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Pilot 8.4.b: Estimating cancer recurrence

Luigino Dal Maso, Fabiola Giudici

Centro di Riferimento Oncologico (CRO), IRCCS, Aviano, Italy

CRO AVIANO

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Italian Association for Cancer Research -
AIRC Foundation

AIRC
Rendiamo il cancro sempre più curabile.

We have no disclosures to declare

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SCIENTIFIC CONTRIBUTORS

CRO AVIANO
L Dal Maso , F Giudici
F Toffolutti, S De Vidi,
D Serraino

RTV
S Guzzinati,
A Andreotti, M Zorzi

ASUGI Azienda Sanitaria Universitaria Giuliano Isontina
REGIONE AUTONOMA FRIULI VENEZIA GIULIA
M Bortul

ISTITUTO SUPERIORE DI SANITÀ
S Francisci,
D Pierannunzio,
A Tavilla, T Lopez

Clínic Barcelona IDIBAPS
F Schettini

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Outline presentation

- Motivation and Context
  - People living after a cancer diagnosis (complete prevalence) are increasing
  - Several indicators of cancer cure are available
  - Information on cancer recurrence can support decisions by oncologists and policy makers on the best follow-up plans and have several important implications for health economic evaluations.

- 8.4.B PILOT: Piloting the estimation of progression to cancer recurrence and long-term side effect
  - Background
  - Pilot protocol: aim/methods-required data
  - Application to Breast Cancer data
  - Remarks and Conclusions

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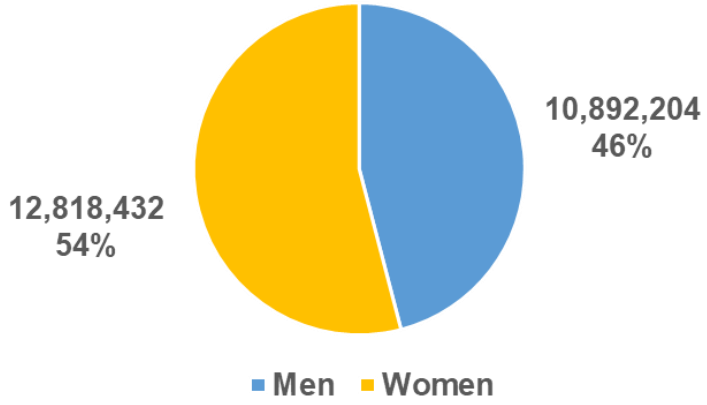
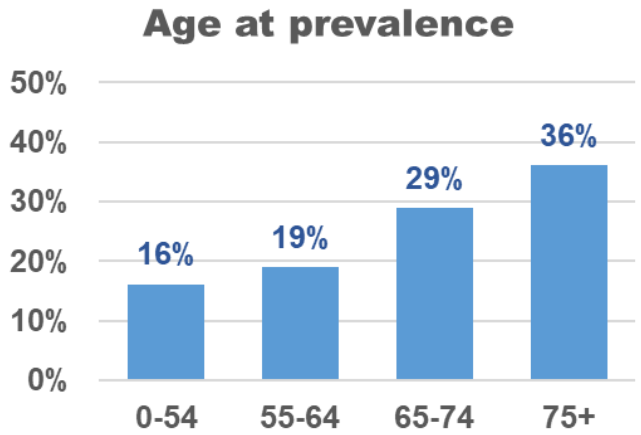
Complete prevalence from in Europe, 2020





23.7 million

- **5%** of the total population (448 mln)
- **54%** women (12.8 mln)
- **35%** below age 65 (8.2 mln)
- **38% long term survivors**, 10+ (9.1 mln)

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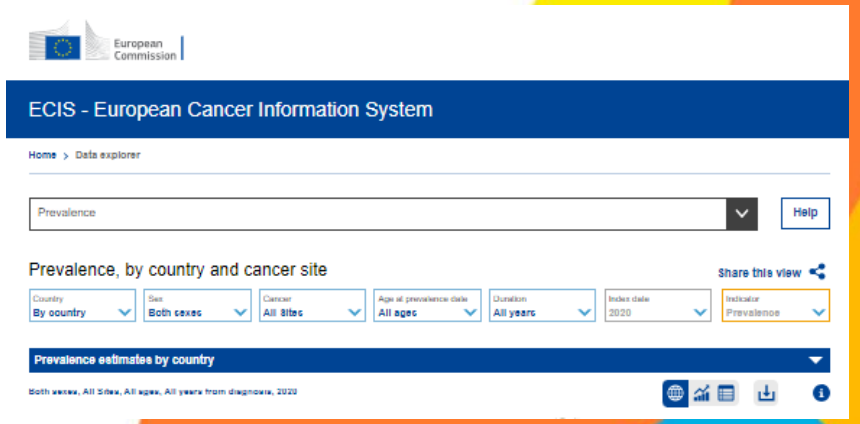
Estimates are accessible for consultation on the EUROPEAN CANCER INFORMATION SYSTEM (ECIS) web-site
https://ecis.jrc.ec.europa.eu/



European Network of Cancer Registries

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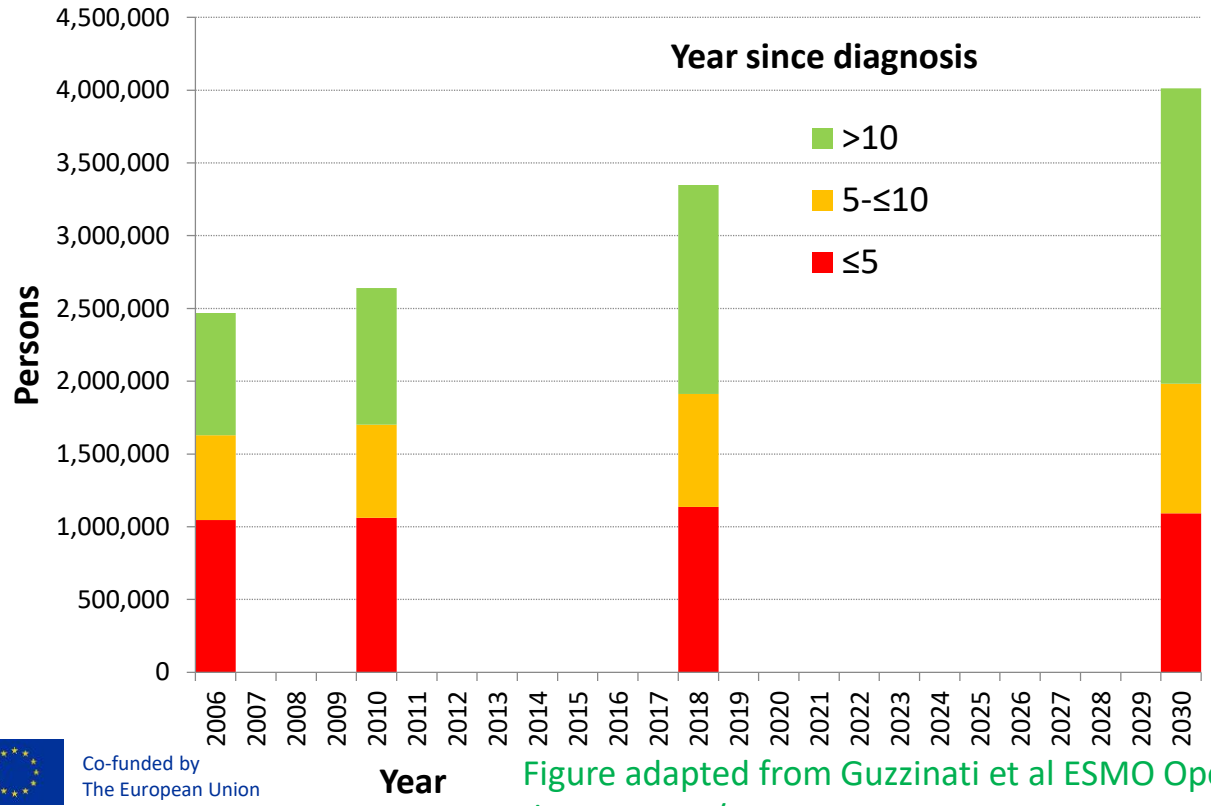
Figure adapted from De Angelis et al. Lancet Oncology 2024
doi: 10.1016/S1470-2045(23)00646-0

Complete prevalence from 2006 to 2018 and projections to 2030 in Italy, by time since diagnosis



4 million Italians will live in 2030,
~7% of italians
2 millions since more than 10 years

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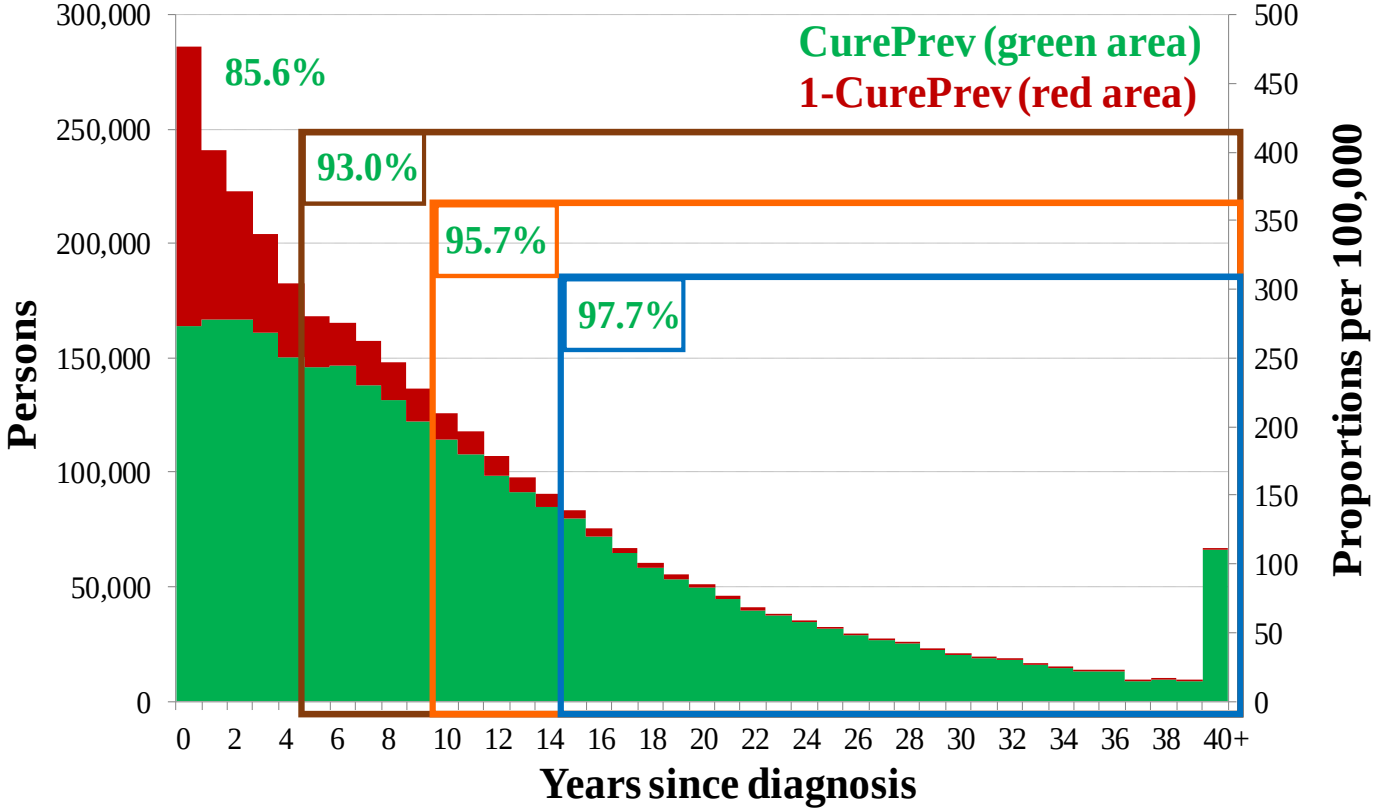
Figure adapted from Guzzinati et al ESMO Open 2024
doi: 10.1016/j.esmoop.2024.103635

Indicators of cure we are able to calculate: Cure prevalence (How many prevalent patients will not die of their disease?)



Squares include people alive at least 5 years after diagnosis (olive), at least 10 years (orange), and at least 15 years after diagnosis (blue).
Corresponding proportions include patients who will not die from the disease in each group.

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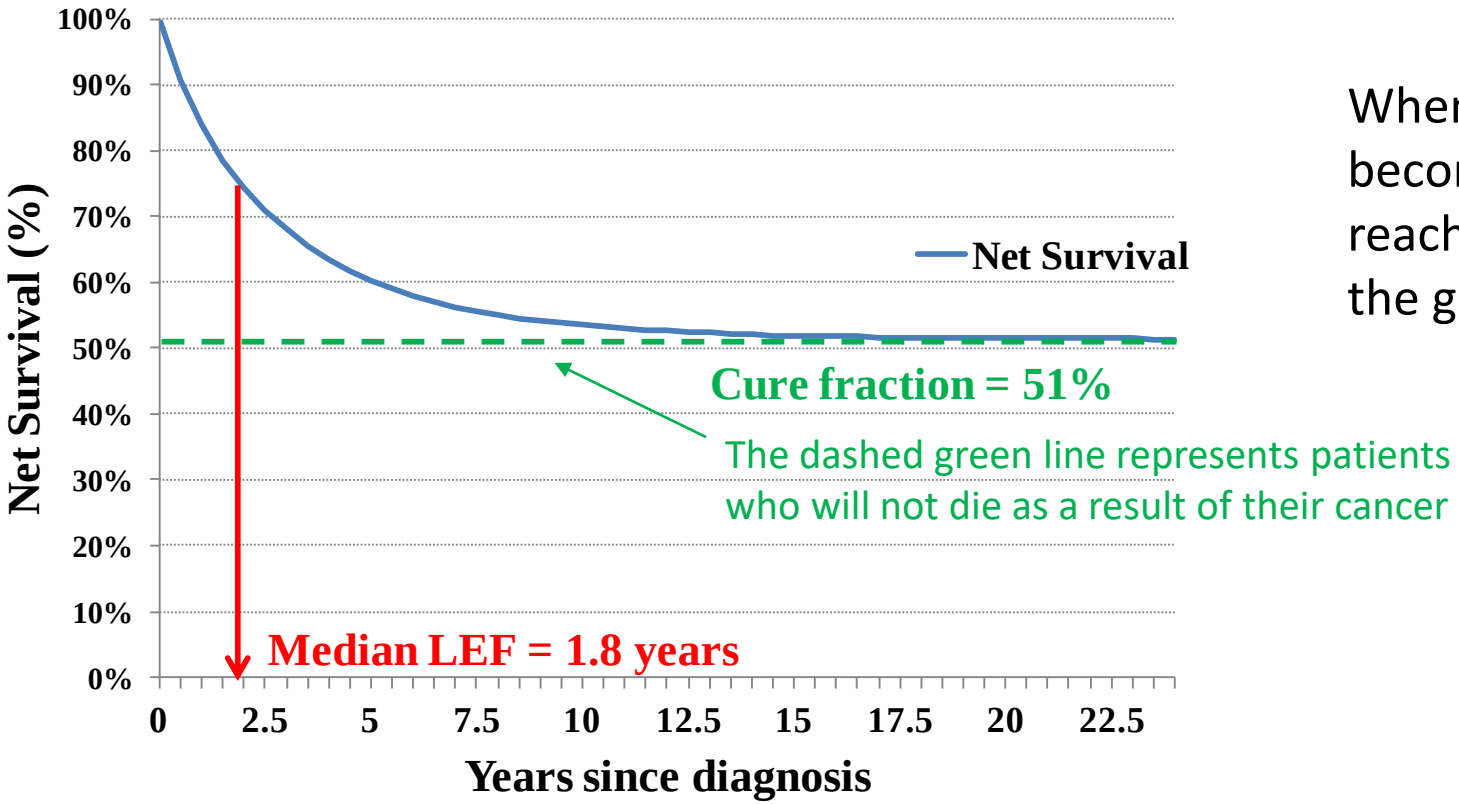
Figure adapted from Guzzinati et al ESMO Open 2024
doi: 10.1016/j.esmoop.2024.103635

Indicators of cure we are able to calculate: Cure fraction (How many patients will be cured?)



When the survival curve becomes flat, cancer cases reach the same death rates of the general population.

The dashed green line represents patients who will not die as a result of their cancer

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Figure adapted from Toffolutti et al. Frontiers Oncol 2023
doi: 10.3389/fonc.2023.1168325

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Background

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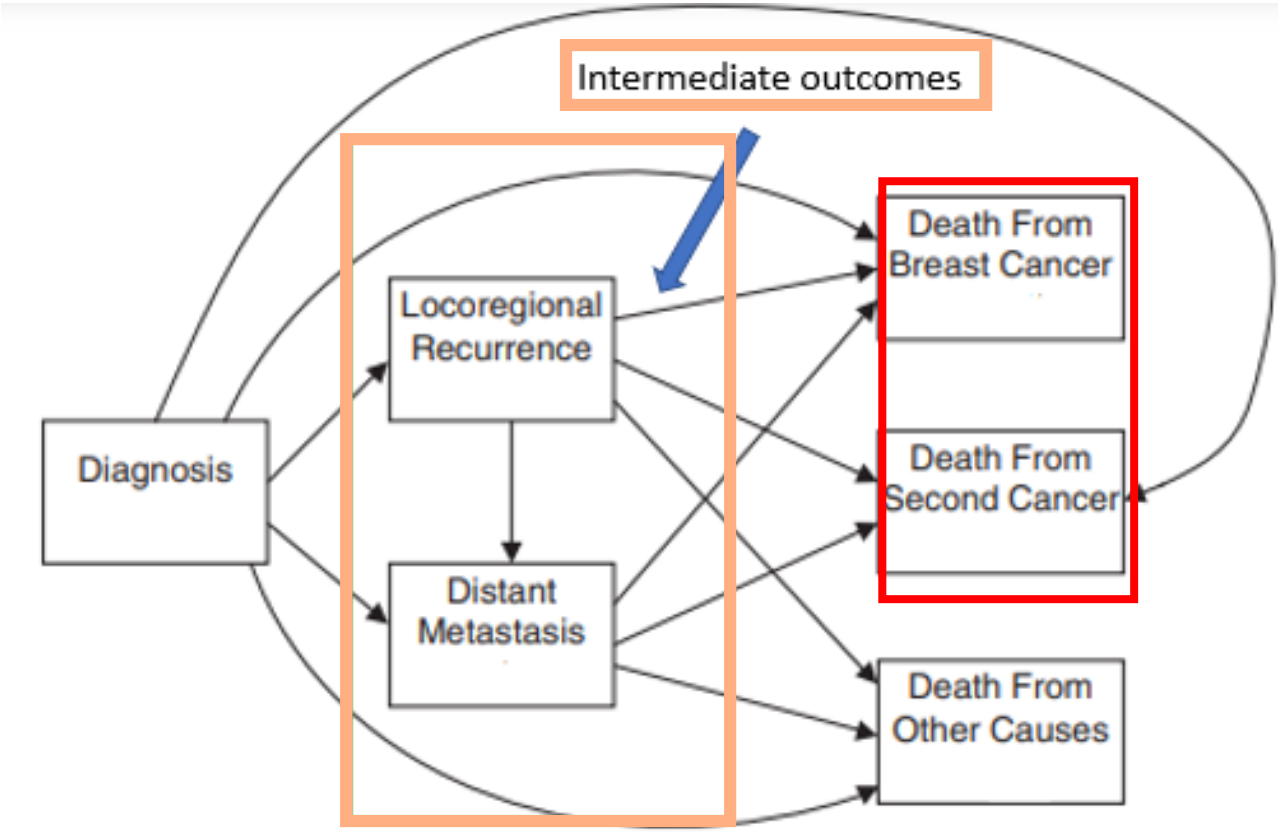

High interest in data collection as well as methods to understand **intermediate outcomes**, including **the number and percent of patients living with recurrence**

This information may support decisions of oncologists and policy makers on the best follow-up plans, in terms of outcomes and costs.

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Figure adapted from Eulenburg C. et al. A Comprehensive Multistate Model Analysing Associations of Various Risk Factors With the Course of Breast Cancer in a Population-Based Cohort of Breast Cancer Cases. AJE (2016) DOI: 10.1093/aje/kwv163.

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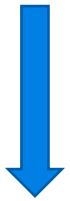
How to retrieve information on recurrence?



Lack of recurrence information has led in recent years to explorations of **several approaches to determine the risk and frequency of cancer recurrence**

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Methods to retrieve information on recurrence?

- **Model-based approaches**

- **Population-based methods**
  - Based on manual revision
  - Based on administrative datasets

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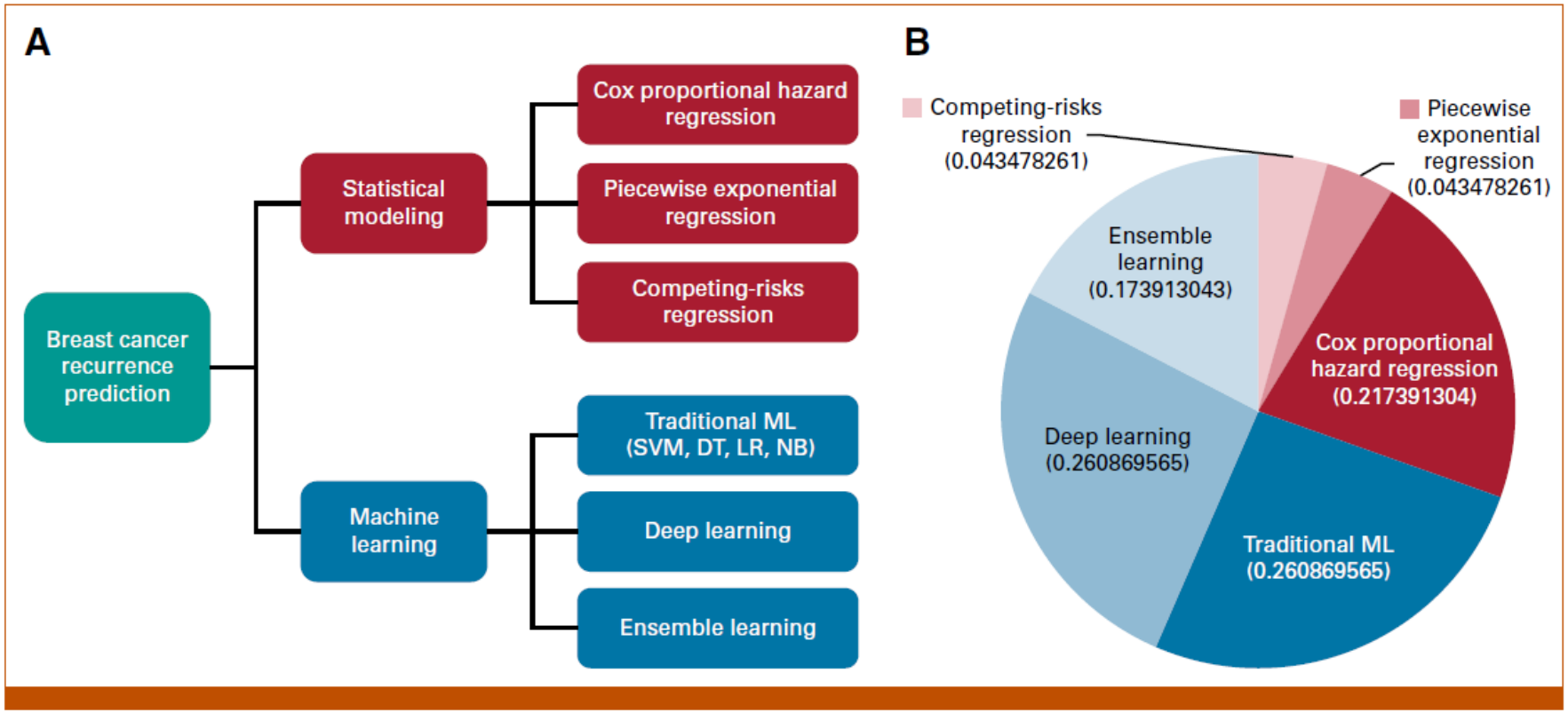
Background

Statistical Modeling and Machine Learning

Evolution of Breast Cancer Recurrence Risk Prediction: A Systematic Review of Statistical and Machine Learning–Based Models

Hasna El Haji, PhD[1,2,3]; Amine Souadka, MD[4]; Bhavik N. Patel, MD, MBA[1,2]; Nada Sbihi, PhD[3]; Gokul Ramasamy, MS[1,2]; Bhavika K. Patel, MD[1]; Mounir Ghogho, PhD[3,5]; and Imon Banerjee, PhD[1,2]

DOI https://doi.org/10.1200/CCI.23.00049



ML-based prediction models exhibit outstanding performance, yet their practical applicability might be hindered by limited interpretability and reduced generalization.

Background

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Population-based cancer registry

Challenge: **population-based data on recurrence is not yet available**

Cancer registry do not routinely collect information on cancer progression or recurrence.

European Network of Cancer Registries

The European Network of Cancer Registries (ENCR) established a multi professional **Working Group on Cancer Recurrences** proposes a new Recommendation for recording recurrence, transformation and progression for population based cancer registries.

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https://www.encr.eu/sites/default/files/Recommendations/Draft%20ENCR%20Recommendation_Recurrences_20240521.docx

Background

European Network of Cancer Registries

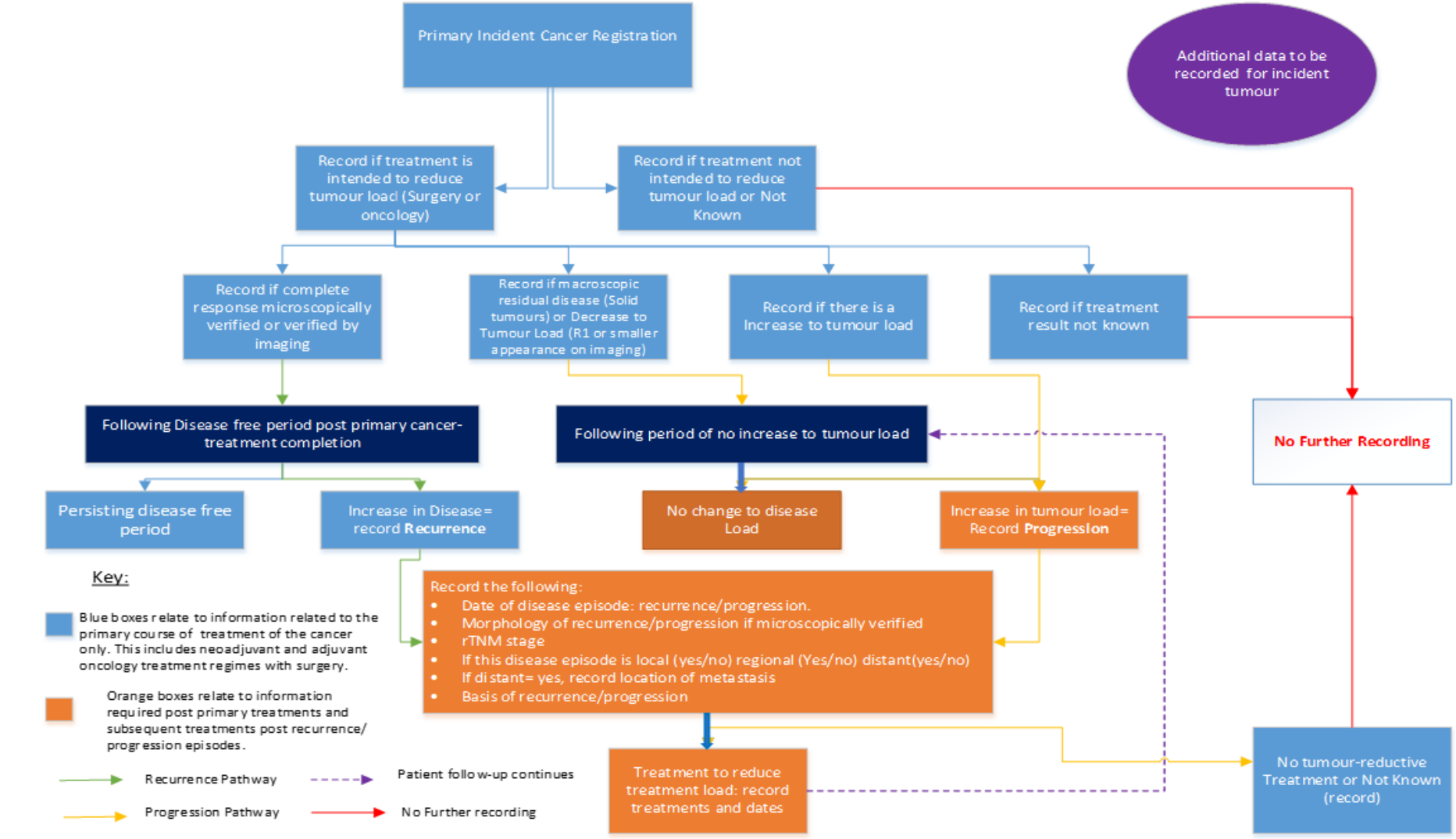
This approach requires

-access to clinical chart

- Identification of recurrence/progression via manual case review

PROS: standardised collection of recurrence/progression data

CONS: time consuming and expensive



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Background

Population-based cancer registry ⟷ administrative healthcare databases

Data-linkage

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Population administrative healthcare databases can potentially be used to estimate breast cancer recurrence rates

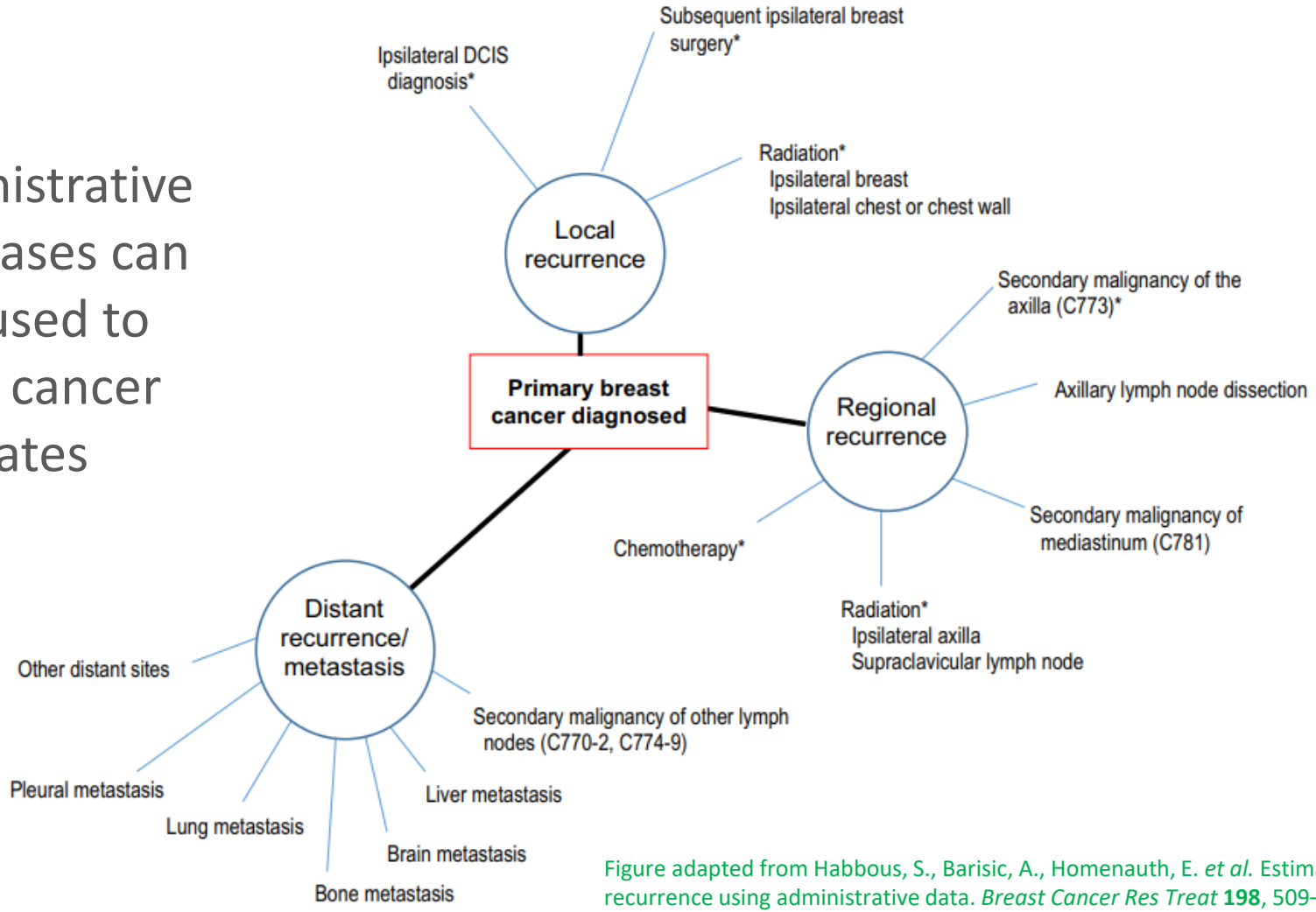

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Figure adapted from Habbous, S., Barisic, A., Homenauth, E. *et al.* Estimating the incidence of breast cancer recurrence using administrative data. *Breast Cancer Res Treat* **198**, 509–522 (2023). https://doi.org/10.1007/s10549-022-06812-z

Protocol (draft)

Aim

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To propose a feasible claims-based procedure to identify the **frequency and type of recurrences** among persons who are living after a diagnosis of cancer through a record-linkage of two data sources

1. population-based cancer registry
2. the health care administrative individual-record databases.

The pilot will be conducted for selected cancer sites

- **Colorectal**
  [males and female ; ICD10 codes C18-C21]
- **Breast**
  [females only; ICD10 code C50]

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Protocol (draft)

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Methods

A) DATA SOURCE: POPULATION BASED-CANCER REGISTRY

-Identification of the population-based retrospective cohort

REQUIRED DATA FROM ITALIAN AND EUROPEAN CENTRES*:

- **1. At least one year of incidence of the selected cancers during 2005-2015, with stage information (TNM) and (if available) other relevant prognostic factors (e.g., molecular profile);**
- **2. Incident cases must have at least 5 years of follow-up since the date of diagnosis**

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* Exclusion criteria will be described in details in the protocol

Protocol (draft)

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Methods

B) DATA SOURCE: ADMINISTRATIVE HEALTH CARE DATABASE

-Identification of the cancer recurrence

REQUIRED DATA FROM ITALIAN AND EUROPEAN CENTRES:

1. Hospital discharge database (HD);
2. Outpatient services database (OSD)

The list of HD and OSD Codes (ICD9-CM) that may indicate a cancer recurrence event will be selected with the collaboration of a multisciplinary group (epidemiologists, oncologists, surgeons….)

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Protocol (draft)

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Methods

-Identification of the date of recurrence

The surveillance period to identify the recurrence through the selected administrative codes will start after a period of no evidence of progression or ongoing disease (remission period) and will be tumour-specific

Assuming that, during primary treatment, procedures follow each other at intervals shorter than 6 months, **the recurrence will be identified by the first procedure occurring at least 6 months after the end of primary treatment**

This time window can be adapted according to the schedule of primary treatments, as defined by current guidelines for the specific neoplasm.

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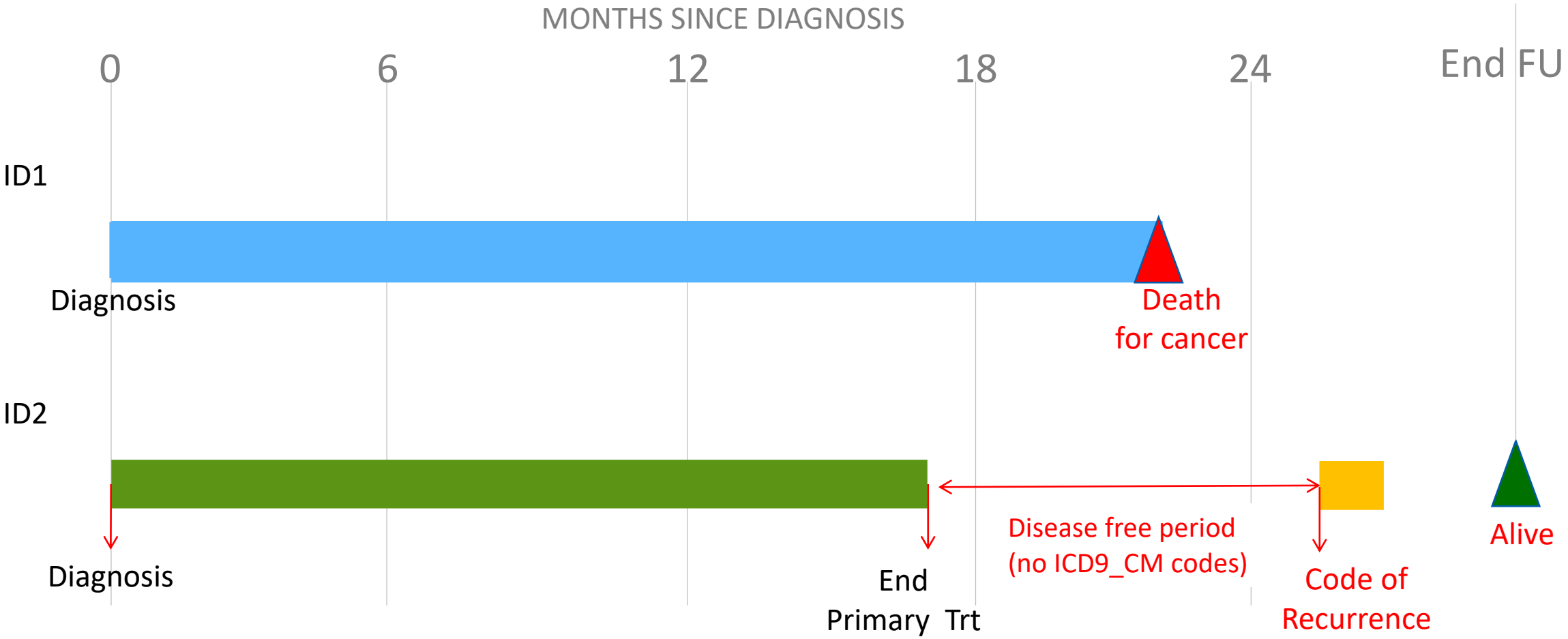
Methods:
how to define cancer recurrence?



Two situation :

ID1 → patient with NO DISEASE FREE PERIOD: cancer PROGRESSION

ID2 → patient with DISEASE FREE PERIOD: cancer RECURRENCE

→ ….secondary aims

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Protocol (draft)
Methods

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This pilot study will also be able to allocate the patients after the diagnosis of primary cancer to the following groups

- Alive and recurrence-free:
- Dead before recurrence (for selected cancer or other causes)
- Second primary tumour before recurrence (alive, dead for selected cancer or dead for other causes
- Alive with recurrence
- Died of selected cancer with recurrence
- Died of other causes with recurrence

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PRELIMINARY RESULTS

An application to Breast Cancer Data using Cancer Registries of Friuli Venezia Giulia and Veneto

INCLUSION CRITERIA

- Women residents in FVG
- Breast cancer diagnosis code (ICD-10: C50)
- Incidence Period: 2004-2010
- Last follow-up: 31/12/2021

EXCLUSION CRITERIA

- DCO and no follow-up
- Age 75+
- Previous or synchronous cancers
- Stage IV
- Missing Stage

5825 women included with a median follow up of 13.5 years

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Pilot 8.4.b: Estimating cancer recurrence

Examples of Hospital and Outpatient Administrative Codes (ICD9-CM) used to Identify Breast Cancer Recurrence

Intervention	ICD9-CM CODE	DESCRIPTION	Database
Chemotherapy	**PROCEDURE**		-Hospital Discharge Database (SDO-Schede di Dimissione Ospedaliera) -Outpatient Services Database (Prestazioni Ambulatoriali)
	99.25	Injection or infusion of cancer chemotherapeutic substance	
	99.28	Injection or infusion of biological response modifier ŸBRM¨ as an antineoplastic agent	
	DIAGNOSIS		Hospital Discharge Database (SDO-Schede di Dimissione Ospedaliera)
	V58.1	Encounter for chemotherapy and immunotherapy for neoplastic conditions	
	V58.11	Encounter for antineoplastic chemotherapy	
	ICD9-CM CODE	**DESCRIPTION**	
Radiotherapy	**PROCEDURE**		-Hospital Discharge Database (SDO-Schede di Dimissione Ospedaliera) -Outpatient Services Database (Prestazioni Ambulatoriali)
	92.23	Radioisotopic teleradiotherapy	
	99.24	Teleradiotherapy using photons	
	92.25	Teleradiotherapy using electrons	
	92.26	Teleradiotherapy of other particulate radiation	
	92.27	Implantation or insertion of radioactive elements	
	92.28	Injection or instillation of radioisotopes	
	92.29	Other radiotherapeutic procedure	
	DIAGNOSIS		
	V580	Radiotherapy	Hospital Discharge Database (SDO-Schede di Dimissione Ospedaliera)
	ICD9-CM CODE	**DESCRIPTION**	
	PROCEDURE		
	85.20	Excision or destruction of breast tissue, not otherwise specified	
	85.21	Local excision of lesion of breast	
	85.22	Resection of quadrant of breast	
	85.23	Subtotal mastectomy	
	85.24	Excision of ectopic breast tissue	

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ICD9-CM = International Classification of Diseases 9th Revision codes: Centers for Disease Control and Prevention. International Classification of Diseases, 9th Revision, Clinical Modifcation
(ICD9-CM). https://www.cdc.gov/nchs/icd/icd9cm.htm. Published 2016. Accessed 4 Nov 2020

Pilot 8.4.b: Estimating cancer recurrence

Hospital and Outpatient Administrative Codes (ICD9-CM) used to Identify Breast Cancer Recurrence

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	ICD9-CM CODE	DESCRIPTION	
Malignant neoplasm of female Breast	174.0	Nipple and areola	Hospital Discharge Database (SDO-Schede di Dimissione Ospedaliera)
	174.1	Central portion	
	174.2	Upper-inner quadrant	
	174.3	Lower-inner quadrant	
	174.4	Upper-outer quadrant	
	174.5	Lower-outer quadrant	
	174.6	Axillary tail	
	174.8	Other specified sites of female breast	
	174.9	Breast (female), unspecified	
Secondary and unspecified malignant neoplasm of lymph nodes	196.0	Lymph nodes of head, face, and neck	Hospital Discharge Database (SDO-Schede di Dimissione Ospedaliera)
	196.1	Intrathoracic lymph nodes	
	196.2	Intra-abdominal lymph nodes	
	196.3	Lymph nodes of axilla and upper limb	
	196.5	Lymph nodes of inguinal region and lower limb	
	196.6	Intrapelvic lymph nodes	
	196.8	Lymph nodes of multiple sites	
	196.9	Site unspecified Lymph nodes NOS	
Secondary malignant neoplasm of respiratory and digestive systems	197.0	Secondary malignant neoplasm of the lung	
	197.1	Secondary malignant neoplasm of the mediastinum	
	197.2	Secondary malignant neoplasm of the pleura	Hospital Discharge Database (SDO-Schede di Dimissione Ospedaliera)
	197.3	Secondary malignant neoplasm of other respiratory organs	
	197.4	Secondary malignant neoplasm of the small intestine, including duodenum	
	197.5	Secondary malignant neoplasm of the large intestine and rectum	
	197.6	Secondary malignant neoplasm of the retroperitoneum and peritoneum	
	197.7	Secondary malignant neoplasm of the liver	
	197.8	Secondary malignant neoplasm of the other digestive organs and spleen	

ICD9-CM = International Classification of Diseases 9th Revision codes: Centers for Disease Control and Prevention. International Classification of Diseases, 9th Revision, Clinical Modifcation (ICD9-CM). https://www.cdc.gov/nchs/icd/icd9cm.htm. Published 2016. Accessed 4 Nov 2020

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Application to Breast Cancer Data

PRELIMINARY RESULTS

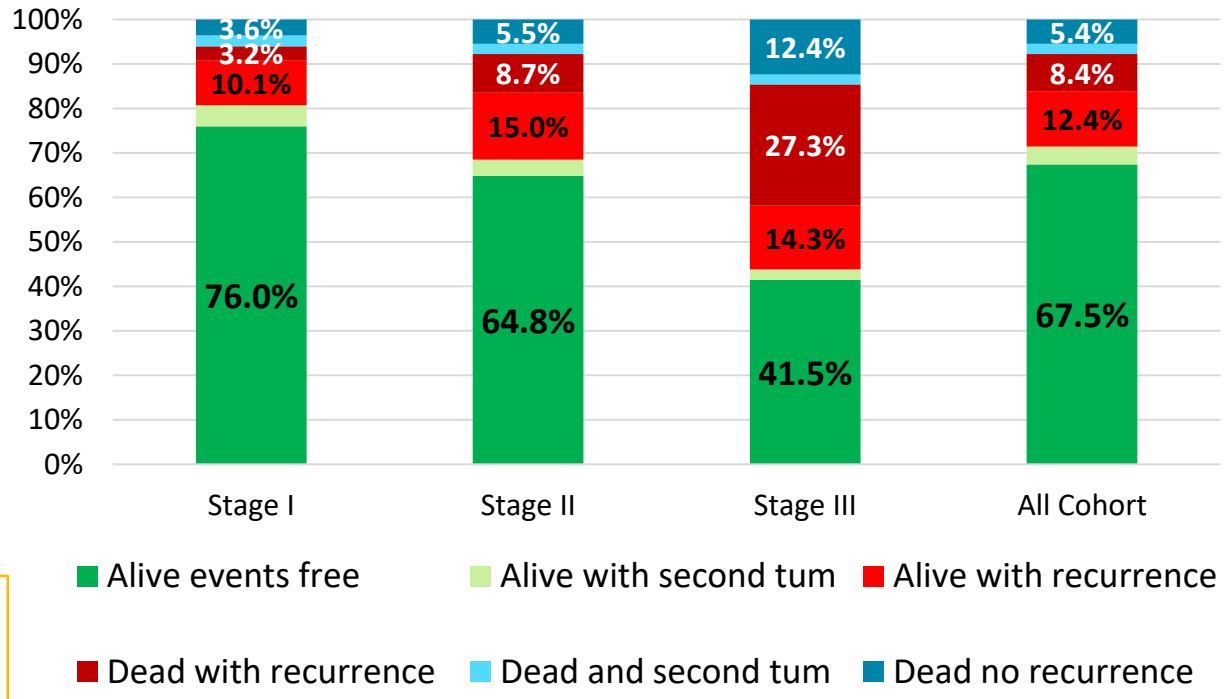
The **overall recurrence rate** in the cohort was **23.9 per 1000 py**
10-year cumulative recurrence (CI) was 20.8%

10-year Cumulative Incidence of recurrence decreased over time: **from 23.7%** in the 2004-2006 period **to 18.5%** in the 2007-2010 period of diagnosis

At 10 years since diagnosis

- **84%** of the women **were alive**
- **68% were alive and without recurrence or other primary tumors**

Follow-up of women with BC at 10 years since diagnosis by TNM Stage



Remarks and Conclusions

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Future developments:

- to complete the detailed protocol for estimation of cancer recurrence using administrative datasets
- to validate the procedure with clinical charts
- to include additional administrative databases (Drug Prescriptions database (DP) , Pathology Registry, ...)

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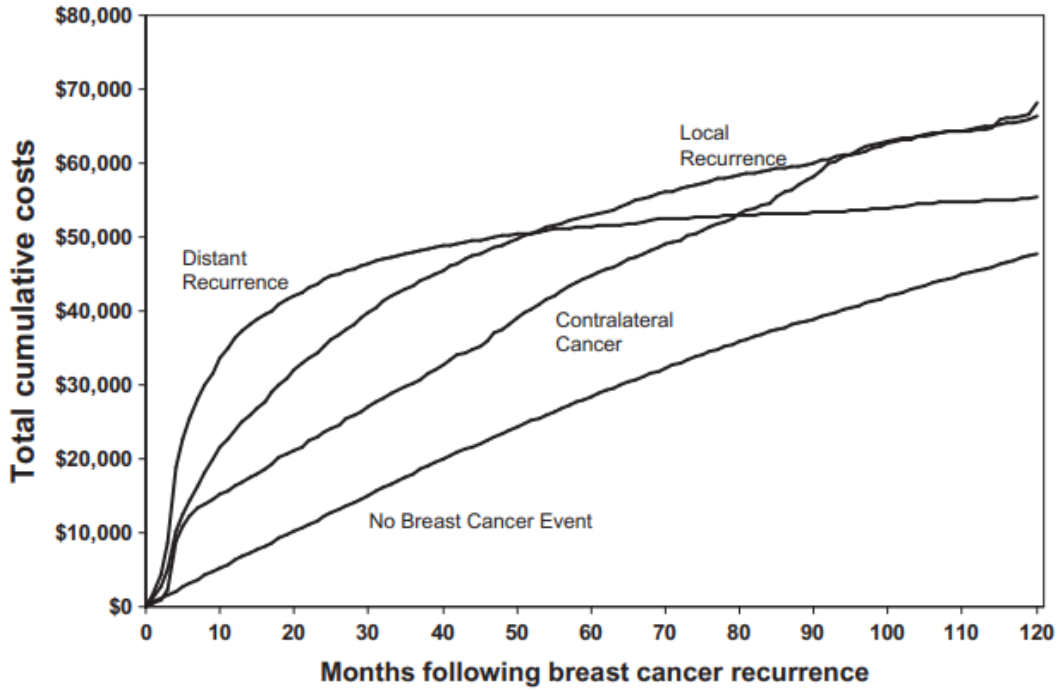
Remarks and Conclusions

This project may be used also for the **estimation of costs** in specific group of patients

Expected cumulative costs of care over 10 years among patients experiencing selected breast cancer events versus no breast cancer event



Volume 11 • Number 2 • 2008
VALUE IN HEALTH

Ten-Year Survival and Cost Following Breast Cancer Recurrence: Estimates from SEER-Medicare Data

Michael E. Stokes, MPH,[1] David Thompson, PhD,[1] Eduardo L. Montoya, BA,[1] Milton C. Weinstein, PhD,[1,2] Eric P. Winer, MD,[3] Craig C. Earle, MD, MSc[3]

[1]i3 Innovus, Medford, MA, USA; [2]Department of Health Policy and Management, Harvard School of Public Health, Boston, MA, USA; [3]Dana Farber Cancer Institute, Boston, MA, USA

Total expected cumulative costs for

Local/distant recurrence
$176,243

No recurrence
$42,005

Thank you for the attention

Questions and proposals are welcome ...

dalmaso@cro.it
fabiola.giudici@cro.it

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