excluded from the matched analyses because they did not have matched controls.

In the unmatched analysis, patients with schizophrenia and cancer died younger (mean age at death 63·6 years [SD 12·8] vs 71·8 years [12·7]), were less socioeconomically deprived, and were more likely to receive specialist care than controls without a diagnosis of mental illness (table 2). They also had more thoracic, CNS, and respiratory system cancers; fewer digestive and male genitalia cancers; and died sooner after cancer was diagnosed than people in the control population (table 2). Patients with schizophrenia and cancer were more likely to have peripheral vascular disease, hemiplegia or paraplegia, mild liver disease, HIV or AIDS, and chronic pulmonary disease, and less likely to have congestive heart failure than were controls (table 2).

In the matched analyses of cases and controls, similar between-group differences were noted in socioeconomic status, time from diagnosis with cancer to death, and likelihood of receiving cancer treatment at a specialist centre (table 3). Patients with schizophrenia were less likely to have metastatic disease than matched controls (table 3). In the multivariate analysis, patients with schizophrenia and cancer had more frequent admissions to palliative care units in the last 31 days of life (adjusted odds ratio 1·61 [95% CI 1·45–1·80];  $p < 0\cdot0001$ ) and in the last 3 days of life (2·52 [2·25–2·82]) and had longer palliative care follow-up before death ( $\beta$  0·36 [SD 0·03]) than were matched controls (table 4). They were less likely to undergo chemotherapy, surgery, imaging, endoscopy, and blood transfusions; less likely to be admitted to acute care units (but had longer stays in these units); and less likely to die in intensive care units or emergency departments than matched controls (table 4).

All the Pearson  $\chi^2$  degrees of freedom results were less than 1, except that for the duration between cancer diagnosis and death, which was greater than 1 but in an acceptable range (1·47; appendix p 3).

## Discussion

In this population-based cohort study, we showed that the 2481 patients with schizophrenia and cancer who died in French hospital care between 2013 and 2016 died younger and sooner after cancer diagnosis than did patients with cancer without a diagnosis of mental illness. Patients with schizophrenia also had more comorbidities, were more likely to have thoracic cancer and to receive specialist cancer care, and were less likely to have metastatic disease or to be socioeconomically deprived than controls. After matching and adjustment, patients with schizophrenia and cancer were more likely to receive palliative care but less likely to receive

	Controls (n=222 477)	Patients with schizophrenia (n=2481)	p value
(Continued from previous page)			
HIV or AIDS	586 (0·3%)	27 (1·1%)	<0·0001
Diabetes with complications	8770 (3·9%)	97 (3·9%)	0·93
Diabetes without complications	38 923 (17·5%)	421 (17·0%)	0·49
Cerebrovascular disease	15 066 (6·8%)	178 (7·2%)	0·42
Chronic pulmonary disease	22 427 (10·1%)	457 (18·4%)	<0·0001
Congestive heart failure	34 679 (15·6%)	299 (12·1%)	<0·0001
Myocardial infarction	14 363 (6·5%)	138 (5·6%)	0·071
Hospital category†			<0·0001
Specialist cancer centre	50 208 (22·6%)	747 (30·1%)	..
Non-specialist centre	172 269 (77·4%)	1734 (69·9%)	..

Data are n (%), unless otherwise specified. Individual p values are provided for binary variables. \*Data are reported by quartile. †Applies to last hospital admission before death.

**Table 2: Characteristics of patients with schizophrenia and controls without a diagnosis of mental illness**

	Matched controls (n=9896)	Patients with schizophrenia (n=2474)	p value
Age at death, years*			
15–62	4702 (47·5%)	1199 (48·5%)	..
63–71	2538 (25·6%)	614 (24·8%)	..
72–81	1735 (17·5%)	430 (17·4%)	..
≥82	921 (9·3%)	231 (9·3%)	..
Sex			
Male	5580 (56·4%)	1395 (56·4%)	..
Female	4316 (43·6%)	1079 (43·6%)	..
Social deprivation index*			<0·0001
More favoured	2431 (24·6%)	717 (29·0%)	..
Favoured	1672 (16·9%)	403 (16·3%)	..
Deprived	3228 (32·6%)	723 (29·2%)	..
More deprived	2401 (24·3%)	570 (23·0%)	..
Missing	164 (1·7%)	61 (2·5%)	..
Year of death	..	..	0·32
2013	2513 (25·4%)	587 (23·7%)	..
2014	2490 (25·2%)	620 (25·1%)	..
2015	2441 (24·7%)	638 (25·8%)	..
2016	2452 (24·8%)	629 (25·4%)	..
Median time from cancer diagnosis to death, days (IQR)	351 (90–767)	290 (70–714)	<0·0001
Primary cancer site			
Digestive system	2580 (26·1%)	645 (26·1%)	..
Thorax	2928 (29·6%)	732 (29·6%)	..
Endocrine system	48 (0·5%)	12 (0·5%)	..
Haematological site	668 (6·8%)	167 (6·8%)	..
Female genitalia	596 (6·0%)	149 (6·0%)	..
Male genitalia	292 (3·0%)	73 (3·0%)	..
Bone	48 (0·5%)	12 (0·5%)	..
Skin	168 (1·7%)	42 (1·7%)	..
Breast	944 (9·5%)	236 (9·5%)	..
CNS	352 (3·6%)	88 (3·6%)	..

(Table 3 continues on next page)



	Matched controls (N=9896)	Patients with schizophrenia (N=2474)	p value
(Continued from previous page)			
Connective tissue	80 (0.8%)	20 (0.8%)	..
Respiratory system	368 (3.7%)	92 (3.7%)	..
Urinary tract	560 (5.7%)	140 (5.7%)	..
Eye	4 (<0.1%)	1 (<0.1%)	..
Unspecified	260 (2.6%)	65 (2.6%)	..
Metastasis	6778 (68.5%)	1600 (64.7%)	<0.0001
Charlson modified Comorbidity Index score	..	..	<0.0001
0	5107 (51.6%)	1003 (40.5%)	..
1-2	3044 (30.8%)	914 (36.9%)	..
≥3	1745 (17.6%)	557 (22.5%)	..
Comorbidities			
Renal disease	728 (7.4%)	237 (9.6%)	<0.0001
Rheumatological disease	81 (0.8%)	20 (0.8%)	0.95
Peripheral vascular disease	479 (4.8%)	194 (7.8%)	<0.0001
Peptic ulcer disease	190 (1.9%)	70 (2.8%)	0.0050
Hemiplegia or paraplegia	906 (9.2%)	237 (9.6%)	0.49
Moderate or severe liver disease	494 (5.0%)	142 (5.7%)	0.12
Mild liver disease	509 (5.1%)	227 (9.2%)	<0.0001
HIV or AIDS	59 (0.6%)	25 (1.0%)	0.025
Diabetes with complications	281 (2.8%)	96 (3.9%)	<0.0001
Diabetes without complications	1426 (14.4%)	420 (17.0%)	0.0011
Cerebrovascular disease	623 (6.3%)	178 (7.2%)	0.094
Chronic pulmonary disease	924 (9.3%)	456 (18.4%)	<0.0001
Congestive heart failure	1069 (10.8%)	297 (12.0%)	0.081
Myocardial infarction	449 (4.5%)	138 (5.6%)	0.029
Hospital category†	..	..	<0.0001
Specialist cancer centre	2555 (25.8%)	742 (30.0%)	..
Non-specialist centre	7341 (74.2%)	1732 (70.0%)	..

Data are n (%), unless otherwise specified. Patients were matched according to age at death ( $\pm 2$  years), sex, and primary cancer location. Seven patients with schizophrenia were excluded from the matched analyses because no matched controls were identified. Individual p values are provided for binary variables. \*Data are reported by quartile. †Applies to last hospital admission before death.

**Table 3: Characteristics of patients with schizophrenia and controls without a diagnosis of mental illness included in matched analyses**

high-intensity end-of-life care than matched controls.

Our study cannot establish with certainty the reasons for these discrepancies in end-of-life outcomes between patients with schizophrenia and control populations without a diagnosis of mental illness. However, as described previously,<sup>3</sup> these discrepancies suggest disparities in health and health care between patients with and without schizophrenia.

Patients with schizophrenia were shown to die 8 years earlier from cancer than were controls without a mental illness diagnosis. The high frequency of comorbidities in patients with schizophrenia recorded in this and previous studies suggests that reductions in life expectancy could be due to somatic causes.<sup>27</sup> The presence of somatic comorbidities might affect the choice of cancer treatment or necessitate dose modifications for chemotherapy or

close collaboration with primary care providers (which might be challenging in patients with advanced psychiatric disease), all of which could negatively affect cancer prognosis. Models of integrated care for people with severe mental disorders and somatic comorbidities should be further developed in France, both for before the occurrence of cancer and for during cancer care.

In our study, patients with schizophrenia died more frequently of tobacco-related cancers (ie, respiratory and thorax cancers) than did controls, even though schizophrenia was not associated with an increased risk of lung cancer in a meta-analysis.<sup>28</sup> However, our finding that tobacco-related cancers could be more lethal in patients with schizophrenia was also noted in a previous French cohort study<sup>9</sup> in the 1990s. Patients with schizophrenia might have delayed cancer diagnoses and present with a more severe form of cancer than people without a diagnosis of mental illness,<sup>4</sup> as suggested by the shorter time from cancer diagnosis to death in these patients in our study. Barriers to lung cancer care have also been reported for patients with schizophrenia.<sup>4</sup> Schizophrenia has been extensively associated with high rates of hard tobacco smoking. 30% of the French general population reports engaging in daily tobacco smoking compared with 52% of outpatients with schizophrenia, a high proportion of whom have severe nicotine dependence.<sup>29</sup> Furthermore, more than two-thirds of excess deaths from natural causes in patients with schizophrenia are due to smoking-related diseases.<sup>30</sup> A high lifetime tobacco smoking dose-effect and not quitting smoking after a cancer diagnosis could increase thoracic cancer mortality in this population.<sup>31</sup> Smoking cessation programmes and cancer screening targeting patients with severe mental illnesses such as schizophrenia should be reinforced to prevent thoracic cancer and to improve cancer prognosis.

In matched analyses, patients with schizophrenia were less likely to have metastases than matched controls, suggesting a difference in cancer stages at first contact with the oncology team. Early identification of cancers in patients with schizophrenia seems unlikely in light of our experience and previous findings.<sup>32</sup> A more probable explanation is that patients with schizophrenia are less likely to undergo additional diagnostic explorations than controls, as suggested by the lower frequency of imaging examinations in the last month of life that we identified. Another plausible explanation is that patients with schizophrenia could be more likely to die from their primary cancer before the development of metastases than are controls because of a lack of or delayed initiation of treatment. If this hypothesis is shown to be true, better cancer screening based on specific and targeted approaches for patients with schizophrenia will be necessary.

Patients with schizophrenia were more likely than controls to be treated at specialist centres, suggesting

	Univariate analysis			Multivariate analysis*	
	Matched controls (n=9896)	Patients with schizophrenia (n=2474)	p value	Adjusted odds ratio (95% CI)	Adjusted p value†
<b>Palliative care</b>					
During the last 31 days of life	6966 (70.4%)	1940 (78.4%)	<0.0001	1.61 (1.45–1.80)	<0.0001
During the last 3 days of life	1244 (12.6%)	638 (25.8%)	<0.0001	2.52 (2.25–2.82)	<0.0001
Median time from initiation of palliative care to death, days (IQR)	19 (8–39)	28 (12–57)	<0.0001	0.36 (0.03)‡	<0.0001
<b>High-intensity end-of-life care</b>					
Intrahospital chemotherapy during the last 14 days of life	1586 (16.0%)	230 (9.3%)	<0.0001	0.53 (0.46–0.62)	<0.0001
Artificial nutrition during the last 31 days of life	369 (3.7%)	121 (4.9%)	0.36	0.85 (0.69–1.05)	0.17
Tracheal intubation during the last 31 days of life	275 (2.8%)	68 (2.7%)	0.93	0.84 (0.63–1.13)	0.34
Mechanical ventilation during the last 31 days of life	1319 (13.3%)	357 (14.4%)	0.15	1.00 (0.88–1.14)	0.98
Gastrostomy (or change in gastrostomy status) during the last 31 days of life	74 (0.7%)	15 (0.6%)	0.45	0.67 (0.34–1.32)	0.34
Cardiopulmonary resuscitation during the last 31 days of life	53 (0.5%)	9 (0.4%)	0.27	0.47 (0.19–1.18)	0.17
Dialysis during the last 31 days of life	119 (1.2%)	32 (1.3%)	0.71	0.80 (0.48–1.35)	0.43
Blood transfusion during the last 31 days of life	1730 (17.5%)	334 (13.5%)	<0.0001	0.72 (0.64–0.83)	<0.0001
Surgery during the last 31 days of life	2012 (20.3%)	408 (16.5%)	<0.0001	0.71 (0.63–0.80)	<0.0001
Imaging during the last 31 days of life	7671 (77.5%)	1751 (70.8%)	<0.0001	0.66 (0.59–0.73)	<0.0001
Endoscopy during the last 31 days of life	1414 (14.3%)	331 (13.4%)	0.24	0.85 (0.74–0.97)	0.031
At least one emergency department admission during the last 31 days of life	4703 (47.5%)	1188 (48.0%)	0.66	0.93 (0.91–1.09)	0.98
At least one intensive-care unit admission during the last 31 days of life	897 (9.1%)	251 (10.1%)	0.092	0.92 (0.80–1.06)	0.79
At least one air extraction chamber (ie, sterile chamber) admission during the last 31 days of life	97 (1.0%)	15 (0.6%)	0.061	0.48 (0.23–0.99)	0.092
More than one admission to acute care unit during the last 31 days of life	5521 (55.8%)	1198 (48.4%)	<0.0001	0.73 (0.67–0.80)	0.0001
Median length of stay in acute care unit during the last 31 days of life, days (IQR)	16 (8–28)	22 (11–31)	<0.0001	1.20 (0.02)‡	<0.0001
Death in emergency department or intensive-care unit	1282 (13.0%)	241 (9.7%)	<0.0001	0.65 (0.56–0.76)	<0.0001

\*Adjusted for social deprivation, year of death, time from cancer diagnosis to death, metastasis, Charlson modified Comorbidity Index score, and hospital type.  
†The false discovery rate was applied when calculating p values. ‡These data are  $\beta$  (SD), and were calculated from a log normal mixed analysis and then back-transformed; a  $\beta$  of 0.36 means that the time from initiation of palliative care to death was 36% longer for patients with schizophrenia than for matched controls.

**Table 4: Univariate and multivariate analyses of end-of-life care in patients with schizophrenia compared with matched controls without a diagnosis of mental illness**

that such patients have less contact with secondary (ie, non-specialist centres) and primary (ie, family physician) care—a pattern that has been previously described in France.<sup>33</sup> Although severe mental disorders have been extensively associated with low socioeconomic status,<sup>34</sup> patients with schizophrenia were less socioeconomically deprived than controls in our sample. Socioeconomically deprived patients with schizophrenia might have an increased risk of early death from other causes of mortality, including cardiovascular diseases, addiction, trauma, and suicide. Socioeconomically deprived patients with schizophrenia who die from cancer might also have reduced access to end-of-life care compared with wealthier patients with schizophrenia. An absence of social support in elderly people with schizophrenia (eg, as a result of their parents' ageing or dying) might be more pronounced in deprived populations, leading to a separation from the health-care system, underdiagnosis of cancer, poor access to cancer

care, adherence issues, and loss to follow-up or death in non-hospital settings.<sup>35</sup>

Patients with schizophrenia did not receive the same care as matched controls in our study. By contrast with the results of previous studies,<sup>19–22</sup> patients with schizophrenia received more palliative care than controls. However, they were less likely to receive high-intensity care, including chemotherapy, surgery, imaging investigations, endoscopies, and blood transfusions. Less frequent chemotherapy and imaging in patients with schizophrenia compared with those without a diagnosis of mental illness were previously reported in a study<sup>22</sup> based on the Taiwanese National Database. That study also showed that surgery was more common in patients with schizophrenia than in those without a diagnosis of mental illness.<sup>22</sup>

There are various potential explanations for our findings about palliative care and high-intensity end-of-life care.<sup>4</sup> First, on a provider level, treating physicians might be

more likely to switch patients with severe mental illnesses to palliative care because prescribing treatments with a high risk of toxic effects and strict administration protocols could be complicated in patients with cognitive impairments who might be less likely to adhere to treatment. This explanation could also account for the lower frequency of chemotherapy in patients with schizophrenia than in controls in our study. Patients with schizophrenia also seem to be at higher risk of postoperative complications—including respiratory failure, sepsis, deep venous thrombosis, pulmonary embolism, paralytic ileus, stroke, and postoperative delirium—than people without a diagnosis of mental illness.<sup>36</sup> This unfavourable risk–benefit balance could explain why surgery was less common in cases than in matched controls in our study. Patients with schizophrenia might be excluded from making decisions about end-of-life care partly because of provider concerns about their emotional fragility and competence.<sup>37</sup> Our results might also reflect mental illness stigma and diagnostic overshadowing (ie, inadequate or delayed treatment as a result of physical symptoms being attributed to patients' mental illness) described in previous works.<sup>6,7</sup>

Second, on a patient level, patients with schizophrenia might be less likely than matched controls without a diagnosis of mental illness to receive high-intensity care because of hostility towards treatment, which could be associated with an increased risk of violence (because of paranoid delusion or psychomotor agitation).<sup>4</sup> In a previous study,<sup>19</sup> patients with schizophrenia more frequently completed do not resuscitate orders than did patients without a diagnosis of mental illness. Third, on a health-systems level, palliative care units have been designed to manage complicated situations—including lack of social support or social isolation, homelessness, and impaired autonomy that can interfere with each step of cancer care<sup>4,38</sup>—which could explain the long duration of follow-up of patients in palliative care units in our study.

Overall, our results should be interpreted with caution. We analysed only deaths, and further studies are needed to establish cancer survival in patients with schizophrenia compared with that in matched controls and to explore overall cancer care in patients with schizophrenia. Data for psychiatric symptoms and psychotropic drugs were not available and were not explored. Our work describes only patients with advanced cancer who died in hospitals, which limits the generalisability of our findings to those with less advanced cancer or those who died at home. However, only 3% of patients with cancer died at home, and only 13% died in nursing homes, in France in 2013.<sup>39</sup> Our patients were matched to controls according to age at death, sex, and primary cancer site, and the results were adjusted for social deprivation, year of death, time from cancer diagnosis to death, metastases, comorbidities, and hospital type, which strengthens our interpretation.

The main strength of this study is that we analysed 4 years of data from a national database of more than

200 000 deaths from cancer in France. It is the largest epidemiological study of end-of-life care in patients with schizophrenia to date, and we used a dedicated method of patient selection, which has been validated by the French National Institute for Cancer.

The differences we identified between patients with schizophrenia and cancer and patients with cancer who do not have a diagnosis of mental illness suggest the existence of disparities in health and health care. Our findings underscore the need for better understanding of health inequalities so that effective interventions can be developed for this vulnerable population. Caring for an individual with schizophrenia and cancer requires knowledge and expertise in both oncology and psychiatry and might necessitate better training of health-care professionals and care coordination or integration.

#### Contributors

GF, SS, KB, P-ML, PA, and LB designed the study. VP and VO managed the data, which VP analysed. GF, SS, KB, and LB wrote the first draft of the Article, which all other authors critically reviewed and approved.

#### Declaration of interests

We declare no competing interests.

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