iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

Co-funded by
the Health Programme
of the European Union

Protocol of the pilot study 7.2 of WP7

Integrating Cancer Registry Data on Care with Administrative and Health Information Sources in Europe

Author(s):	Lead author: Milena Sant Co-authors: Pamela Minicozzi, Roberto Lillini
Version	1.1
Date	27/05/2021

Contents

This report arises from the Innovative Partnership for Action Against Cancer Joint Action, which has received funding from the European Union through the Consumers, Health, Agriculture and Food Executive Agency of the European Commission, in the framework of the Health Programme 2014-2020. The European Commission is not responsible for the content of this report. The sole responsibility for the report lies with the authors, and the Consumers, Health, Agriculture and Food Executive Agency is not responsible for any use that may be made of the information contained herein. The authors are not responsible for any further and future use of the report by third parties and third-party translations.

Abbreviations

ATC	Anatomical Therapeutic Chemical
CC	Colon Cancer
CR	Population based Cancer registry
DRG	Diagnosis-related group
ECOG	Eastern Cooperative Oncology Group Performance Status score
ENCR	Network of European Population based Cancer Registries
EoL	End of Life
EUROCARE	Cancer Registry Based study on survival and care of European cancer patients
HR	high-resolution population-based studies
ICD9-CM	International Classification of Diseases, 9th revision - Clinical Modification
ICDO3	International Classification Of Diseases For Oncology – Third revision
PC	Pancreatic cancer
PROMs	Patients' reported outcomes measures
R0	Surgery with no residual cancer
RC	Rectal cancer
SM	Skin melanoma
TNM	**T**umour **N**odes **M**etastasis Cancer Staging system

Executive summary

This document describes the study protocol to evaluate the feasibility of linking individual patient's data included in population-based CRs, with administrative and health data, in order to describe the complete pathway of cancer patients from diagnosis to rehabilitation or terminal care, and assess the adherence of procedures to clinical guidelines

1. Background

In the last 10 years, „high-resolution“ population-based (HR) studies [HR studies, 2015], collecting more detailed clinical data than those available in the routine CR activity (such as stage at diagnosis, diagnostic procedures and main treatments), have been conducted in several European countries on samples of cases representative of the whole cancer incidence population, in order to explain reasons of outcomes differences and to assess the adherence of treatments to standard guidelines in the participating countries.

However, the HR studies rely on a limited number of cases, impairing generalization on the results to the entire cancer population and limiting the study robustness and power. Furthermore, the HR studies only collect primary treatment after diagnosis, and do not focus on further therapies administered during the disease course, either for maintenance, disease progression (relapse, distant metastases), palliation, or end of life. Moreover, they usually investigate relapses or disease progression, if any, within few years since diagnosis, advantaging of the natural gap existing between cancer registration and completion of cancer incidence. Major obstacles in collecting this detailed clinical information for the whole incident cases are: i) the amount of resources needed to consult patients' clinical documentation, often archived in various hospitals (where patients refer to be treated); ii) the need to consult clinical documentation also many years after diagnosis, with the possibility that the clinical documentation is archived in places different from the hospital where the main treatment was administered. Hospital registries and health administrative databases may help in capturing the entire clinical pathway for all cancer cases incident in the area covered by the population-based CRs.

2. Aims

Pilot 7.2 will evaluate the feasibility of linking individual patient's data included in the participating population-based CRs, with administrative and health data, in order to:

1. describe the complete pathway of cancer patients from diagnosis to rehabilitation or terminal care, including the use of health care resources at the end of life;
2. assess the adherence of the administered treatments to standard clinical guidelines.

Furthermore, taking into consideration the availability and type of administrative and health data, we will also explore the feasibility of:

- investigating pathological events (e.g., relapse, unwanted effects of anticancer treatments) occurring during the disease course;
- investigating 1) and 2) taking co-morbidities and socio-economic status into account
- integrating clinical data with patients' reported outcomes measures (PROMs).

3. Study Design

In order to optimise the amount of work performed by CRs and to provide as much as possible country-specific pilot results, pilots 7.2 and 7.3 will share the same study design.

Invasive, primary, malignant neoplasms of rectum (International Classification of Diseases for Oncology, 3rd revision – ICDO3 [Fritz A et al, 2000] topography C19-20), colon (ICDO3 topography C18), pancreas (ICDO3 topography C25), and skin melanoma (ICDO3 topography C44, morphology 8720-8790) diagnosed in adult (aged ≥15 years) patients are eligible for inclusion in the pilot study (these are called index tumours).
The study cohort will include patients diagnosed with the index tumours during all years of activity of the CR and still alive at the prevalence date (prevalence cohort). The prevalence date is the most recent one for which the CR database has been updated; an entire year of follow-up (life status) after the prevalence year must be available for the entire cohort.
Individual CR data will be linked to different administrative/health care data sources and to the mortality file, in order to reconstruct patterns of care of study cohort patients in a 3-year period spanning from 2 years before the prevalence date to one year after the prevalence date (study period). A visual concept of the study design is provided in **Figure 1**

3.1 Study indicators

The data made available through the present pilot study will allow us to investigate at least one cancer-specific indicator of standard care among the following ones.
The definition of the selected cancer-specific indicators is the result of the synergy between task 7.2 and WP10.

Indicators of standard care for colon cancer [Labianca R et al, 2013; Van Cutsem E et al, 2014]
- Percentage of screen detected (by organised or opportunistic screening) colon cancer patients;

- Percentage of colon cancer patients diagnosed by endoscopy who received a complete colonoscopy;
- Percentage of stage III resected colon cancer patients treated with adjuvant chemotherapy [if feasible, only R0 resections included] (in common with WP10);
- Percentage of metastatic colon cancer patients treated with
- Percentage of resected colon cancer patients died within 30/90 days from surgery (in common with WP10).

Indicators of standard care for rectal cancer [Glynne-Jones R et al, 2017]
- Percentage of screened-detected (by organised or opportunistic screening) rectal cancer patients;
- Percentage of rectal cancer patients diagnosed by endoscopy with biopsy;
- Percentage of stage III resected rectal cancer patients treated with neo-adjuvant radiotherapy [if feasible, only R0 resections included] (in common with WP10) ;
- Percentage of metastatic rectal cancer patients treated with biological drugs (molecular targeted, monoclonal antibodies);
- Percentage of resected rectal cancer patients died within 30/90 days from surgery (in common with WP10).

Indicators of standard care for skin melanoma [Dummer R et al, 2015]
- Percentage of stage IV skin melanomas receiving mutation testing;
- Percentage of skin melanomas with information on the maximum thickness in millimetres (Breslow) ;
- Percentage of skin melanoma patients with clinically negative nodes (cN0) and tumour thickness of >1 mm receiving sentinel lymph node biopsy;
- Percentage of metastatic skin melanoma patients treated with immunotherapy.

Indicators of standard care for pancreatic cancer [Ducreux M et al, 2015]
- Percentage of pancreatic cancer patients receiving CT scan at diagnosis;
- Percentage of resectable pancreatic cancer patient treated with curative surgery;
-Percentage of metastatic pancreatic cancer patients with information on ECOG performance status;

- Percentage of resected pancreatic cancer patients died within 30/90 days from surgery (in common with WP10).

Furthermore, for each tumour under study we consider:

Type of hospital (oncological, general hospital, oncological department within general hospital) where patients received the main treatments.

Indicators of quality of care at the end of life [Barbera et al, 2015], taking into account that in this phase high hospitalisation or anticancer drugs use are considered indicator of inappropriate care:
- A new hospital admission in the last 30 days of life;
- An intensive care unit (ICU) admission in the last 30 days of life;
- Chemotherapy use in the last 2 weeks of life;
- Percentage of dead cancer patients with information on place of death;
- Enrolment in specialist palliative care programm.

3.2 Information and data sources required

For each cancer case, the CR will provide all variables included in the 2015 ENCR-JRC Call for Data study protocol [EUROCARE-6, 2015]. In particular,

- the information on stage at diagnosis is requested only for prevalent cases with diagnosis up to 12 months before the prevalence date
- all tumours occurred before the prevalence date should be provided
- in case of prevalent cases with multiple primaries, all multiple primaries should be provided; patients with index tumours to be included in the study cohort will be defined centrally (by Task 7.2 coordination group) by selecting: a) patients with index tumours diagnosed as most recently as possible; and b) other primaries (any cancer type) that occurred 5 or more years before the index tumour diagnosis date.

To each cancer case, the CR will link the patient's record with all the available administrative/health care data sources and to the mortality file in order to trace access to health services, drug prescription or pathological events of interest during the follow up time.

The datasets (one for each health care source) will include a record per patient included in the prevalence cohort and per procedure (i.e multiple procedures for the same patient correspond to multiple records).

As contents of administrative/health care data sources considered for the linkage might vary according to the country health care data system, the number and type of administrative/health care data sources needed to evaluate the study indicators will vary according to country.

However, from administrative/health care data sources information should be extracted on:

- multiple diagnostic codes, including those not related to the cancer under study (main diagnosis, secondary diagnoses up to the maximum number available);
- multiple treatment codes (secondary treatments up to the maximum treatments available) ;
- type of treatments (e.g., ACT codes for establishing type of drug);
- quantity of treatments (e.g., total dose and fractions of radiotherapy);
- DRG code;
- type of hospital (eg teaching or general hospital);

and the main dates included in each data source, in order to investigate timing of treatments and pathological events occurring during the disease course, as well as the presence of co-morbidity.

In addition to this basic information, we will examine and discuss the feasibility of collecting information on:

- Type of procedure (diagnostic procedures, outpatient procedures and visits) classified according to the ICD9-CM or ICD10-CM classifications;
- Date of procedure;
- Quantity of procedure;
- Socio-economic status (or information to estimate it) ;
- Patients Outcomes Reports (PROMs).

Moreover, from the mortality file information should be extracted on:

- Patient-ID (the same one used in the CR database sent for the pilot study)
- Date of death;
- Cause of death.

4. Figures and Tables

Figure 1

Example of 7.2 and 7.3 study design, taking as prevalence date January 2013, 1st.

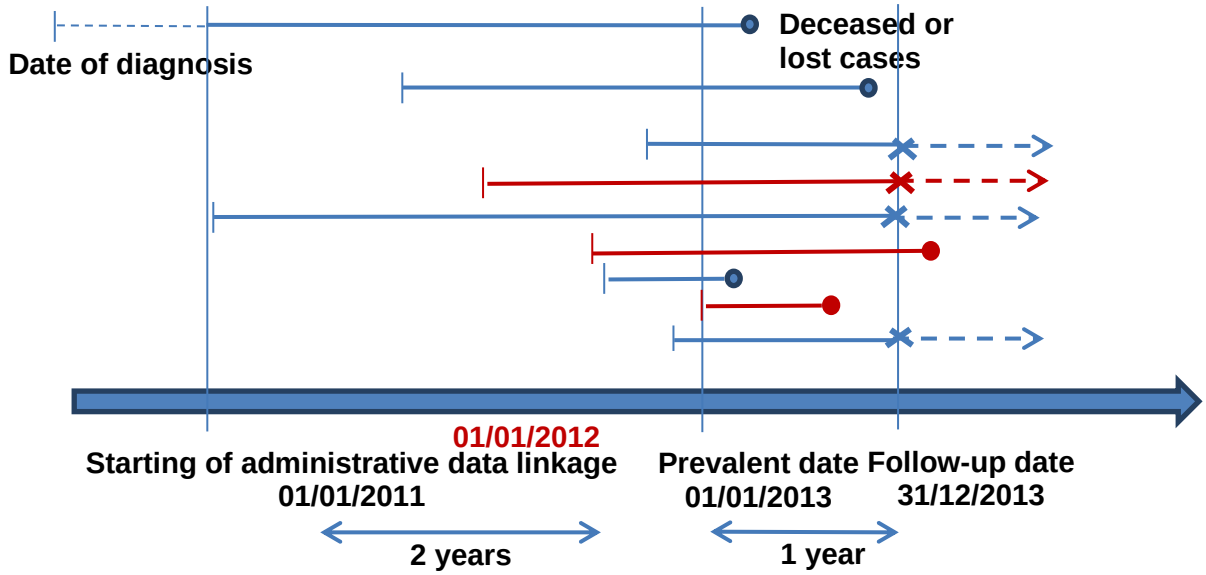

Table 1

Required information for each selected indicator for colon (CC), rectal (RC) and pancreatic (PC) cancers, skin melanoma (SM), and for investigating patients' end of life (EoL) in all patients

Topic	Indicator	Required information
CC	Percentage of screen detected *(by organised or opportunistic screening)* CC	Screen detection and date, type of screening
RC	Percentage of screen detected *(by organised or opportunistic screening)* RC	
CC	Percentage of CC patients diagnosed by endoscopy with biopsy	Stage at diagnosis, diagnostic procedure and date
RC	Percentage of RC patients diagnosed by endoscopy with biopsy	
SM	Percentage of stage IV SM receiving mutation testing	Stage, mutation testing procedure
PC	Percentage of PC patients receiving CT scan at diagnosis	Diagnostic procedure and date
SM	Percentage of SM patients with clinically negative nodes (cN0) and tumour thickness ~~of~~ >1 mm receiving sentinel lymph node biopsy	Pathological and clinical stage, thickness / Breslow (the latter could be indirectly reconstructed by pT); sentinel node biopsy
CC	Percentage of stage III resected CC patients treated with adjuvant chemotherapy	Stage, All treatments (type or category of drugs) and their dates *(important for distinguishing between pre or post-operative, for primary cancer or relapse/progression)*
CC	Percentage of metastatic CC patients treated with targeted therapy or monoclonal antibodies	
RC	Percentage of stage III resected RC patients treated with neo-adjuvant radiotherapy	Type of radiotherapic treatments
RC	Percentage of metastatic RC patients treated with targeted therapy	Stage, treatment (type or category of drugs)
SM	Percentage of metastatic SM patients treated with immunotherapy	Stage; treatment (type or category of drugs)
PC	Percentage of resectable PC patient treated with curative surgery	Stage; treatment
EoL	Chemotherapy use in the last 2 weeks of life	Dates (dd,mm,yy); treatment (type or category of drugs)
SM	Percentage of SM with information on the maximum thickness in millimetres (Breslow)	Stage at diagnosis with thickness / Breslow (it could be indirectly reconstructed by pT)
PC	Percentage of metastatic PC patients with information on ECOG performance status	Stage, ECOG
CC	Percentage of resected CC patients died within 30 days from surgery	Dates of death (dd,mm,yy), life status, date of surgery
RC	Percentage of resected RC patients died within 30 days from surgery	

PC	Percentage of resected PC patients died within 30 days from surgery	
EoL	Percentage of dead cancer patients with information on place of death	Place of death
EoL	A hospital admission in the last 30 days of life	All hospital admissions and their dates
EoL	An intensive care unit (ICU) admission in the last 30 days of life	Unit of hospital admission (e.g., emergency room, etc.)
EoL	Enrolment in a specialist palliative care programme	It includes information on setting where palliative care (Pcare) was administered, e.g.: • home specialised Pcare service • hospice admission • residential hospice admission • hospital Pcare consultation • inpatient hospital Pcare admission • outpatient Pcare clinic

Table 2a

List of Variables to be collected from the cancer registry or other sources, with the aim to collect them and justification for their use

VARIABLE	Description	AIM
Identification code*	Unique patient id code used at the CR	To link cancer registry (CR) data with administrative data files
Tumour identification code*	If available, in addition to patient's id code	To identify multiple tumours for the same patient (time sequential number)
Gender *		To study differences in care provision and outcomes by gender
Education	Scholarity title or total years education	Proxy of socio-economic status
Marital status	At diagnosis/prevalence date	Indicator of social support/isolation
Current occupation	Occupation at diagnosis/ prevalence date.	Proxy of social support/socio-economic status
Receipt of Social benefits	At diagnosis/prevalence date	Proxy of social support/socio-economic status

Unemployment	At diagnosis/prevalence date	Proxy of socio-economic status
Date of birth* (including day, month and year)	Day, month, year	To calculate the exact age at diagnosis
Birth nationality	Country of birth	Proxy of socio-economic status
Place of residence at diagnosis		To study socio-economic status
Date of incidence * (including day, month and year)	Incidence date as recorded in the CR (day, month, year)	It is the starting date for the calculation of care provision and/or survival
Age at diagnosis	As recorded in the CR	Required if the complete date of birth and/or incidence are not available
Basis of diagnosis *	Coded as as provided to ENCR and EUROCARE-6	
Topography*	Coded according to ICD-O morpho and topography codes, as provided to ENCR and EUROCARE-6	
Morphology*		
Laterality*		
Multifocality*		
Behaviour*		
Grade*		
Autopsy*		
Vital status*	Coded as as provided to ENCR and EUROCARE-6	To distinguish between alive and dead cases, and correctly identify the study cohort for each proposed indicator, particularly those referring to care at the end of life
Duration of survival in days	To be provided if complete date of incidence and/or date of last known vital status cannot be provided	To study survival

Date of last known vital status*	as recorded in the CR (day, month, year)	
Screen detection	Diagnosis made in asymptomatic phase; type of screening (opportunistic, organised);	To study the proposed indicator (=percentage of screen detected cases)
Stage at diagnosis*: pTNM cTNM, stage grouping Breslow thickness for melanoma*	According to the TNM manual rules, and coded as provided to ENCR and EUROCARE-6	To study treatments and the proposed cancer-related indicators, sccording to tumour stage
summary extent of disease*	Coded as provided to ENCR and EUROCARE-6	To be provided if TNM stage not available
TNM manual version used to code stage*		To help standardise the stage categorization
Number of positive and examined lymph nodes*	Coded as provided to ENCR and EUROCARE-6	To be used in multivariable models, as explanatory and/ or confounding factors
Sentinel lymph node biopsy		To study the proposed indicator for skin melanoma
Resectability	Only for pancreatic cancer	To study the proposed indicator for pancreatic cancer
Recurrence	0= none; 1= local; 2= on regional nodes or adjacent tissues/organs; 3= distant metastases; 9= unknown	To distinguish the disease phase
Date of recurrence (including day, month, year	(If available) Day, month, year	To distinguish if the treatment was done for the tumour under study or for recurrence

Distance between date of diagnosis and date of first recurrence in days	Number of days	The distance in days is required if the complete date of incidence and/or date of recurrence cannot be provided

* Variables required by ENCR and EUROCARE-6

Table 2b

Variables from the mortality database

VARIABLE	DESCRIPTION	AIM
Identification code	Unique patient id code used at the CR	to link CR data with administrative data files
Date of death (including day, month, year)	Day, month, year	To analyse the proposed indicators on care at the end of life
Distance between date of diagnosis and date of death in days	Number od days	Duration in days is required if complete date of incidence and/or date of death cannot be provided.
Cause of death	ICD10 code for cause of death, coded as provided to ENCR and EUROCARE-6	To distinguish between patients dead for the tumour under study, any further multiple tumour, or other causes different from cancer
Place of death	Hospital versus non-hospital	To study the proposed indicator for care at the end of life (e.g quality of life differences in dying at home, at hospital, or other places)

5. References

- Albreht T, Borras J, Conroy F, Dalmas M, Federici A, Gorgojo L, et al. European Guide for Quality National Cancer Control Programmes. 2015. Available at https://webgate.ec.europa.eu/chafea_pdb/assets/files/pdb/20102202/20102202_d10-00_en_ps_european_guide_on_quality_national_cancer_control_programmes.pdf

- Barbera et al. Quality of end-of-life cancer care in Canada: a retrospective four-province study using administrative health care data. Curr Oncol. 2015;22:341-55

- Ducreux M et al. Cancer of the pancreas: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015;26: v56-68.

- Dummer R et al. Cutaneous melanoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015;26: v136-132.

- EPICOST. Available at http://www.epicost.it; 2012.

- EUROCARE-6. Protocol for updating population-based cancer survival in Europe. Available at: http://www.eurocare.it/LinkClick.aspx?fileticket=99eJdjrCq18%3D&tabid=93; 2015.

- European Commission. Cancer control joint action e policy papers, 2017. Available at https://cancercontrol.eu/archived/uploads/PolicyPapers27032017/Policy_Paper_2_NCCP.pdf

- European Commission. Innovative Partnership Action Against Cancer, 2018. https://www.ipaac.eu

- Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, Whelan S, eds. International classification of diseases for oncology (ICD-O), 3rd ed. Geneva: World Health Organisation, 2000.

- Glynne-Jones R et al. Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017;28:iv22-40.

- HR studies. European High Resolution studies, 2015. http://www.hrstudies.eu

- Jonsson B et al. The cost and burden of cancer in the European Union 1995-2014. European Journal of Cancer 66 (2016) 162-170

- Labianca R et al. Early colon cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24:vi64-72.

- Parry C, Kent EE, Mariotto AB, Alfano CM, Rowland JH. Cancer Survivors: A Booming Population. Cancer Epidemiol Biomarkers Prev. 2011; 20(10): 1996–2005. doi:10.1158/1055-9965.EPI-11-0729.

- Sullivan R, Peppercorn J, Sikora K, Zalcberg J, Meropol NJ, Amir E et al. Delivering affordable cancer in high -income countries. Lancet Oncol 2011; 12: 933–80.

- Trama A, Botta L, Foschi R et al. Survival of European adolescents and young adults diagnosed with cancer in 2000-07: population-based data from EUROCARE-5. Lancet Oncol. 2016 Jul;17(7):896-906.

- Van Cutsem E et al. Metastatic colorectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2014;25:iii1-9.)