Intensity of Care, Expenditure, and Place of Death in French Women in the Year Before Their Death From Breast Cancer: A Population-Based Study

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Abstract

Health care utilization of women with breast cancer (BC) during the last year of life, together with the causes and place of death and associated expenditure have been poorly described. Women treated for BC (2014-2015) with BC as a cause of death in 2015 and covered by the national health insurance general scheme (77% of the population) were identified in the French health data system (n = 6,696, mean age: 68.7 years, SD ± 15). Almost 70% died in short-stay hospitals (SSH), 4% in hospital-at-home (HaH), 9% in Rehab, 5% in skilled nursing homes (SNH) and 12% at home. One-third presented cardiovascular comorbidity. During the last year, 90% were hospitalized at least once in SSH, 25% in Rehab, 13% in HaH and 71% received hospital palliative care (HPC), but only 5% prior to their end-of-life stay. During the last month, 85% of women were admitted at least once to a SSH, 42% via the emergency department, 10% to an ICU, 24% received inpatient chemotherapy and 18% received outpatient chemotherapy. Among the 83% of women who died in hospital, independent factors for HPC use were cardiovascular comorbidity (adjusted odds ratio, aOR: 0.83; 95%CI: 0.72–0.95) and, in the 30 days before death, at least one SNH stay (aOR: 0.52; 95%CI: 0.36-0.76), ICU stay (aOR: 0.36; 95%CI: 0.30-0.43), inpatient chemotherapy (aOR: 0.55; 95%CI: 0.48-0.63), outpatient chemotherapy (aOR: 0.60; 95%CI: 0.51-0.70), death in Rehab (aOR: 1.4; 95%CI: 1.05-1.86) or HAH (aOR: 4.5; 95%CI: 2.47-8.1) vs SSH. Overall mean expenditure reimbursed per woman was €38,734 and €42,209 for those with PC. Women with inpatient or outpatient chemotherapy during the last month had lower rates of HPC, suggesting declining use of HPC before death. This study also indicates SSH-centered management with increased use of HPC in HaH and Rehab units and decreased access to HPC in SNH.

Keywords

breast cancer, expenditure, end of life, healthcare, observational study, palliative care

Introduction

The end-of-life care pathway of individuals with certain incurable cancers has been described as a progressive decline over several years, followed by a marked and sudden deterioration during the last weeks or months.[1,2] Early access to palliative care (PC) provides patients with improved comfort and better quality of life prior to their death.[2,3] Indicators proposed to measure the intensity of end-of-life care of cancer patients

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during the last month or last 2 weeks of life suggest high rates of healthcare use.[4] For example, high rates of hospitalization, emergency department visits, intensive care unit (ICU) admissions and chemotherapy have been reported for women with breast cancer (BC).[5-7] Detection of the palliative care needs and end-of-life planning are therefore becoming increasingly important.

BC is the most common cancer in women with an estimated incidence in France of 59,000 cases in 2017.[8] For women diagnosed with BC between 2005 and 2010, the net 5-year survival rate was 88%.[9] The expenditure for national health insurance of patients managed for BC in 2014, regardless of stage, was €2,515 million, i.e. 19% of all cancer-related expenditure and 2% of total reimbursed expenditure.[10] This expenditure was estimated by means of the *Système National des Données de Santé* (SNDS) [National Health Data System], which is being progressively deployed in France.[11] Few large observational studies of women who died from BC, focusing on intensity of care, place of death and expenditure, are available.

The objective of this observational study, based on SNDS data, was to describe the causes of death of women managed for BC during the year before their death in 2015, and, for women who died from BC, their characteristics and comorbidities, the hospital pathway during the last year of life and the expenditure reimbursed by French national health insurance, the intensity of care during the last month of life and factors associated with HPC management at the end of life for those who died in hospital.

Patients and Methods

Setting

All the 66 million inhabitants in France had public health insurance. At the end of 2015, the general scheme covers salaried employees of the private sector and their dependents were selected (i.e. about 77% of the population living in France), as well as people covered by *Sections Locales Mutualistes* (SLM) [local mutualist sections], essentially civil servants, employees of territorial collectivities and public hospitals and students, i.e. about 11% of the population. Other schemes cover the rest of the population.[11]

Data Source

The SNDS includes, for each individual, information about reimbursed hospital and outpatient health care utilization, including hospital palliative care (HPC), as well as the possible causes of death.[11-13] It comprehensively collects individual outpatient data (age, sex, etc.), as well as healthcare prescriptions and procedures reimbursed by French national health insurance, but it does not provide any clinical data concerning the results of physician visits, prescriptions or examinations. Nevertheless, it includes information on the presence of long-term chronic diseases (LTD) eligible for 100% reimbursement of healthcare expenditure, when requested by the

patient's general practitioner and after approval by the health insurance medical consultant. Using a pseudonymized identification number, all this information is linked, via the national hospital discharge database, to data concerning public and private hospital stays: short-stay hospitals (SSH), Rehabilitation (Rehab) and hospital-at-home (HaH) and a specific database indicating whether or not the person is a resident of a skilled nursing home (SNH). Hospital discharge diagnoses and LTD diagnoses are coded according to the International Classification of Diseases 10th revision (ICD 10). Primary and secondary causes of death (ICD 10) are collected and analyzed by the Epidemiology Centre on Medical Causes of Death (Inserm-CépiDc). These data are linked in the SNDS using an indirect matching and deterministic procedure, prior to the introduction of a common identifier. Several common variables were used: full date of death, month and year of birth, gender, and place of residence. The overall matching rate was 93% in 2015. The SNDS databases are mainly devoted to healthcare reimbursement and public health policies, and consequently comprise very few missing data.

Selection of Cases and Study Population

The *Caisse Nationale d'Assurance Maladie* (CNAM), the general health scheme fund, has developed a tool based on SNDS data with algorithms designed to identify beneficiaries reimbursed for chronic diseases and common, serious or expensive diseases and treatments each year, in order to study these diseases in terms of numbers, prevalence and incidence rates, expenditure and annual growth.[12,13] Algorithms identify 56 non-exclusive groups of diseases, classified into 13 main categories, based on principal diagnoses, related or significant associated diagnoses in short-stay hospitals and psychiatric hospitals, LTD, dispensing of specific drugs, and specific procedures.[14] In this tool, algorithms designed to identify people on cardiovascular prevention drugs (antihypertensives or lipid-lowering drugs) or psychotropic drugs are considered on the basis of 3 annual reimbursements. Cancer is defined by short-stay hospitalizations over a 5-year period and/or LTD status based on specific cancer diagnoses. BC cases are distinguished according to the presence of active treatment or surveillance. Cases with active treatment are defined as those requiring, over a 2-year period, either hospitalization for treatment, with the exception of hospitalizations for assessment only, or hospitalization for metastasis, or initiation of management for an LTD, or specific treatment, excluding long-term administration of aromatase inhibitors and anti-oestrogens for prevention of recurrence. Actively treated cancers were included in preference to cancers under surveillance.

This retrospective observational study concerned all French national health insurance general scheme beneficiaries, who died in 2015 and who were identified by an active BC treated in 2014 or 2015. Women who died from BC were then selected for detailed analyses. The study was confined to these schemes because, at this time, the other schemes did not systematically record the vital status of their beneficiaries.

Description of Variables

All data used for this study were derived from SNDS. In France, palliative care is provided by various types of hospitals or institutions: SSH have acute wards and palliative care facilities (specific wards, mobile teams providing palliative care advice and expertise to other healthcare professionals in other wards) and specific beds; rehab hospitals, to which people are usually admitted after an acute hospital stay and which are devoted to rehabilitation as well as palliative care depending on their rehabilitation specialization; and HaH care delivered at home by hospital teams. Data concerning HaH were analyzed separately, as HaH constitutes a specific type of management. Palliative care is also provided at home and in skilled nursing homes (SNH) by ambulatory teams not attached to hospital units, but this information is not available in the SNDS. In this study, the concept of HPC comprises palliative care during hospital stay, in specific wards or not, and delivered during the year, either before death or at the time of death. HPC were identified using ICD code (Z51.5) and stay in specific beds dedicated to palliative care.

Chemotherapy not administered by the IV route consisted of drugs dispensed by a retail pharmacy and reimbursed by national health insurance, including subcutaneous injections using ATC codes (antineoplastic and immunomodulating agents).

Information on the place of death is available for deaths occurring during hospital stays (SSH, Rehab or HaH) or in SNH. However, among "other places" of death, death at home cannot be distinguished from death outside home: in a retirement home, in public places, etc.

For all health care benefits (drugs, clinical pathology procedures, consultations, sick-leaves and disability benefits, etc.) reimbursed by French national health insurance, SNDS indicates, in particular, the sums corresponding to the expenditure billed to the beneficiary, the reimbursable expenditure (i.e. reimbursement basis) and the sum reimbursed to the beneficiary. All these expenditures are calculated from the CNAM's perspective. Drugs dispensed during a hospital stay are not individually reimbursed and are integrated in the global cost of the stay. It is therefore not possible to precisely identify which drugs are prescribed to the patient during hospital stays or chemotherapy sessions, except for specific drugs billed by the hospital in addition to diagnosis-related group funding. Reimbursed inpatient and outpatient health care were included in the study for all selected patients.

Analyses

Data are expressed as the mean $\pm$ standard deviation (SD). The rates of at least one healthcare reimbursement during the study period were reported. Means were calculated only for those people with at least one reimbursement during the period considered. The total and mean lengths of stay during the 365 days prior to death per patient in the same type of hospital were determined. Percentages were compared by Chi-square test,

ANOVA or Student's t test and medians were compared by Wilcoxon's test or Kruskal-Wallis test. A Sankey diagram was used to illustrate patient flow according to the presence and the types of hospitalization during the year or during the last 28 days before death. To study the variables independently associated with the presence of HPC during the end-of-life stay for women who died in hospital, univariate and multivariate logistic regression modeling was performed using a backward elimination procedure for multivariate analysis. All variables associated with a P-value < 0.20 on univariate analysis were tested in this model. All statistical analyses were 2-tailed and the results were considered to be statistically significant for P-values < 0.05.

SAS software (version 7.11, SAS Institute Inc., Cary, NC, USA) was used for statistical analysis and R software (4.0.2.) was used for Sankey diagrams.

The CNAM, as a health research institute, has permanent access to the pseudonymized SNDS database approved by decree and the French data protection authority (*Commission Nationale de l'Informatique et des Libertés*).

Results

Causes of Death of Women Managed for BC

A total of 10,490 women managed for active BC during the previous year (2014-2015) died in 2015, and the cause of death was available in the SNDS for 9,790 (93.3%) of these women (Table 1). Cancer was reported as the cause of death for 84% of women. This proportion decreased with age (93% for women younger than 60 and 58% for women 90 years and older) and varied according to the place of death: almost 90% in hospital, 75% at home and 61% in skilled nursing home (SNH) and in the presence of hospital palliative care (HPC) (92% versus 69% in the absence of HPC). The second most common group of diseases was cardiovascular disease (5%), which was more frequent in SNH (10%) and with increasing age (15% for women 90 years and older). The third most common causes of death consisted of ill-defined conditions (4%), with 8% at home and in SNH.

BC was reported as the cause of death for 68% of women managed for active BC (58% of deaths at home, 72% of deaths in SSH or Rehab and 74% of deaths in HaH). Higher rates of BC as cause of death were observed among younger women with less frequent comorbidities (82% for women younger than 60 years).

Characteristics of Women With BC as the Cause of Death

Among the 6,696 women retained, they had a mean age of 69 years (SD 15 years), 28% were younger than 60 years and 28% were 80 years or older (Table 2). Almost 70% of women died in short-stay hospitals (SSH), 4% died in HaH, 9% died in Rehab units, 5% died in SNH and 12% died at home. On average, women who died in SSH or HaH were younger (mean age: 66 years and 68 years, respectively) and women who died at home (72 years), in Rehab (75 years) and in SNH (85 years) were older.

Table 1. Causes of Death of Women Managed for Breast Cancer Who Died in 2015.

	Total	Place of death						Hospital palliative care			Age (years)					
		Homeor other	SNH	HaH	Rehab	SSH	p	No	Yes	p	<60	60-69	70-79	80-89	≥90	p
All causes																
N (%)	9,790 (100)	1,354 (13.8)	651 (6.6)	416 (4.2)	793 (8.1)	6,576 (67.3)	***	3,554 (36.3)	6,236 (63.7)	***	2,251 (23.0)	2,105 (21.5)	2,094 (21.4)	2,531 (25.8)	809 (8.3)	***
Tumors	83.9	75.0	60.5	91.3	89.4	86.9	***	69.3	92.3	***	93.1	91	86.5	76	58	***
Cardiovascular	4.8	7.3	10.4	1.9	2.9	4.2		9.4	2.2		0.8	2.5	3.9	7.8	15.0	
Ill-defined conditions	3.7	7.8	8.1	4.8	3.2	2.4		5.8	2.5		3.2	2.6	3.2	4.6	6.7	
Respiratory system	1.5	1.6	2.5	0.5	0.5	1.6		3.0	0.6		0.3	0.4	1.2	2.4	5.4	
External causes	1.4	3.4	3.2	0.2	0.5	1.0		3.2	0.4		1.0	1.0	1.4	1.7	3.1	
Gastrointestinal system	1.1	0.9	0.9	0.5	0.3	1.2		2.1	0.5		0.6	1.1	1.3	1.1	1.4	
Neurodegenerative	1.0	1.4	5.2	0	0.8	0.6		1.8	0.5		0.3	0.2	0.6	2.0	2.6	
Endocrine	0.6	1.1	2.2	0.2	0.5	0.4		1.2	0.3		0.2	0.3	0.3	1.2	1.7	
Infectious	0.5	0.1	1.2	0	0.5	0.5		1.1	0.1		0.2	0.4	0.4	0.5	1.6	
Genitourinary	0.4	0.2	0.2	0.2	0.6	0.4		0.7	0.2		0	0	0.4	0.7	0.9	
Other	1.1	1.2	5.6	0.4	0.8	0.8		2.4	0.4		0.3	0.5	0.8	2.0	3.6	
Tumor details																
Breast	68.4	58.0	49.3	74.1	72.2	71.6	***	55.0	76.0	***	82.1	72.5	67.8	60.2	46.8	***
Larynx, trachea, bronchus, lung	3.4	3.7	4.7	7.1	6.7	0.6		2.8	3.8		2.6	5.1	4.0	2.7	1.7	
Ovary	1.1	0.7	1.2	3.2	1.3	0.2		0.6	1.4		1.0	1.8	1.0	0.9	0.1	
Lymphatic tissue	0.9	1.0	1.2	2.0	2.0	0.2		1.2	0.8		0.5	0.7	1.4	1.3	0.6	
Colon	0.9	1.4	1.2	3.2	2.2	0.1		0.9	0.9		0.3	0.9	1.2	1.1	1.0	
Pancreas	0.8	1.0	0.8	2.7	1.3	0.2		0.6	1.0		0.5	1.4	1.0	0.9	0.1	
Kidney	0.8	0.8	3.1	2.7	0.9	0.1		0.8	0.8		1.0	0.7	0.7	0.8	0.8	
Body of uterus	0.8	0.4	0.8	2.0	1.8	0.1		0.4	0.9		0.3	0.9	1.0	0.7	0.9	
Liver	0.4	0.8	0.8	0.0	0.4	0.1		0.3	0.6		0.1	0.3	0.9	0.5	0.3	
Rectum, anus	0.4	0.2	1.6	2.7	0.5	0.1		0.1	0.6		0.2	0.4	0.8	0.3	0.5	
Other, not specified	5.9	7.2	13.4	20.8	7.6	1.0		6.4	5.5		4.6	6.3	6.8	6.5	5.0	

*** p < 0.001.
Abbreviations: HaH, hospital-at-home; Rehab, rehabilitation; SNH, Skilled nursing home; SSH, short-stay hospital.
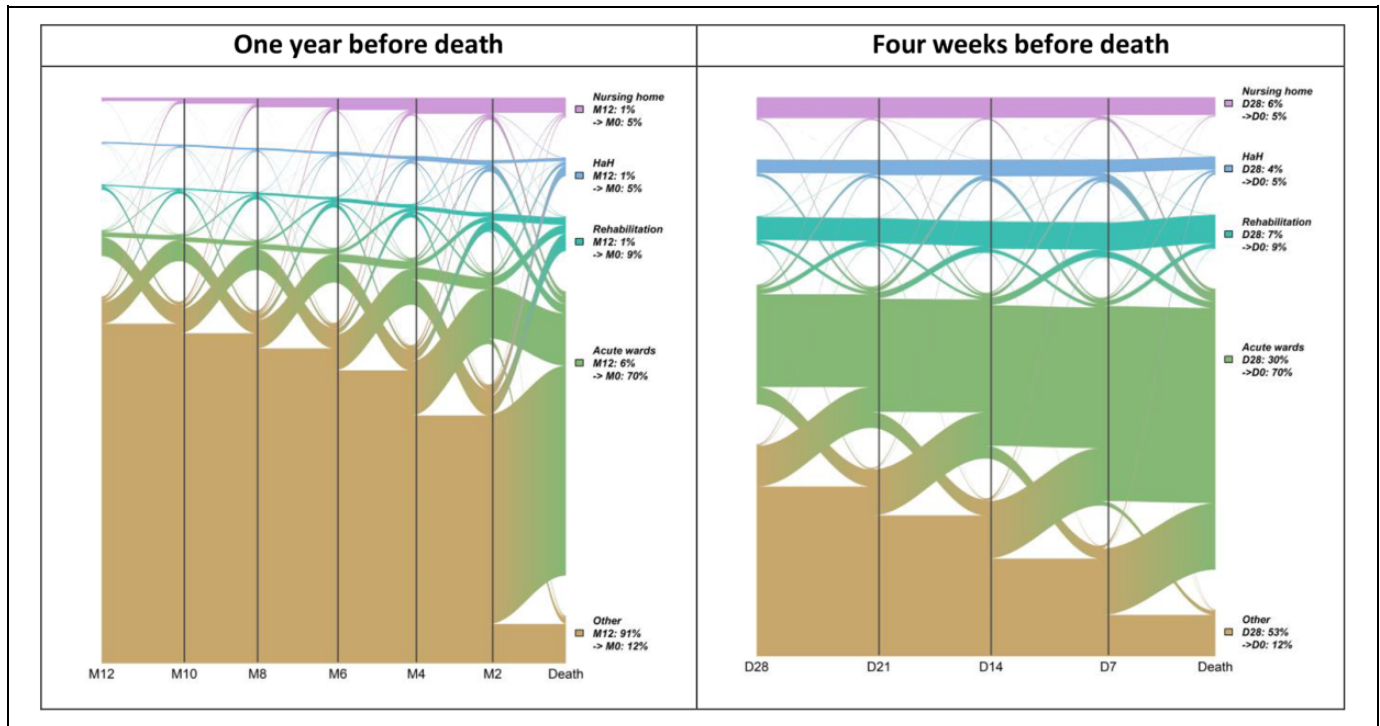
Figure 1. Hospital and SNH care pathway for women who died in 2015 and who had been managed for breast cancer during the last year and the last 4 weeks of life. In this diagram, percentages reflect the distribution of patients according to their place of stay each month or week (last month) before death and their flow from one place to another each month or week. HaH indicates hospital-at-home.

At least one other cancer, either actively treated or under surveillance during the previous 5 years, was identified for 17%, with a lower rate of other cancers for women who died in SSH or HaH (16%) and a higher rate for women who died in SNH (23%) or Rehab (21%). During the year before death, more than one-third of women presented cardiovascular comorbidity, 17% had chronic respiratory disease, 15% had diabetes, and 9% had a neurological or degenerative disease. These frequencies differed according to the place of death, with 46% of women presenting cardiovascular diseases and 39% presenting neurological and degenerative diseases in SNH, in which women are generally older (mean age: 85 years). Women who had received HPC at least once, i.e. 71% of women (including 5% prior to the end-of-life stay), were younger (mean age: 67 years vs 71 years) and less often presented cardiovascular diseases (31% vs 36%). These women more often had at least one HaH (18%), Rehab (29%) or SSH (92%) stay in the year before death, but were less often admitted to SNH (5% vs 14%). About 34% of the women who died in SNH and 33% of the women who died at home had received HPC compared to 96% in HaH, 86% in Rehab and 76% in SSH.

Hospitalizations and Hospital Pathways

During the year before death, almost all (91%) women were hospitalized at least once, with an annual mean length of stay of 74 days: 90% in SSH (mean length of stay: 53 days), 25% in Rehab, 13% in HaH and 8% in SNH (Table 1). The mean annual length of stay in the presence of HPC was 83 days vs 50 days in the absence of HPC.

Figure 1 illustrates the flows of women between the various places of management during the year before death. More intense flows were observed during the last 2 months of life, predominantly from home to acute wards in SSH and, to a lesser extent, from acute wards in SSH to Rehab. When focusing on the last 28 days, flows from home to acute wards intensified before death, especially during the last week: 53% of women were at home at the beginning of the last month and 12% were at home at the time of death, while 30% of women were in acute wards at the beginning of the last month versus 70% at the time of death. These proportions were relatively stable for HaH and SNH.

Intensity of End-of-Life Care

During the month before death (Table 3), 85% of women were admitted at least once to SSH, with a mean of 2 stays. Hospitalization rates and the number of stays decreased for older women. At least one emergency department visit was identified for 42% of women, regardless of their place of death and, according to the place of death: SSH (43%), Rehab (42%), HaH (32%), SNH (51%), home (27%). During hospital stays, 10% of women were admitted to an intensive care unit (8% with HPC, 14% without HPC), 24% received a chemotherapy session (13% during the last 14 days of life). These frequencies were higher for women who died in SSH (29% and 16%) and in the

Table 2. Characteristics, Comorbidities and Treatments of Women With Breast Cancer as a Cause of Death in 2015 and Who Had Been Managed for Their Breast Cancer During the Year Before.

	Total	Place of death						Hospital palliative care		
		Home or other	SNH	HaH	Rehab	SSH	p	No	Yes	p
N	6,696	785	321	308	573	4,709		1,955	4,741	
%	100.0	11.7	4.8	4.6	8.6	70.3		29.2	70.8	
	%	%	%	%	%	%		%	%	
Age at inclusion (years)										
mean (years) ± SD	68.7 ± 14.6	72.2 ± 14.3	85.1 ± 8.0	68.4 ± 14.2	74.6 ± 12.2	66.4 ± 14.3	**	71.2 ± 14.7	67.2 ± 14.3	***
<60 years	27.6	20.5	0.9	26.3	12.4	32.5	***	22.9	29.6	***
60-69 years	22.8	20.1	4.4	26.0	19.6	24.7		19.8	24.0	
70-79 years	21.2	22.0	15.0	22.7	26.5	20.7		21.4	21.1	
80-89 years	22.8	28.3	48.0	20.1	33.9	18.9		26.6	21.2	
≥ 90 years	5.7	9.0	31.8	4.9	7.7	3.1		9.4	4.1	
Comorbidities										
Lung cancer	0.8	0.5	–	1.0	0.3	0.9	.	0.6	0.8	.
Colorectal cancer	1.4	1.8	1.6	0.3	1.9	1.3	.	1.2	1.5	.
Other cancers	15.0	16.1	21.2	14.6	19.2	13.9	***	15.9	14.6	.
Cardiovascular/neurovascular	32.7	31.9	45.5	26.6	34.7	32.1	***	36.3	31.2	***
Diabetes	14.5	14.1	16.2	16.6	18.0	13.8	**	15.5	14.0	.
Psychiatric	8.3	7.7	17.4	6.2	9.2	7.9	***	8.8	8.2	*
Neurological or degenerative	9.3	10.8	38.9	7.5	12.9	6.6	***	12.2	8.0	***
Chronic respiratory	16.9	16.8	14.0	14.9	15.4	17.5	.	17.1	16.9	.
Chronic inflammatory	3.0	2.6	2.8	2.3	2.6	3.2	.	2.4	3.3	.
Rare diseases	0.3	0.4	0.3	–	0.3	0.4	.	0.5	0.3	.
HIV or AIDS	0.2	–	–	–	0.2	0.3	.	0.2	0.2	.
Chronic dialysis	0.3	0.1	0.3	0.3	0.2	0.4	.	0.4	0.3	.
Liver or pancreas	12.0	6.1	1.9	4.6	5.6	15.0	***	11.2	12.4	.
Treatments										
Psychotropic drugs	52.3	53.9	67.9	54.9	53.4	50.7	***	51.0	52.9	*
Hypnotics	19.4	17.7	24.3	19.8	19.4	19.3	.	18.7	19.7	.
Anxiolytics	35.2	38.3	46.7	34.4	36.8	33.7	**	34.5	35.5	.
Neuroleptics	4.4	5.5	11.5	3.3	4.4	3.8	***	5.1	4.1	.
Antidepressants	26.2	30.3	39.9	27.3	25.7	24.6	***	25.8	26.4	*
Antihypertensives	53.6	57.3	66.7	48.7	60.2	51.6	***	55.7	52.7	***
Lipid-lowering drugs	19.3	17.0	18.7	21.1	22.2	19.2	.	20.7	18.7	.
At least one stay in the year										
SSH	89.9	82.0	74.5	86.7	90.2	100.0	***	84.0	92.3	***
Mean total length of stay	53.0 ±	38.4 ±	35.6 ±	49.0 ±	50.9 ±	56.6 ±	***	38.7 ±	58.4 ±	***
(SD)	42.3	34.3	31.7	38.1	39.8	43.7		35.3	43.5	
HaH	13.2	5.1	2.5	100.0	5.8	10.6	***	2.6	17.6	***
Rehab	25.4	16.8	35.8	15.9	100.0	17.6	***	16.9	28.9	***
All types$	90.9	88.5	83.2	100.0	100.0	100.0	***	92.4	100.0	***
Mean total length of stay	73.9 ±	53.3 ±	68.4 ±	98.1 ±	108.4 ±	71.5 ±	***	50.3 ±	82.9 ±	***
(SD)	69.0	58.9	71.0	81.5	78.1	66.3		53.7	72.0	
SNH	7.5	1.5	100.0	6.5	2.4	2.9	***	13.7	5.0	***
Hospital palliative care	70.8	33.1	34.3	96.4	85.5	76.1	***	–	100.0	***
Other than the end-of-life stay	4.8	16.7	11.8	2.0	2.3	2.8	***	–	6.8	***

$ Sum of SSH+Rehab+HaH stays.

° Palliative care in SSH+Rehab+HaH, at home and in SNH cannot be identified.

***p < 0.001, ** p < 0.01, *p < 0.05.

Abbreviations: HaH, hospital-at-home; Rehab, rehabilitation; SD, standard deviation; SNH, Skilled nursing home; SSH, short-stay hospital.

Table 3. Presence of at least One Utilization of the Various Intensity of Care Indicators During the Last 30 Days of Life in 2015.

	Total	Place of death					Hospital palliative care		Age-group				
		Home	SNH	HaH	Rehab	SSH	No	Yes	< 60 years	60-69 years	70-79 years	80-89 years	≥ 90 years
N	6,696	785	321	308	573	4,709	1,955	4,741	1,848	1,526	1,419	1,524	379
%	100%	11.7%	4.8%	4.6%	8.6%	70.3%	29.2%	70.8%	27.6%	22.8%	21.2%	22.8%	5.7%
SSH stay													
At least one stay	85.0	46.1	27.4	54.9	63.2	100.0	74.1	89.5	94.2	90.0	84.6	75.7	58.6
Number of stays*	1.9 ± 1.6	2.0 ± 1.9	1.2 ± 0.5	1.5 ± 0.8	1.7 ± 1.6	2.1 ± 1.5	2.1 ± 1.7	2.0 ± 1.4	2.4 ± 1.7	2.1 ± 1.5	1.9 ± 1.4	1.6 ± 1.2	1.4 ± 1.1
Length of stay (days ± SD)*	17.9 ± 9.8	10.7 ± 9.5	13.3 ± 10.1	13.7 ± 9.8	17.1 ± 9.5	17.8 ± 9.6	13.4 ± 9.4	18.4 ± 9.6	17.5 ± 9.7	16.7 ± 9.9	17.6 ± 9.9	17.1 ± 9.9	15.0 ± 9.0
Rehab stay													
At least one stay	15.2	4.5	8.1	3.6	100.0	7.9	8.5	17.9	8.3	13.6	19.2	20.3	19.5
HaH stay													
At least one stay	11.0	2.7	1.3	100.0	3.0	8.1	1.5	14.9	14.6	12.5	9.7	7.4	6.1
Emergency department visit													
At least one visit	41.8	26.5	51.1	32.0	42.0	43.1	48.4	39.5	37.9	38.6	40.5	50.3	54.5
Followed by hospitalization	34.7	11.6	13.7	16.6	26.5	42.2	34.9	34.7°	34.5	34.1	33.5	37.5	31.7
Number of visits*	1.1 ± 0.4	1.0 ± 0.3	1.0 ± 0.2	1.0 ± 0.4	1.1 ± 0.2	1.1 ± 0.4	1.1 ± 0.4	1.1 ± 0.4°	1.1 ± 0.5	1.1 ± 0.4	1.1 ± 0.3	1.1 ± 0.4	1.1 ± 0.3
ICU stay													
At least one stay	9.5	2.2	1.3	2.0	3.5	12.6	14.1	7.6	12.5	10.7	9.8	6.2	2.9
Chemotherapy (At least one)													
Last 30 days													
Inpatient	24.3	17.3	2.2	15.9	14.3	28.8	27.4	23.1	39.0	30.5	20.0	10.0	1.9
Outpatient	18.2	24.7	22.1	10.1	5.8	18.9	25.8	15.0	18.2	18.0	16.1	19.5	21.9
Last 14 days													
Inpatient	13.3	10.3	1.2	7.5	8.6	15.6	19.3	10.8	20.1	17.3	11.8	5.4	1.1
Outpatient	6.6	12.2	8.1	2.6	1.7	6.4	11.3	4.6	6.3	7.0	5.9	6.9	7.7
Radiotherapy (At least one session)													
Last 30 days	5.7	2.8	1.6	3.9	6.5	6.5	5.0	6.0°	8.6	6.1	5.1	3.5	1.3
Last 14 days	4.0	1.7	0.9	2.9	3.5	4.8	4.6	3.8	5.8	4.7	3.8	2.0	1.3

*among those women with at least one visit with or without an overnight stay.

° p-value not significant.

Abbreviations: HaH, hospital-at-home; Rehab, rehabilitation; SNH, Skilled nursing home; SSH, short-stay hospital.

Table 4. Characteristics and at Least One Utilization of the Various Intensity-of-Care Indicators During the Last 30 days Before Death in 2015 Associated With Hospital Palliative Care During the Last Stay For Women Who Died in Hospital.

	Crude OR	95%CI	p	Adjusted OR	95% CI	p
Age						
<60 years	1		ns			
60-69 years	0.98	0.83-1.15				
70-79 years	0.91	0.77-1.07				
80-89 years	0.92	0.77-1.09				
$\geq$ 90 years	0.94	0.67-1.3				
Comorbidities vs no comorbidities						
Other cancers	0.97	0.83-1.14	ns			
Cardiovascular/neurovascular	0.76	0.67-0.86	<.0001	0.83	0.72-0.95	0.008
Diabetes	0.89	0.75-1.05	ns			
Psychiatric	0.91	0.73-1.13	ns			
Neurological or degenerative	0.98	0.78-1.23	ns			
Chronic respiratory	0.85	0.73-0.99	0.03			
Liver or pancreas	0.83	0.70-0.98	0.03			
Other diseases	1.03	0.76-1.4	ns			
Place of death						
SSH	1		<.0001			<.0001
Rehab	1.64	1.32-2.04		1.4	1.05-1.86	
HaH	6.82	4.2-11.2		4.5	2.47-8.1	
At least one during the last 30 days						
SNH stay	0.60	0.43-0.84	<.0001	0.52	0.36-0.76	0.0007
Number of SSH stays	0.90	0.87-0.94	<.0001			
ICU stay	0.34	0.28-0.40	<.0001	0.36	0.30-0.43	<.0001
Chemotherapy						
Inpatient	0.57	0.50-0.65	<.0001	0.55	0.48-0.63	<.0001
Outpatient	0.56	0.49-0.65	<.0001	0.60	0.51-0.70	<.0001
Radiotherapy (session)	1.09	0.85-1.40	ns			
At least one during the last 14 days						
Chemotherapy						
Inpatient	0.5	0.42-0.58	<.0001			
Outpatient	0.41	0.33-0.52	<.0001			
Radiotherapy (session)	0.95	0.72-1.27	ns			

Ns: not significant.
Abbreviations: CI, confidence interval; HaH, hospital-at-home; OR, odd-ratio; Rehab, rehabilitation; SNH, Skilled nursing home; SSH, short-stay hospital.

absence of HPC. Chemotherapy was dispensed by a retail pharmacy to 18% of women during the last month and to 7% of women during the last 2 weeks of life. The oldest women and those died in SNH or at home were more frequently reimbursed for chemotherapy dispensed by a retail pharmacy. Radiotherapy sessions were relatively uncommon (6% during the last 30 days and 4% during the last 14 days).

Independent Factors Associated With HPC Access During the End-of-Life Stay

Poorer access to HPC was observed for women with cardiovascular or neurovascular comorbidities (adjusted odds ratio, aOR: 0.83; 95% Confidence Interval, 95%CI: 0.72–0.95) and at least one SNH stay (aOR: 0.52; 95%CI: 0.36-0.76), ICU stay (aOR: 0.36; 95%CI: 0.30-0.43), inpatient chemotherapy (aOR: 0.55; 95%CI: 0.48-0.63), outpatient chemotherapy (aOR: 0.60; 95%CI: 0.51-0.70) during the 30 days before death (Table 4). Better access to HPC was observed for women who died in

Rehab (aOR: 1.4; 95%CI: 1.05-1.86) or HAH (aOR: 4.5; 95%CI: 2.47-8.1).

Expenditure of the Last Year of Life

The global French national health insurance expenditure for the last year of life for all women managed for BC included in this study was €259 million (€200 million with HPC, €59 million without HPC), including €155 million for hospital expenditure, €92 million for office medicine expenditure and €12 million for other benefits. The mean annual expenditure per woman was €38,734 (€42,209 with HPC, €30,297 without HPC). The mean monthly expenditure accelerated during the last month of life (Figure 2) and was always higher in the presence of HPC, even during the first months with a more marked difference closer to the end of life.

Discussion

This observational study based on real-world data concerning women with BC as cause of death described their care
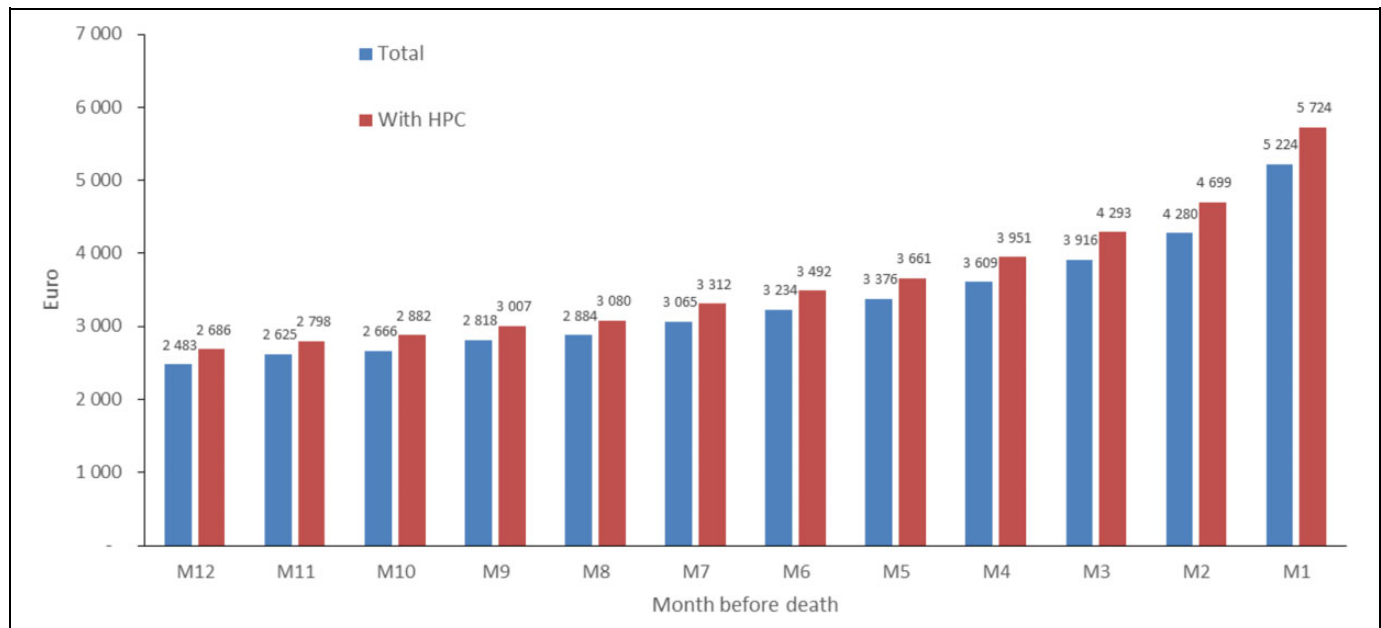
Figure 2. Growth of the mean monthly national health insurance expenditure for women who died in 2015 and who had been managed for breast cancer during the previous year, and details concerning the presence of hospital palliative care (HPC).

pathways, which involved several types of institutions, with intense flows during the last month of life from home to SSH, the main place of death, as well as Rehab units and HaH, representing a total of about 85% of all deaths. About 71% of women with BC as cause of death received HPC at the end of life, but only a small proportion received HPC prior to their end-of-life stay. Emergency department visits and inpatient and outpatient chemotherapy sessions were frequent during the last month of life, but less frequent for women who died in hospitals with HPC.

Causes of Death

The active BC inclusion algorithm identified 82% of all women with BC as the cause of death in the source population of this study. The remaining women were classified as BC under surveillance in 1% of cases, other active cancers in 4% of cases, other cancers under surveillance in 9% of cases, while no BC or other active cancer or cancer under surveillance was detected by the algorithms in 4% of cases. The presence of other active cancers can be explained by the fact that about 16% of women with BC who died in 2015 also presented another cancer, either actively treated or under surveillance and presented major disease progression justifying specific health care and a cause of death other than BC. An American study linked cancer registry patients to their cause of death (1973-2012) and revealed a decreasing proportion of patients for whom the main cause of death was BC since the beginning of the 1970s (70%) that reached 30% in 2012.[15] In contrast, a slight increase in the proportion of deaths due to other cancers was observed (12% in 2012). Cardiovascular disease accounted for almost 20% of deaths.[15] The proportion of deaths due to BC was

higher in our study (64%), with also high proportions of deaths due to other cancers (16%) and a lower proportions of deaths due to cardiovascular disease (5%). These differences are probably related to epidemiological differences. Nevertheless, about one-third of women in our study who died with BC presented cardiovascular comorbidity, which was negatively associated with HPC use among women who died from BC in hospital. Another American study also revealed an age-related increase in the proportion of deaths due to cardiovascular disease.[16]

Health Care Indicators

Few published studies have described health care indicators for BC apart from the frequency of chemotherapy.[5-7] A French study, also based on SNDS data, specifically devoted to chemotherapy in the overall population of patients with metastatic cancer who died between 2010 and 2013, reported that 19% of patients received chemotherapy during the last month of life (11% during the last 2 weeks of life),[17] similar to the frequencies observed for BC in our study (21% and 12%). Factors associated with the use of chemotherapy toward the end of life were younger age, limited comorbidities, a chemosensitive cancer associated with significant life expectancy, and the absence of HPC in hospital or in the private sector.[17] In the United States (2010-2014), 23% of women with metastatic BC received chemotherapy during the last 4 weeks of life and 12% received chemotherapy during the last 2 weeks of life, i.e. similar proportions for chemotherapy use observed in our study.[6] No study has included the rates of chemotherapy using drugs purchased from a retail pharmacy consisting of targeted therapies (anti-HER2, anti-VEGF) and endocrine therapy

(18%, 30 days before death), more often used by women who died at home or in SNH. Frequent intercurrent and long-term hospitalizations during the last month of life (mean of 2 stays) could have limited the use of these drugs purchased from retail pharmacies. Nevertheless, our study also shows that chemotherapy (oral or intravenous) 1 month before death is negatively associated with HPC use at the end of life for women who died in hospital, which could suggest that decreased use of chemotherapy may have been planned in women with planned end of life and HPC. In other women without HPC, the end of life may have been unexpected, possibly due to rapid deterioration of the patient's health status or comorbidities such as cardiovascular disease. The hypothesis of planned end of life could be supported by the low chemotherapy rates observed for women who died in HAH or Rehab units associated with high HPC access on multivariate analysis.

High values were also observed for other intensity-of-care indicators, especially for patients who died in SSH. For example, during the last month of life, 14% of patients who died in SSH were managed in an ICU and 85% had at least one hospital stay and 49% had at least 2 hospital stays. SNH stays and ICU stays are independent negative predictive factors for HPC use among women who died in hospital. In a study comparing all cancers in 7 countries in 2010, the proportion of people with at least one SSH stay during the last month of life ranged from 44% in The Netherlands to 64% in Norway, lower than that observed in our study.[18] The presence of at least one ICU stay for all cancer patients in 4 countries ranged from 9% in Germany to 18% in Belgium, and was 11% for BC in our study.[19] The proportion of patients attending the emergency department in these 4 countries ranged from 27% in Germany to 58% in England and 37% for BC in our study.[19] In our study, as only emergency visits followed by hospitalization were recorded, the emergency visits was probably underestimated. Our study identified radiotherapy sessions for 6% of women during the last month of life, but our study did not include community radiotherapy sessions. The indication for radiotherapy, for metastasis, for example, was not available in the database, but a review of the literature estimated that 5% to 10% of patients under the age of 65 years received at least one palliative radiotherapy session during the last month of life.[20] All of these indicators were higher in patients under the age of 65 compared to older patients, as in the United States.[21]

Palliative Care

Utilization of palliative care, especially at an early stage of the disease, has been shown to have a positive impact on the patient's quality of life with decreased intensity of health care and the use of less aggressive treatments during the last month of life.[2,3,5-7,22-24] The presence of HPC during the last year of life or at the time of death was identified for 71% of women in this study, but only for 5% of women prior to their end-of-life stay. As in other studies, patients managed by palliative care were younger and presented fewer comorbidities.[5] In the present study, patients managed by HPC were more often admitted

to various types of hospitalization with a longer mean annual length of stay. Patients managed by HPC were also more frequently hospitalized during the last month of life, especially in HaH and Rehab units with increased access to HPC compared to SSH, suggesting a planned end of life considering the relative increase of patient flows during the last month of life.

Place of Death

End-of-life management for women dying from BC is essentially hospital-centered in France, but among the 17% of women who died at home or in SNH, about 15% had received HPC. A similar study conducted in France on all cancer patients (mean age: 73 years) who died in 2013 showed that 67% of deaths occurred in SSH, 8% in Rehab, 4% in HaH, 5% in SNH and 15% at home or other places.[12] These proportions were similar to those observed for women with BC as cause of death in this study: 70%, 9%, 5%, 5% and 12%, respectively. The proportion of 67% of cancer patients who died in SSH is higher than that reported in 7 other countries in 2010, ranging from 29% in The Netherlands to 54% in Canada.[18] Another study conducted in 6 European countries on the proportion of cancer deaths strictly at home in 2003 revealed proportions ranging from 12% in Norway to 45% in The Netherlands,[25] i.e. much higher proportions than those observed in France: 15% at home and 19% at home or in HaH. Few studies have specifically reported the place of death of breast cancer patients. In the United States, in a cohort of 123 patients with metastatic BC, 53% died at home[23] and, in another cohort of 947 patients, 25% died in hospital.[5] The proportion of each place of death and the mode of management may vary according to the definition of the cases included, either people who died with a managed cancer or, inversely, people for whom a cancer was the main cause of death, the study period, but also according to age, the type of cancer, its stage and its history, and any comorbidities, including concomitant cancers and the development and organization of palliative care.[5-7,21-33] Observed frequencies also vary according to organization of end-of-life care or palliative care in each country, either mainly in short-stay hospitals, as in France, or by preferring discharge from hospital and management at home or in hospices.

Expenditure

Few studies have reported the expenditure related to the last year of life in a large cohort of patients treated for BC and calculated from the national health insurance perspective. A study on the monthly expenditure reimbursed during the last 6 months of life revealed a progressive increase from $8,956 to $19,326 during the last month of life,[33] higher than the expenditures observed in our study. Expenditures related to sick leave were also higher for women with metastatic breast cancer compared to women with early stage cancer or controls.[34] In this study, a higher mean expenditure was observed for women managed by HPC. It is difficult to assess the possible impact of HPC in this study, as only a small proportion of HPC was

administered before the end-of-life stay and patients managed by HPC therefore probably had more advanced disease already associated with more intense health care utilization during the last year of life.

Strengths and Limitations

The main strengths of this study are the use of the SNDS population database comprising almost 77% of the French population. The diseases identified by multisource algorithms have been submitted to sensitivity analyses and expert reviews.[13] However, they depend on the use, offer and access to care. The data analyzed in this study were derived from administrative databases with their classical limitations i.e. data collection limited and coding.

The absence of information concerning the initial stage of disease or at the time of transfers from one hospital to another or to emergency departments does not allow more detailed analysis of whether these flows were scheduled or corresponded to emergency situations. The levels of quality indicators described here therefore cannot be used to assess the appropriate or inappropriate nature of care, as certain clinical factors and personal preferences may or may not justify the same level of care or an intercurrent event may have been the cause of death. Nevertheless, linkage between the SNDS and cancer registries, although they cover only about 20% of the French population, but based on specific methodologies, could be helpful, as they may enrich information about patient and cancer characteristics (stage, metastasis, etc.) and also provide confirmation of the ICD codes used by the SNDS.

In the present study, based on 77% of the French population and 93% linkage with the national cause of death database, BC was the main cause of 6,696 deaths corresponding, by crude extrapolation, to a larger sample of 9,351. This is smaller than the 11,913 deaths published by the Epidemiology Centre on Medical Causes of Death for all of France in 2015,[9] bearing in mind that the characteristics of populations not included on the basis of their national health insurance scheme are probably different (age, socioeconomic conditions, etc.).

Overall access to palliative care was probably underestimated, as the SNDS databases do not contain information on care provided at home or in any other outpatient palliative care PC setting, (e.g., care delivered in SNH, care delivered after a mobile palliative care team intervention). Nevertheless, HPC was sometimes administered before death in an SNH or in another place, suggesting return home or to a SNH for subsequent management, but the intensity of this care cannot be analyzed.

Conclusion

This study suggests a high level of hospital and HPC use in France for women with BC during the last year of life and a high proportion of hospital deaths related to the use of HPC mainly during the end-of-life stay. Women with inpatient or outpatient chemotherapy during the last month were less frequently managed by HPC, suggesting a planned decrease before death. This study also indicates SSH-centered management with intensive use of HPC and increased use of HPC in HaH and Rehab units and decreased access to HPC for women living in SNH. In the context of a reflection on the end-of-life national plan, these results must be confirmed and refined in order to detail specific fields of end-of-life care (diseases, disparity of uses, etc.) based on SNDS data, to guide and evaluate policies and improve monitoring and early access to HPC.

Abbreviations

ATC	Anatomical Therapeutic Chemical;
BC	breast cancer;
CNAM	*Caisse Nationale d'Assurance Maladie* general health scheme fund;
ICD-10	International Classification of Diseases, 10th edition;
ICU	intensive care unit;
IQR	interquartile range
LTD	long-term diseases;
SNDS	*Système National des données de santé* [National Health data Information System];
PC	palliative care;
HPC	hospital palliative care;
SSH	short-stay hospital;
HaH	hospital-at-home, Rehab: rehabilitation;
SNH	Skilled nursing home.

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