ISRCTN69229101 https://doi.org/10.1186/ISRCTN69229101

Development of a tool for effective comparisons of breast cancer survival between hospitals

Submission date
10/04/2022

Recruitment status
No longer recruiting

Registration date
14/11/2022

Overall study status
Completed

Last Edited
16/06/2025

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Breast cancer is the most common cancer among Swedish women. Thanks to improved diagnostics and treatment, fewer women die from breast cancer today than 60 years ago despite that twice the number of women are diagnosed. However, despite an increased number of treatment options for breast cancer in the past 15 years, breast cancer survival in Sweden has not improved as much as expected. This could be due to inequalities in breast cancer care. Breast cancer prognosis depends on several factors including how biologically aggressive the breast cancer is as well as other patient-related factors (for example other diseases). Comparing survival rates for patients with breast cancer between Swedish hospitals does not take into consideration that different hospitals might have underlying differences in their patient populations that impact the chance of survival. It is therefore hard to interpret whether the hospital with the highest survival has the best breast cancer care or if that hospital happens to have the patients with the best prerequsites to survive their diagnosis.
This study aims to create a tool for the patient, healthcare and policymakers for continuous follow-up of breast cancer care nationally and in the long-term internationally. This enables more transparent and effective comparisons of breast cancer survival between Swedish hospitals. It is hoped that this will lead to an even more equal and high-quality breast cancer care in Sweden.

Who can participate?
This is a register-based study meaning that the researchers use data on patients that got their breast cancer diagnosis between 01/01/2007 and 31/12/2014. The study includes all patients aged 18 years and over that were registered in the Swedish national breast cancer registry during this time period.

What does this study involve?
The study involves retrieving data on included patients from a database called BcBaSe 3.0. This database has linked the Swedish breast cancer registry with other Swedish government registries. The data will be used to create a tool that can better distinguish if the difference in survival between two hospitals is due to healthcare performance.

What are the possible benefits and risks of participating?
As this study includes patients that have already received their breast cancer diagnosis many years ago there are no direct benefits for the study participants. There are no physical risks for the included participants. However, as the researchers will need to use data on for example participants' income, educational level and other medical conditions this is an integrity risk. The researchers mitigate this risk by pseudonymising the data. This means that all participants are coded as a number so that no one can identify individual participants in the database.

Where is the study run from?
Karolinska Institute (Sweden)

When is the study starting and how long is it expected to run for?
April 2022 to December 2022

Who is funding the study?
Innovative Medicines Initiative (Belgium)

Who is the main contact?
Dr Elham Hedayati
elham.hedayati@ki.se

Contact information

Type(s)
Principal investigator

Contact name
Dr Elham Hedayati

Contact details
Karolinska Universitetssjukhuset
FoU-ledningen
Eugeniavägen 18 (Princton)
Solna
Sweden
171 64
+46 (0)709261035
elham.hedayati@ki.se

Type(s)
Scientific

Contact name
Mr Jacob Thurell

Contact details
Karolinska University Hospital, Theme Cancer
Eugeniavägen 3
171 76 Solna
Lidingö

Sweden
18155
+46 (0)761299934
jacob.thurell@ki.se

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Development and validation of a risk-adjustment model for breast cancer survival - a retrospective registry-based study on Swedish breast cancer patients

Study objectives
Breast cancer care is rapidly developing with new treatment options and more personalised medicine to ensure the best survival chance at minimum risks of treatment-related complications for each patient. A challenge for Swedish as well as for international breast cancer care is to follow up outcomes such as survival in different patient subgroups. Benchmarking of health outcomes is one well-established method for comparing performance between hospitals. Risk adjustment is a key component of benchmarking to ensure that we compare "apples with apples". Without risk adjustment it is not possible to tell whether the observed differences in outcome are explained by health care performance or underlying differences in compared patient populations.

There are to the researchers' knowledge no validated risk-adjustment models for breast cancer outcomes. The aim of this study is to develop such models for several survival-related outcomes for breast cancer based on a large Swedish breast cancer cohort.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/11/2021, Swedish Ethical Review Authority (Etikprövningsmyndigheten, Box 2110, 750 02, Uppsala, Sweden; +46 10-475 08 00; registrator@etikprovning.se) ref: 2021-05189

Study design
Registry-based observation longitudinal cohort study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Breast cancer

Interventions
Population:
A Swedish database (i.e. BcBaSe 3.0) has been constructed linking the Swedish National Registry for Breast Cancer (NCBR) with several other Swedish government registries. The database contains approximately 90,000 Swedish patients who have been diagnosed with breast cancer between 01/01/2007 and 31/12/2019. The database contains information on both tumour biological characteristics (e.g. tumour stage at diagnosis, histological grade) as well as patient-level sociodemographic information (e.g. income, educational level). For the current project patients diagnosed between 01/01/2007 and 31/12/2014 (approx. 45,000 patients) will be analysed for 5-year survival outcomes while patients diagnosed between 01/01/2007 and 31/12 /2009 (approx. 11,000 patients) will be analysed for 10-year survival outcomes. Power calculations estimate the need of 3,108 participants to detect a 1 % impact of an independent variable on the outcome variable with 95 % power and a 5 % significance level if 20 independent variables are included. The database has a sufficient number of patients both for 5- and 10-year survival outcomes except for 10-year survival in the subgroups of HER2-positive breast cancer and triple-negative breast cancer. These subgroup analyses will be underpowered.

Variables:
Independent variables that will be tested for impact on the dependent variable (i.e. outcome variable) include:

Tumour biological factors:
Tumour size, number of positive lymph nodes, estrogen receptor (ER) status, progesterone receptor status, HER2 status, TNM stage and histological grade.

Socioeconomic factors:
Overall socioeconomic status, household income, education level, first-generation immigrant, working status, gender, marital status and age.

Comorbidities and heredity:
Comorbidity burden (according to Charlson Comorbidity Index) and heredity for breast cancer defined as one first grade relative with breast cancer diagnosis under 50 years old.

Statistical analyses:
Multiple regression analyses will be applied to analyse how different independent variables impact outcome variables. Descriptive statistics will be performed on all candidate independent variable (IV)s to control for missing data and outliers. Univariable analyses will be performed on all independent variables using the Student's T-test, Qi-square and ANOVA test. Significant variables will be tested for multicollinearity using a correlation matrix. Stepwise regression will then be performed with a threshold for inclusion $p < 0.10$ and exclusion $p < 0.05$. A model evaluation will be performed evaluating model fit through tests such as the Brier test (overall performance), C-statistic (discrimination) and goodness of fit (calibration). Overall model multicollinearity will be tested by generating VIF values. Except for the model based on all included patients, the patients will also be divided into the clinical subgroups ER-positive breast cancer, HER2-positive breast cancer and triple negative breast cancer as these three groups have different prognosis and treatment options. The subgroup-specific models will be compared on

performance with the model including all patients in terms of prediction capacity in each subgroup. Internal validation will be performed for 5-year outcomes on the patients diagnosed with breast cancer between 01/01/2014 and 31/12/2014.

Intervention Type
Other

Primary outcome(s)
Overall model performance, discrimination and calibration of a model on 5-year relative survival

Key secondary outcome(s))
Overall model performance, discrimination and calibration for models on:
1. 5-year overall survival
2. 5-year disease-free survival
3. 10-year relative survival
4. 10-year overall survival
5. 10-year disease-free survival
6. 5-year relative survival of patients with triple-negative breast cancer based on this subgroup of patients
7. 5-year relative survival of patients with ER-positive breast cancer based on this subgroup of patients
8. 5-year relative survival of patients with HER2-positive breast cancer based on this subgroup of patients
9. 5-year observed survival of patients with triple-negative breast cancer based on this subgroup of patients
10. 5-year observed survival of patients with ER-positive breast cancer based on this subgroup of patients
11. 5-year observed survival of patients with HER2-positive breast cancer based on this subgroup of patients
12. 5-year disease-free survival of patients with triple-negative breast cancer based on this subgroup of patients
13. 5-year disease-free survival of patients with ER-positive breast cancer based on this subgroup of patients
14. 5-year disease-free survival of patients with HER2-positive breast cancer based on this subgroup of patients
15. 10-year relative survival of patients with triple-negative breast cancer based on this subgroup of patients (under-powered)
16. 10-year relative survival of patients with ER-positive breast cancer based on this subgroup of patients
17. 10-year relative survival of patients with HER2-positive breast cancer based on this subgroup of patients (under-powered)
18. 10-year observed survival of patients with triple-negative breast cancer based on this subgroup of patients (under-powered)
19. 10-year observed survival of patients with ER-positive breast cancer based on this subgroup of patients
20. 10-year observed survival of patients with HER2-positive breast cancer based on this subgroup of patients (under-powered)
21. 10-year disease-free survival of patients with triple-negative breast cancer based on this subgroup of patients (under-powered)
22. 10-year disease-free survival of patients with ER-positive breast cancer based on this subgroup of patients

23. 10-year disease-free survival of patients with HER2-positive negative breast cancer based on this subgroup of patients (under-powered)

Completion date
31/12/2022

Eligibility

Key inclusion criteria
1. Aged 18 years or older
2. Breast cancer diagnosis between 01/01/2007 and 31/12/2014
3. Treated for breast cancer in Sweden
4. Stage I-III at diagnosis (no distant metastasis)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
45441

Key exclusion criteria
De novo (or within 3 months of diagnosis) metastatic breast cancer (stage IV breast cancer)

Date of first enrolment
01/01/2007

Date of final enrolment
31/12/2014

Locations

Countries of recruitment
Sweden

Study participating centre

Karolinska Institute
Solnavägen 1
Solna
Sweden
17177

Sponsor information

Organisation
Karolinska University Hospital

ROR
https://ror.org/00m8d6786

Funder(s)

Funder type
Industry

Funder Name
Innovative Medicines Initiative

Alternative Name(s)
The Innovative Medicines Initiative, Europe's Innovative Medicines Initiative, EU Innovative Medicines Initiative, IMI

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Belgium

Results and Publications

Individual participant data (IPD) sharing plan
Patient-level data will not be shared for patient integrity reasons. However, the researchers will supplement the publication with a detailed variable list of all analysed variables.

IPD sharing plan summary

Stored in non-publicly available repository, Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/06/2023	16/06/2025	Yes	No