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# Treatment pattern, risk for hospitalization and mortality in elderly patients with triple-negative breast cancer

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Version 2

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## Abstract

### Introduction

Triple-negative breast cancer (TNBC) has limited treatment options, as chemotherapy is the only systemic therapy. This poses a challenge in the elderly population due to the limited research done, but also the increased risk for adverse events.

### Aim

To describe the treatment pattern, identify the risk of hospitalization and potential risk factors for hospitalization within 1 year from diagnosis, and investigate the causes of death in elderly with TNBC and possible predictors for mortality.

### Methods

We performed a registry-based cohort study using the BCBaSe database which links cases of breast cancer from 3 Swedish healthcare regions with socioeconomic factors, hospitalizations and causes of death. Women  $\geq 70$  years old with non-metastatic TNBC, between 1/1 2007 and 31/12 2012 were chosen (n = 413). Logistic regression and Cox proportional hazards regression analyses were used.

### Results

Age, stage and comorbidities influenced administration of chemotherapy. The risk of hospitalization overall was increased in the group receiving chemotherapy (OR 2.35, 95% CI 1.30 – 4.26) mainly due to toxicities. Chemotherapy use was not associated with either breast cancer-specific (HR 0.95, 95% CI 0.51 – 1.79) or overall survival (HR 0.72, 95% CI 0.44 – 1.18). Stage at diagnosis and comorbidities were associated with both breast cancer-specific mortality and overall mortality, whereas age was only associated with overall mortality.

### Conclusions

In elderly TNBC patients, chemotherapy use was associated with increased risk for hospitalization within 1 year from diagnosis without improving breast cancer-specific or overall survival. No benefit regarding mortality was seen in those who were administered chemotherapy.

**Keywords:** Triple-negative breast cancer; elderly; chemotherapy; hospitalization; treatment

## Abbreviations

TNBC	Triple-negative breast cancer
ER	Oestrogen receptor
PgR	Progesterone receptor
BCBaSe	The Breast Cancer DataBase Sweden
LISA	Longitudinal integration database for health insurance and labour market studies
CCI	Charlson Comorbidity Index
SD	Standard deviation
OR	Odds ratio
HR	Hazard ratio

## Introduction

Breast cancer is the most common type of cancer for women worldwide [1]. In 2017, more than 7 800 women were diagnosed with breast cancer in Sweden, and 1 400 died [2].

Advances in screening, diagnosis, and treatment have led to a decreased mortality over the last decades [3].

Breast cancer is divided into distinct subtypes depending on pathological features including tumour grade and expressions of different receptors; the oestrogen receptor (ER), the progesterone receptor (PgR), and overexpression of the Her2 protein [4]. One of the more aggressive subtypes of breast cancer is the triple-negative breast cancer (TNBC) [5], which does not express any of these markers. The lack of receptor expression rules out the ability to treat these patients with endocrine therapy and anti-Her2 treatment. Even though new therapies are on the horizon, this currently leaves chemotherapy as the only systemic treatment option [6,7].

With advancing age, the incidence of breast cancer increases [8]. However, elderly patients are often underrepresented in breast cancer clinical trials, which pose challenges in treatment decision making [9]. Elderly patients also have a higher rate of hospitalization after receiving chemotherapy due to side effects [10], including pain, nausea and neutropenia [11]. Despite this, adjuvant chemotherapy has been found to increase both all-cause and cancer-specific survival in elderly patients with breast cancer, especially in those with hormone-receptor negative disease and lymph node involvement [12,13].

Older patients with other forms of cancer have been examined more thoroughly than those with TNBC. In fact, elderly with colorectal cancer and lung cancer seem to derive benefit from chemotherapy which is comparable to younger patients [14,15].

## Aim

The aims of this study were to:

- 1) describe the treatment pattern in elderly patients with TNBC.
- 2) identify risk factors for hospitalization within 12 months after breast cancer diagnosis.
- 3) investigate the causes of death in elderly TNBC patients and potential predictors of breast cancer-specific mortality, non-breast cancer mortality, and overall mortality.

## Material and Methods

### Study design

The study was a register-based, population-based cohort study.

## Data source

The data used in this project stem from BCBaSe. BCBaSe is a database that links together the Longitudinal integration database for health insurance and labour market studies (LISA), the Swedish Inpatient Register, the Swedish Prescribed Drug Register and the Cause of Death registry with the Regional Breast Cancer Clinical Quality Registers from Uppsala/Örebro, Stockholm/Gotland and the Northern regions of Sweden. Comorbidities in BCBaSe was measured with the Charlson Comorbidity Index (CCI) [16].

## Identification of study cohort

All women 70 years old and over who received the diagnosis TNBC without distant metastasis between January 1, 2007 and December 31, 2012 were included in the study. These women were at the time of diagnosis residing in the regions of either Uppsala/Örebro, Stockholm-Gotland or the Northern regions of Sweden. TNBC was defined as oestrogen-receptor < 10%, progesterone-receptor < 10%, and Her2-negative breast cancer according to the National Guidelines for breast cancer [17]. Since the data on Her2 status was unreliable before 2007, this year was used as the cut-off point for study entry.

## Outcomes of interest

The following outcomes were of interest for the study:

1. Proportion of patients receiving chemotherapy in the study population and in specific subgroups (age, stage, comorbidity index, region where treatment was received, educational status and marital status).
2. Overall mortality, breast cancer mortality and non-breast cancer mortality in the study population and in specific subgroups (age, stage, comorbidity index, region where treatment was received, marital status, adjuvant radiotherapy and if chemotherapy was given).
3. Hospitalization rate in patients receiving adjuvant chemotherapy in the study population and in specific subgroups (age, stage, comorbidity index, region, educational status, type of surgery and type of chemotherapy). Only hospitalizations within 12 months from breast cancer diagnoses were included in the analyses, with causes related to surgery excluded. Hospitalizations were categorised to be associated with chemotherapy toxicity when the primary diagnosis at hospitalization was one of the following: infection, fever, neutropenia, thrombocytopenia, anaemia, adverse effects of chemotherapy, dehydration, or delirium. In the event of multiple hospitalizations, those who had at least one admission due to toxicity was counted as such, and otherwise counted in other causes.

## Statistical analysis

Categorical variables were analysed and presented with the number of patients and the percentages in each group. Continuous variables were analysed and presented with minimum, maximum and median.

For bivariate analysis chi-square was used with categorical variables and either t-test or Mann-Whitney U-test was used on continuous variables, depending on distribution. For determining whether the continuous variables had a normal distribution or not, the Kolmogorov–Smirnov test was used.

Logistic regression analysis was used to identify potential factors for receiving chemotherapy and risk factors for hospitalization. The variables included in logistic regression analyses were chosen from two approaches: variables that were statistically significant in bivariate analyses and variables that in earlier studies have shown to have an impact. Multivariable Cox proportional hazards regression analyses were performed to investigate the impact of different variables on overall mortality, breast-cancer specific mortality, and non-breast cancer mortality.

All analyses were performed according to complete case approach and patients with missing data were excluded from the multivariate analyses.

For all analyses, p-values of statistical tests were two-tailed and  $p < 0.05$  was taken to be statistically significant. All analyses were performed using the software SPSS [18].

## Ethical discussion

The data used in this study were extracted by a statistician working on the BCBSaSe project. Only the relevant data (patients aged 70 years or older within the defined dates) were taken for further analysis. The data were pseudonymized and then passed on to a remote server. The project is approved by the Swedish Ethical Review Authority with the registration number 2013/1272-31/4.

## Results

### Study cohort

From a total of 20 680 patients in BCBSaSe, 413 were eligible to study cohort (Figure 1). The characteristics of study cohort are shown in Table 1. The median age at diagnosis was 77 years (range: 70 – 96). The patients were followed until death or end of follow up (31/12 2012). The median follow-up was 32.6 months.

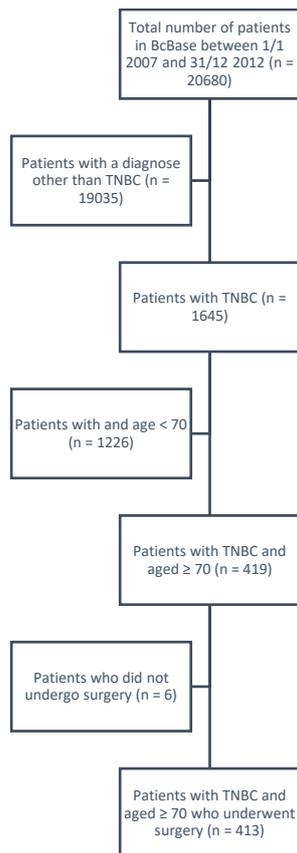


Figure 1. Flow chart for patient selection.

### Factors associated with chemotherapy use

Table 1 summarizes potential factors associated with chemotherapy use. In the logistic regression, advanced age (OR: 0.74; 95% CI: 0.69 – 0.80) and higher comorbidity index (for index 1 OR: 0.34; 95% CI: 0.15 – 0.80; for index 2 OR: 0.35; 95% CI: 0.12 – 1.00; for index  $\geq 3$  OR: 0.14; 95% CI: 0.03 – 0.69) were independently associated with lower chemotherapy use whereas more advanced stage at diagnosis with higher chemotherapy use (for stage II OR: 3.29; 95% CI: 1.75 – 6.16; for stage III OR: 3.82; 95% CI: 1.31 – 11.15).

Table 1. Characteristics of study cohort by chemotherapy use (n = 413).

	Chemotherapy	No chemotherapy	P-value
	n (%)	n (%)	
<i>n</i>	168 (40.7)	245 (59.3)	
<i>Region</i>			0.542
<i>Stockholm/Gotland</i>	57 (33.9)	81 (33.1)	
<i>Uppsala-Örebro</i>	73 (43.5)	118 (48.2)	
<i>Norr</i>	38 (22.6)	46 (18.8)	
<i>Age</i>			< 0.001

70 - 74	98 (58.3)	45 (18.4)	
75 - 79	62 (36.9)	49 (20)	
80 - 84	8 (4.8)	71 (29)	
85 - 89	0 (0)	60 (24.5)	
90 +	0 (0)	20 (8.2)	
<i>Stage</i>			0.306
<i>I</i>	40 (24.1)	75 (30.9)	
<i>II</i>	112 (67.5)	147 (60.5)	
<i>III</i>	14 (8.4)	21 (8.6)	
<i>T stage</i>			0.545
<i>0</i>	5 (3)	2 (0.8)	
<i>1</i>	51 (30.4)	82 (33.5)	
<i>2</i>	96 (57.1)	137 (55.9)	
<i>3</i>	14 (8.3)	21 (8.6)	
<i>4</i>	2 (1.2)	3 (1.2)	
<i>N stage</i>			0.19
<i>0</i>	109 (65.3)	182 (74.9)	
<i>1</i>	51 (30.5)	54 (22.2)	
<i>2</i>	4 (2.4)	3 (1.2)	
<i>3</i>	3 (1.8)	4 (1.6)	
<i>Comorbidity index</i>			< 0.001
<i>0</i>	148 (88.1)	143 (58.4)	
<i>1</i>	10 (6)	52 (21.2)	
<i>2</i>	8 (4.8)	26 (10.6)	
<i>3+</i>	2 (1.2)	24 (9.8)	
<i>Civil status</i>			< 0.001
<i>Single</i>	18 (10.7)	16 (6.6)	
<i>Married</i>	87 (51.8)	71 (29.1)	
<i>Divorced</i>	25 (14.9)	32 (13.1)	
<i>Widow</i>	38 (22.6)	125 (51.2)	
<i>Socioeconomic status</i>			0.08
<i>Low</i>	95 (58.6)	149 (61.8)	
<i>High</i>	63 (38.9)	70 (29)	

<i>Not gainfully employed</i>	4 (2.5)	22 (9.1)
<i>Educational status</i>		< 0.001
<i>Low</i>	55 (33.5)	129 (53.3)
<i>Middle</i>	66 (40.2)	81 (33.5)
<i>High</i>	43 (26.2)	32 (13.2)

### Reasons and risk factors for hospitalization

In total, there were 198 (47.9%) patients with at least one hospitalization within one year from diagnosis. No patients were admitted to the hospital during the period due to dehydration or delirium (Table 2).

Table 2. Reason for hospitalization within 1 year from breast cancer diagnosis (n = 198).

<i>Reason for hospitalization</i>	<i>n (%)</i>
<i>Any hospitalization</i>	198 (47.9)
<i>Due to chemotherapy-related toxicity</i>	53 (26.8)
<i>Infection-related</i>	33 (16.7)
<i>Haematological toxicity</i>	8 (4)
<i>Gastrointestinal toxicity</i>	12 (6.1)
<i>Hospitalization due to other causes</i>	145 (73.2)

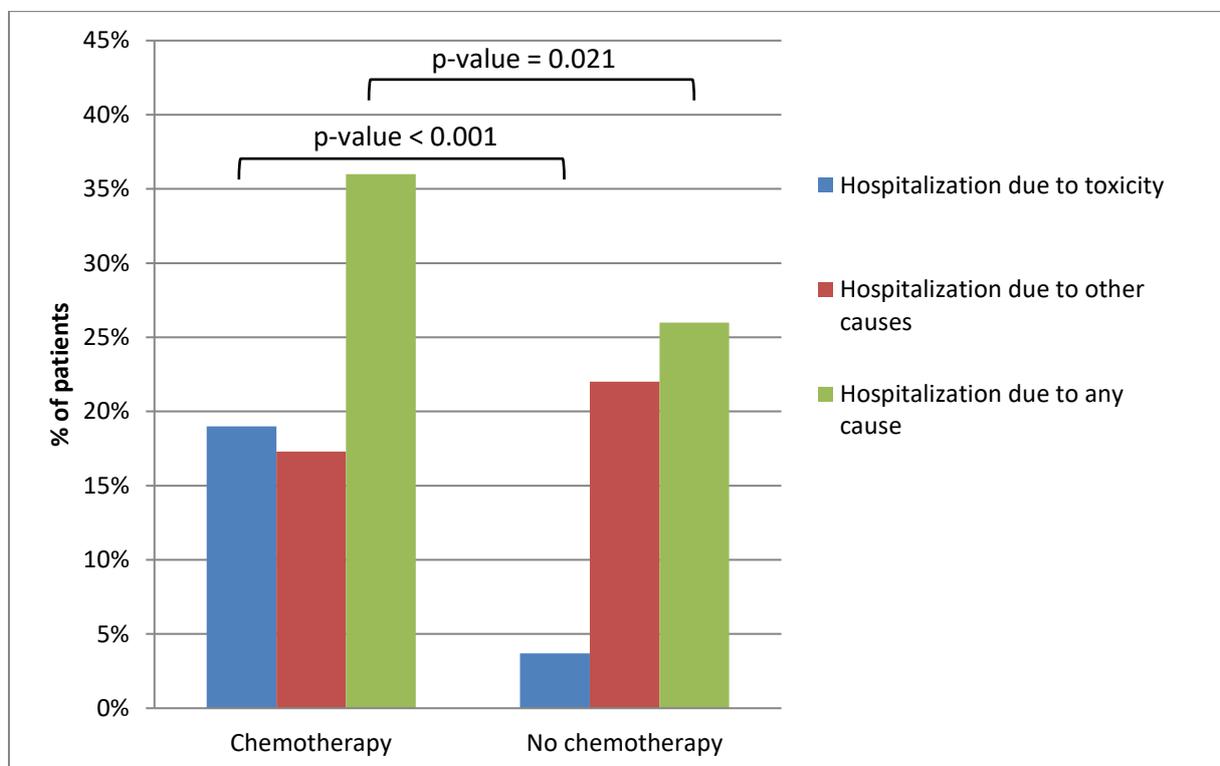


Figure 2. Hospitalization in the group receiving chemotherapy (n = 168) and those who did not (n = 245).

Figure 2 shows how the group that received chemotherapy differs from those who did not in terms of hospitalizations, analysed with the chi-square test. Chemotherapy use was significantly associated to risk for hospitalization both due to any cause and due to toxicity. In the logistic regression analysis, only chemotherapy use was independently associated with higher risk for hospitalization when adjusted to several potential variables of interest (Table 3). Different types of chemotherapy did not influence the risk for hospitalization.

Table 3. Multivariate analysis for risk factors for hospitalization

<i>Variable</i>	<i>Odds ratio</i>	<i>95% Confidence Interval</i>	<i>p-value</i>
<i>Age</i>	1.04	.99 - 1.09	0.101
<i>Stage</i>			
<i>Stage 1</i>	1		
<i>Stage 2</i>	0.93	0.53 - 1.62	0.798
<i>Stage 3</i>	1.24	0.50 - 3.08	0.641
<i>Region</i>			
<i>Stockholm/Gotland</i>	1		
<i>Uppsala - Örebro</i>	0.90	0.55 - 1.49	0.690
<i>Norr</i>	0.61	0.31 - 1.21	0.155
<i>Education</i>			
<i>Low</i>	1		
<i>Middle</i>	1.43	0.85 - 2.41	0.176
<i>High</i>	1.73	0.93 - 3.23	0.085
<i>Single/Divorced/Widow</i>	1.114	0.70 - 1.86	0.602
<i>Comorbidity index</i>			
<i>0</i>	1		
<i>1</i>	1.00	0.59 - 1.95	0.987
<i>2</i>	1.45	0.63 - 3.30	0.382
<i>≥ 3</i>	2.30	0.92 - 5.72	0.074
<i>Mastectomy</i>	1.22	0.71 - 2.12	0.471
<i>Chemotherapy use</i>	2.35	1.30 - 4.26	.005

#### Causes and predictors of mortality

Mortality from breast cancer, non-breast cancer and overall analysed by multivariate Cox regression analyses are presented in Table 4. For overall mortality, advanced age, higher stage of the disease, and higher comorbidity index significantly increased mortality. For breast

cancer-specific mortality, higher stage of the disease and number of comorbidities were significantly correlated with mortality.

For non-breast cancer-specific mortality, higher comorbidity index was associated with increased mortality whereas chemotherapy use with lower mortality rate. However, chemotherapy use was not associated with breast-cancer specific or overall mortality.

Radiotherapy did not affect overall mortality, breast cancer mortality and non-breast cancer mortality either.

Table 4. Multivariate Cox proportional hazards models on the risk for breast cancer mortality, non-breast cancer mortality, and overall mortality in the study cohort.

Variable	Breast cancer mortality			Non-breast cancer mortality			Overall mortality		
	HR	95% CI	P	HR	95% CI		HR	95% CI	P
<i>Region</i>									
<i>Stockholm/Gotland</i>	1			1			1		
<i>Uppsala - Örebro</i>	0.75	0.45 - 1.25	0.270	0.87	0.46 - 1.66	0.668	0.75	0.51 - 1.12	0.160
<i>Norr</i>	0.96	0.49 - 1.87	0.900	1.88	0.95 - 3.73	0.071	1.27	0.79 - 2.02	0.324
<i>Age</i>	1.04	0.99 - 1.09	0.166	1.04	0.99 - 1.09	0.14	1.04	1.00 - 1.08	0.041
<i>Stage at diagnosis</i>									
<i>Stage 1</i>	1			1			1		
<i>Stage 2</i>	2.64	1.16 - 5.99	0.021	1.21	0.63 - 2.31	0.562	1.69	1.03 - 2.78	0.039
<i>Stage 3</i>	21.30	8.97 - 50.54	< 0.001	1.94	0.53 - 7.02	0.314	9.85	5.48 - 17.71	< 0.001
<i>Radiotherapy</i>	1.06	0.62- 1.80	0.836	0.57	0.30 - 1.06	0.076	0.79	0.53 - 1.17	0.243
<i>Comorbidity index</i>									
<i>0</i>	1			1			1		
<i>1</i>	1.04	0.48 - 2.26	0.915	2.02	1.01 - 4.01	0.046	1.44	0.87 - 2.37	0.158
<i>2</i>	2.58	1.27 - 5.28	0.009	3.23	1.41 - 7.38	0.006	2.79	1.63 - 4.78	< 0.001
<i>≥ 3</i>	1.69	0.75 - 3.83	0.205	3.51	1.62 - 7.60	0.001	2.46	1.42 - 4.25	0.001
<i>Single/ Divorced/Widow</i>	1.03	0.61 - 1.75	0.900	1.15	0.61 - 2.18	0.669	1.09	0.73 - 1.63	0.687
<i>Chemotherapy use</i>	0.95	0.51 - 1.79	0.877	0.40	0.16 - 0.96	0.040	0.72	0.44 - 1.18	0.191

During the study follow up, the 5-year overall mortality rate was 41% (95% CI: 35% – 47%), the breast cancer-specific mortality was 24% (95% CI: 18% – 30%), and the non-breast cancer-specific mortality was 22 % (95% CI: 16% - 28%) (Figure 3).

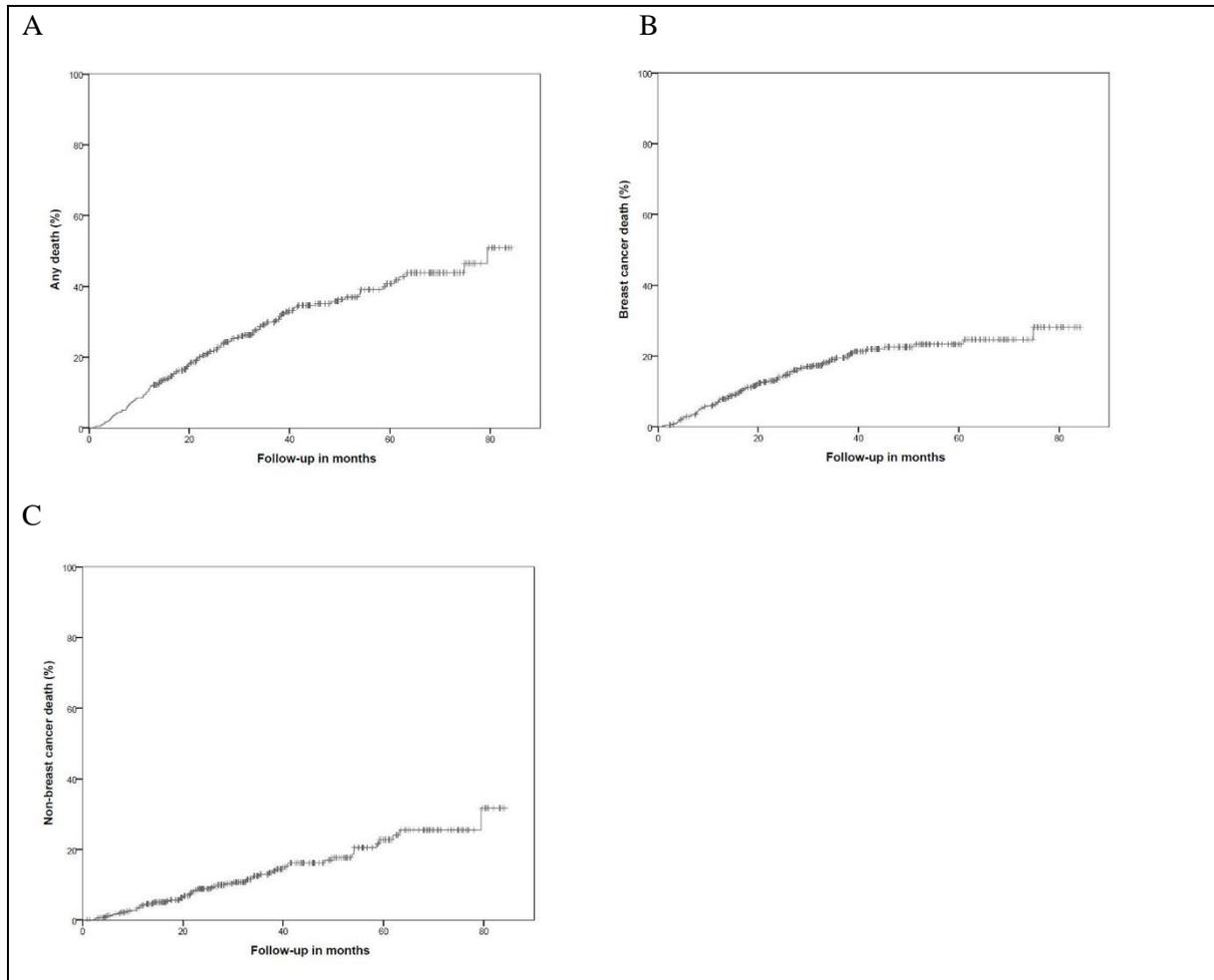


Figure 3. Kaplan-Meier curves for the entire study cohort (A) overall mortality; (B) breast cancer mortality; (C) non-breast cancer mortality.

## Discussion and conclusion

In our study cohort of elderly patients with TNBC, we found that less than half of the patients received chemotherapy as a part of curative treatment. Chemotherapy use was associated with higher risk for hospitalization within 1 year from breast cancer diagnosis without improving breast cancer-specific or overall survival. In addition, comorbidities were independently associated with breast cancer-specific mortality, non-breast cancer mortality, and overall mortality.

According to the latest treatment recommendations, chemotherapy should be based on tumour characteristics and not on age [19]. We found that age of the patient, tumour stage at diagnosis and number of comorbidities affected chemotherapy administration in our study

cohort [20,21]. The Swedish treatment recommendations say that the aggressiveness of the disease and functional status should dictate the chemotherapy administration. This is partly matched by our results, given that the decision to administer chemotherapy was influenced by a factor that reflects tumour aggressiveness (stage at diagnosis) and one that indirectly reflects functional status (CCI) [17]. Age however should not be the sole factor in deciding chemotherapy administration.

Regarding risk of hospitalization, of all the examined risk factors only chemotherapy was deemed significant. Our results are in accordance with an earlier study done on all forms of early stage breast cancer and found an increased risk for hospitalization due to chemotherapy [10]. In addition, they found that anthracycline-based chemotherapy was associated with a higher risk of hospitalization, an observation that we could not confirm. Potential explanations for this discrepancy could be the low number of patients in the specific subgroups in our study and the fact that our study included only patients with TNBC, in contrast to the aforementioned study that included all breast cancer patients irrespective of subtype.

When we analysed the impact of chemotherapy on breast-cancer and overall mortality, we could not find that chemotherapy improved prognosis. The lack of association between chemotherapy use and prognosis is in accordance with a large retrospective study showing that the effectiveness of chemotherapy was declined by age in breast cancer patients [12] but differs from older studies that showed an improved outcome when chemotherapy was administered in elderly patients with ER-negative breast cancer [13,22]. Our study adds to the current literature since we only included patients with TNBC and used a more strict cut-off age for elderly (70 years) compared to 65 years in most of the prior studies.

One of the few prior studies that has been done in this area so far was only presented at a meeting and focused on elderly patients with TNBC, the treatment pattern, and survival in relation to chemotherapy [23]. They used 10 694 patients from the SEER (Surveillance, Epidemiology, and End Results) cancer registry, and found that untreated patients had a higher risk of death (HR = 1.28; 95% CI = 1.19-1.38). They also found that tumour size and grade, comorbidities, age and stage all increased the mortality. The risk factors of mortality are largely in accordance with our results; however, the results regarding chemotherapy differ. This discrepancy could be explained by some key differences in the study designs. The SEER-based study included women aged 66 years and older, compared to 70 years and older in our study, and the inclusion of younger patients could partially explain the different results. In addition, some interesting variables are lacking from the SEER database, including

baseline health information, type of chemotherapy, and extent of radiotherapy. The lack of association in our study cohort could also be explained by the smaller number of patients included in our study compared with the SEER-based study.

However, the lack of association could be a real observation with biological rationale. TNBC is a heterogeneous disease with substantial clinical, molecular and prognostic differences among distinct subgroups. A recent study revealed significant differences in molecular subtyping of TNBC between younger and older patients [24]. In fact, older patients had higher expression of the ERBB2 gene, lower expression of proliferation-associated genes, and a lower percentage had the basal-like subtype. As a result, the effectiveness of chemotherapy on this patient group might be limited.

The small protective effect of chemotherapy use seen in non-breast cancer-specific mortality could have two potential explanations not related to an innate protective chemotherapy attribute. Firstly, this observation could reflect an unrevealed selection bias on chemotherapy use; it is more likely to administer chemotherapy in less vulnerable patients with better non-breast cancer-specific survival. Secondly, patients treated with chemotherapy do have a closer monitoring and, as we observed, a higher risk to be hospitalized. We hypothesize that the more frequent contact with healthcare providers can discover health problems at an earlier stage. These problems could easily have been missed if they had emerged at home.

One interesting finding in our study was that radiotherapy did not affect either breast cancer-specific survival or overall survival. Radiotherapy after breast-conserving surgery as well as after axillary dissection in node-positive disease has been associated with increased breast cancer-specific survival in overall breast cancer population [27,28]. However, in elderly patients with ER-positive breast cancer radiotherapy after breast conserving surgery can be omitted without jeopardizing prognosis [29,30]. Our findings imply that radiotherapy might not been necessary in some elderly patients with TNBC as well. Nonetheless, this research question was not part of the aim of the study and should therefore be considered as a hypothesis-generating finding that needs further large-scale studies to accurately assess the role of radiotherapy in this patient group.

Our results confirm previous findings regarding the prognostic role of comorbidities in both breast-cancer and overall survival, i.e. decreasing the survival [25,26]. It is, therefore, essential to manage comorbidities in breast cancer patients and take them into account in a greater degree in treatment decision making.

The 5-year mortality rate in our study cohort was 41%, with mortality due to breast cancer and due to other causes making up roughly equal proportions; each accounted for half of the

recorded deaths. This observation shows that this patient group is rather vulnerable and burdened with age-related, non-cancer diseases that account for nearly half of expected deaths.

Our study has several limitations that need to be discussed. The retrospective nature of this study is inherently by design victim to several biases; recall bias and indication bias. We tried to assess the risk for indication bias and imbalance between different patient groups using multivariate analyses including various factors that could potentially influence the results.

In addition, the number of patients in our study cohort became somewhat limited in some subgroups. This has to do both with the unintended imposed limitation of the BCBSaSe database which is restricted to cases between 2007 where there are reliable data on Her2-status and 2012, but also reflects the reality of the relative scarce number of elderly patients with TNBC. Finally, there were no detailed records of chemotherapy administration, e.g. dose and duration. This information would be valuable in comparing different therapy regimens to each other.

In conclusion, treatment of TNBC in elderly is influenced by age, stage and comorbidities. Patients who receive chemotherapy are admitted to hospital in a higher frequency, and chemotherapy did not lower overall mortality and breast cancer mortality in our study cohort. Our study highlights the need to individualize treatment decision making regarding use of chemotherapy in elderly patients with TNBC by taking all these aspects into account. Future research should focus on several aspects mentioned in this paper, which could be classifying TNBC based on molecular subtyping, investigating the potential role of different treatment strategies in the light of molecular background and patients functional status and examine the impact of radiotherapy on mortality.

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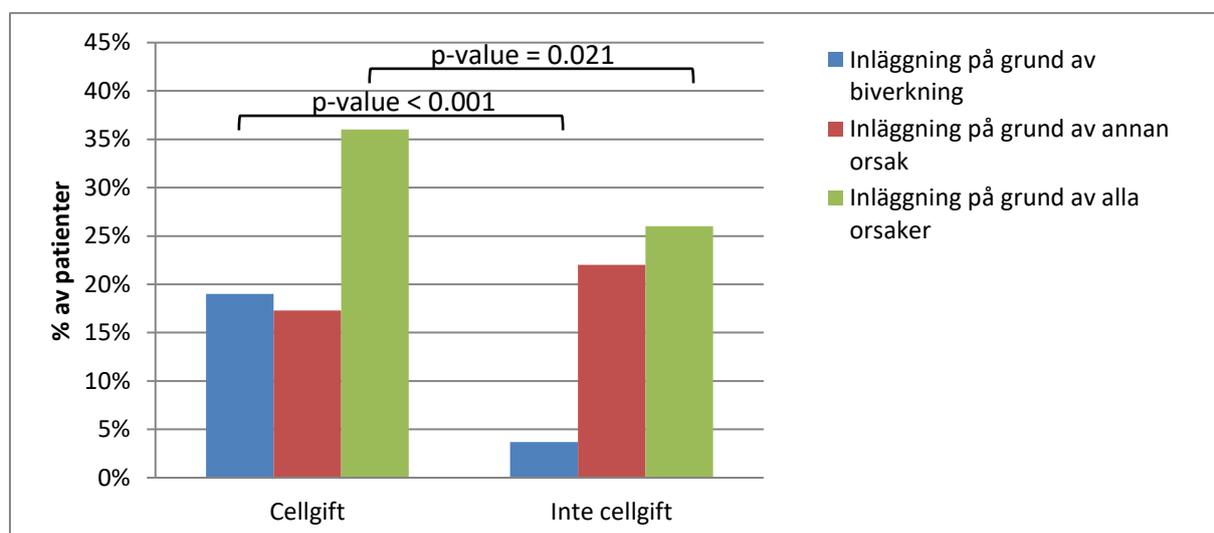
## Populärvetenskaplig sammanfattning

En allt mer åldrande befolkning ställer nya krav på vård och samhälle, då många sjukdomar i större grad drabbar äldre. Samtidigt är äldre som grupp underrepresenterade i forskningsstudier, vilket leder till sämre och mer ojämlig vård.

En av de sjukdomar vars prevalens ökar med åldern är bröstcancer. Bröstcancer i sig delas in i olika undergrupper, och den allvarligaste heter trippelnegativ bröstcancer. Denna typ av bröstcancer kan bara behandlas medicinskt med cellgifter, till skillnad från andra varianter som utöver cellgifter har målinriktad behandling som alternativ. Trots detta är forskningsläget oklart om äldre patienter med trippelnegativ bröstcancer blir hjälpta av cellgifter; biverkningarna kan vara allvarliga och accentueras med stigande ålder.

Vår studie undersökte vad som påverkar cellgiftsordinerings till patienter, om dödligheten minskar och om sjukhusinläggningarna påverkas. Studien genomfördes med ett nationellt cancerregister med över 20 000 patienter. Våra resultat blev följande: tumörstadium, ålder och övrig sjuklighet påverkade cellgiftsadministrationen. Patienterna som fick cellgifter blev oftare inlagda på sjukhus. Ingen minskad mortalitet sågs i gruppen som fick cellgifter jämfört med de som inte fick.

Överbehandling av patienter är alltid dåligt, speciellt i de fall med allvarliga biverkningar som kan uppkomma vid cellgiftsbehandling. Ett undvikande av denna risk genom att inte ordinera cellgift utan att påverka överlevnaden negativt skulle både innebära minskat lidande för patienter och anhöriga, men även minskade kostnader för samhället på grund av minskad medicinanvändning och minskad användning av sjukhusresurser.



## Cover letter

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Dr. David Collingridge  
Editor-in-Chief  
*The Lancet Oncology*

23/6 2019

Dear Dr. Collingridge:

I am happy to submit to you my master thesis done at Örebro University, “Treatment pattern, risk for hospitalization and mortality in elderly patients with triple-negative breast cancer” for consideration for publication in *The Lancet Oncology*.

In the study, we show that age, comorbidities and tumour stage all had an impact if chemotherapy was administered or not. However, chemotherapy also significantly increased the number of patients that was admitted to hospital due to different side effects, one of which was different types of infections. At the same time, we could not find a mortality decrease in those who were administered chemotherapy. Instead, it was age, stage of the disease and number of comorbidities that affected survival negatively.

Our findings are interesting since this group of patients is not well studied. Because of this, doctors must rely on clinical experience and not evidence-based guidelines. This leads to different treatment depending on which doctor handles the treatment. Our study isn't an answer to this problem; larger studies are needed to accurately establish new guidelines. However, a paper like this paves the way for future prospective studies in the area.

Thank you for the consideration.

Regards,

Pontus Nyström, Bachelor of Medicine  
Örebro University

## Etisk reflektion

Jag har gjort en registerstudie om trippelnegativ bröstcancer. Det är inte den vanligaste subtypen av bröstcancer (prevalens på 16%<sup>1</sup>). I sig är inte det problematiskt, men lägg till det faktum att vi har register där folk läggs in på rutin i den kliniska verksamheten. Patienterna får kanske frågan om de vill vara med i dessa register när de är mitt uppe i en livskris som en cancerdiagnos innebär. Detta gör att de kanske inte tänker så mycket på vad konsekvenserna blir i slutändan. Eftersom register generellt innehåller ganska detaljerad information om de olika deltagarna såsom region, ålder, insjuknandedatum och liknande går det trots anonymisering få ut en hel del information.

Det vi får i min studie är då en konflikt mellan göra gott och inte skada. I och med att det blir en relativt ”sällsynt” diagnos för det med sig en större risk att patienten eventuellt kan identifieras och därmed lida men, speciellt när man helt är på nåder av de som handskas med databasen och hur den lämnas ut.

Denna oförmåga att gå ur är samtidigt en styrka från andra hållet sätt. Kompletta register vilket innebär större underlag och längre uppföljningstider. Detta är såklart viktigt i register kring alla sjukdomar, men kanske framförallt om sjukdomen har låg incidens. Då måste det göras så lätt som möjligt att forska på detta, på grund av det lilla ”ointresse” som kanske dyker upp om det inte är en vanlig diagnos.

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<sup>1</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5804056/>