

PROTOCOL OF THE RITA DATA QUALITY STUDY

INTRODUCTION

The RITA project is aimed at estimating the burden of rare malignant tumours in Italy using the population based cancer registries (CRs) data. One of the major objectives of the project is to improve data quality in rare cancers registration. It is appropriate, therefore, to assess the validity, completeness and standardisation of CRs data on rare cancers between registries. The improvement of the quality of data will consequently improve the comparability of incidence, prevalence and survival of rare cancers among Italian and European population-based CRs.

On the basis of past experience of the analysis of rare cancers [Lancet Oncology, 2006], data quality for rare cancers doesn't seem as good as that for non rare tumours. The major reason is that rare tumour entities, as defined by the RITA and RARECARE projects, are a combination of ICD-O topography and morphology codes. Sometimes although topography is detailed to the 4th digit (sub-site) and morphology codes refer to a rare morphology, there are well known problems in diagnostic accuracy. An additional difficulty is due to the changes of the ICD-O classifications. The inclusion of new morphology and topography codes has forced registries to update not only the new but also the old data leading to additional efforts and raising comparability issues.

In this context, the main objectives of the RITA study are:

- To assess the comparability of data among CRs.
- To assess the validity of CRs data for rare cancers
- To verify the completeness of data on rare cancers.
- To verify the availability of information on stage, treatment and place of treatment.

Because previous experiences demonstrated that the revision of the pathological reports can improve the quality of the morphology and of the topography this study aims at assessing the data quality for rare cancers through the revision of information/reports available at the CRs offices.

This study will focus on the rare tumours of the so called 'short list', a group of rare tumours with high priority. These tumours have been selected because of their relevance for primary prevention, early diagnosis, diagnostic accuracy, quality of care, clinical research feasibility or because of their poor data quality in rare cancer registration.

Rare tumours to be included in the study with their related relevance for primary prevention, early diagnosis, accuracy of diagnosis, availability of treatment and poor data quality in rare cancer registration are listed in Table 1.

Table 1. Rare tumours to be studied for data quality and reasons for their relevance.

Rare tumour	Primary prevention	Early diagnosis	Diagnostic accuracy	Quality of care	Clinical research feasibility	Poor data quality
Mesothelioma	+++	?	++	+	++	+
Liver angiosarcoma	+++	?	+	++	+	+
Sarcomas	++	++	+++	++	+	++
Oral cavity tumours	++	+++	+	++	++	+
CNS tumours	++	++	++	+++	++	++
Germ cell tumors	+	+	+	+++	+	+
Leukaemia	++	+	++	+++	+	++
Endocrine tumours	+	?	++	++	++	+++

+++ very high relevance, ++ high relevance; + relevant; ? no data on the efficacy

For the revision of the morphology and/or of the primary cancer site, the documents/files to be revised will be the pathologic reports and the clinical dossiers **filed at cancer registry offices**. If necessary and feasible also the revision of the source documents such as medical records available at the hospital will be considered.

Pathological reports will be used also to check the availability of information on the stage of the tumours. The CRs internal dossiers of the case will be reviewed to verify the availability of information on treatment and place of treatment.

The mortality files will be reviewed **only** for mesothelioma and central nervous system tumours in order to check the vital status.

The period of diagnosis of cases to be revised is 1995-2002. The study will focus on malignant tumours only (5th digit of the morphology codes ≥ 3).

MESOTHELIOMA

The review will focus on long term survivors with ICD-O morphology 9050-9053 of **any sites** and of all cases with pleural cancers that are not coded as mesothelioma.

For this lethal cancer, we expect a very low proportion of cases alive two or more years after diagnosis thus, all the incident cases diagnosed during the study period, alive two (or three) years after the diagnosis have to be checked.

For these cases the revision should:

- confirm the diagnosis, this may be the case for patients surgically treated, or for patients that have undergone multimodal treatment (surgery, plus chemo/radiotherapy)

or

- change the diagnosis specifying the new code if it was a non malignant lesion of the pleura. Actually, pulmonary pleura in asbestos exposed people could be site of nodules, inflammatory pseudo-tumour, atypical adenomatous hyperplasia, etc. Furthermore, the pleura could be site of distant metastasis.

and

- correct the life status of the patient because the death certificate was not correctly linked.

In order to ascertain the completeness of mesothelioma of the pleura, all the pleura non-mesothelioma cases have to be checked.

LIVER ANGIOSARCOMA

To identify missing cases, the revision will focus on all liver cancers (topography ICD10 C22.0) microscopically verified and with a morphologic code **different from**:

8160	(cholangiocarcinoma),
8161	(cystadenocarcinoma),
8170	(hepatocellular carcinoma),
8171	(fibrolamellaire hepatocellular carcinoma),
8180	(hepato-cholangioma),
9590, 9591	(lymphoma),
8970	(hepatoblastoma),

The above listed cancers are the most frequent usual primary liver cancers and so, with a high degree of probability to be well coded in the database.

The quality of diagnosis and the completeness of incidence will be checked also through the revision of all sarcoma (not otherwise specified) NOS of the liver (only microscopically verified cases).

For these cases the revision should confirm the diagnosis or change the diagnosis reporting the new code.

SARCOMAS

Diagnosis of sarcoma is difficult. Sometimes the right diagnosis comes after several months since the first unspecific diagnosis of sarcoma or epithelial tumour.

For this exercise, it is suggested to revise all the sarcoma NOS (8800) and the descriptive ICD-O3 morphology codes 8801-8806, of any site (except liver because these cases will be checked as part of the review of the angiosarcoma of the liver). We expect to increase the number of Gastro Intestinal Stromal Tumours (GIST) and of all the new morphology codes included in the ICD-O3. It is worth stressing that it is possible to have a diagnosis of sarcoma NOS, since also expert pathologists may give this diagnosis.

For these cases the revision should confirm the diagnosis or change the diagnosis reporting the new code.

TUMOURS OF ORAL CAVITY

The revision will focus on morphology codes 8000, 8001, 8010, 8011 (carcinoma NOS) for the ICD-O site codes C02.0-02.3, 2.9, 03.0-05.0, 06.0-06.9 (oral cavity) and the unspecific site codes (2.8 and 5.9) in order to distinguish between oral cavity and oropharynx.

It is expected to increase the number of squamous cell carcinoma of the oral cavity.

For these cases the revision should confirm or change **both the morphology and topography codes** specifying the new codes.

CENTRAL NERVOUS SYSTEM TUMOURS

Some of the Central Nervous System (CNS) tumours are characterized by the availability of effective treatment, e.g. selected gliomas, pinealoma, germ-cell tumours, lymphomas etc.

However, several problems such as method and accuracy of diagnosis, high proportion of DCO, incompleteness of incidence, benign/borderline malignancies, etc. can affect the quality of CNS tumours data and the calculation of the epidemiologic indicators.

The review will focus on:

- Long-term survivors with a diagnosis of unspecified morphology codes (8000, 8001, 8010). The review should clarify whether the long-term survivors are brain malignant tumours. In addition the revision should verify if the life status is correct.
- Cases with diagnosis of Glioma NOS (9380), microscopically verified. The review should confirm or change the diagnosis, specifying the new code. If available, the information on grading should be added.

GONADAL GERM CELL TUMOURS

These tumours are characterised by the availability of treatment.

The review will focus on the morphology NOS (8000-8010) cases of the testis (C62, C63.0, C63.1) and of the ovary (C56). ONLY microscopically verified cases will be reviewed.

For these cases the revision should confirm the diagnosis or change the diagnosis reporting the new code.

LEUKAEMIA

Different leukaemias have different prognosis and division into main diagnostic groups is necessary to analyse treatment and prognosis of leukaemia. Therefore the number of unspecified leukaemia cases should be as low as possible. Unspecified codes are: 9801, 9820 and 9860. The two major types of CML: typical (9875) and atypical (9876) have different prognosis, because of the availability of treatment for typical CML. Consequently, also the number of CML, NOS (M9863) should be as low as possible.

The review will focus on:

- all the leukaemias, NOS (9800, 9801, 9820, 9860),
- CML, NOS (ICD-O3 9863)

For these cases the revision should confirm the diagnosis or change the diagnosis reporting the new code.

MALIGNANT DIGESTIVE ENDOCRINE TUMOUR (MDET)

Some registries have difficulties to identify small-cell MDET, which are major prognostic factors (the 5-year relative survival rate being 8% compared to 58% for well-differentiated MDET).

Well differentiated endocrine tumours include the following codes, pancreatic insular carcinoma (8150/3), insulinoma (8151/3), gastrinoma (8153/3), vipoma (8155/3), glucagonoma (8152/3), non secreting endocrine carcinoma (8246/3), (those tumours being pancreatic tumours) and carcinoïd (8240, 8241, 8243, 8244/3) which can be found at all digestive site.

Small cell tumours include small cell endocrine carcinoma (8041/3) and oat cell carcinoma (8042/3) (this code is very rarely used). In some registries small cell endocrine tumours are not identified. Their identification may require a review of pathology reports concerning undifferentiated carcinoma (8020/3, 8021/3) of the digestive tract (topography codes C15 to C25). The objective is to find in the pathology reports the term “round” or “fusiform” cells which suggest endocrine tumour. In the case that the terms “round” or “fusiform” are in the reports, the code should be changed in 8041.

High incidence and survival rates of MDET have been related to a high proportion of appendix MDET. These tumours are usually benign suggesting that tumours of undetermined malignancy were recorded among MDET. We invite to review the pathological reports of all carcinoid tumours (8240-8244) in order to distinguish between borderline and malignant. The following criteria should be used to identify the behaviour (**ATTENTION: these criteria are proposed and have to be used ONLY for this study**):

- Invasion of the muscularis propria
- Dimension of the tumour
- Proliferation index (Ki67)

The behaviour is equal to 3 if:

- the tumour invades the muscularis propria (stomach, small intestine and colon and rectum), invades the visceral peritoneum (appendix), has an extra-pancreatic extension (pancreas);
AND
- the size is more than 1 cm (stomach and small intestine) or more than 2 cm (large intestine, appendix and pancreas).

Additional information confirming the malignant behaviour are:

- mitotic index 2 to 10;
- proliferation index (Ki67) 2 to 15%;
- angioinvasion.

Please refer to Table 2 for more details.

The revision will focus on the topography codes: C16-25

Table 2. Criteria to identify the behavior of endocrine tumours (ET) (in situ vs malignant).
(ATTENTION: these criteria are proposed and have to be used ONLY for this study)

	Well differentiated benign and bordeline ET	Well differentiated endocrine carcinoma	Undifferentiated endocrine carcinoma
Differentiation	Well differentiated	Well differentiated	Undifferentiated
Angioinvasion	No	Possible	Possible
Size	Stomach, Small intestine: ≤ 1 cm Appendix, colon, rectum : ≤ 2 cm Pancreas : < 2 cm	Stomach, Small intestine : >1 cm Appendix, colon, rectum : > 2 cm Pancreas : >2 cm	
Mitotic Index	≤ 2	2 to 10	> 10
Proliferation Index (Ki67)	≤ 2 %	2 to 15 %	> 15 %
Local invasion	Digestive tumour : mucosae/submucosae Pancreas : intra-pancreatic	Digestive tumour (out appendix): > Muscularis propria Appendix : invasion of the visceral peritoneum Pancreas : extra-pancreatic extension	
Metastases	no	Possible	Possible
Behavior: /1 ↓ /3 /3			

For all these rare tumours the revision have to specify whether information of stage, treatment and place of diagnosis and treatment are available.