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Incidence of cancer in the Belgian province of Limburg in 1996: First experiences of a new cancer incidence registry.

by

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Abstract

Background: *Epidemiological research on occurrence and determinants of cancer requires reliable age and sex adjusted incidence rates for all cancer groups.The absolute numbers and age-specific data are also valuable for cancer research and planning health services.The Limburg Cancer Registry has been established to collect such data.*

Aim: *To provide the opportunity of continuously follow cancer incidence rates and to analyse the relation of occurrence with a number of determinants (age, sex, regional differences etc.)*

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Methods: *All cytologically and/or pathologically confirmed cancers in inhabitants of the Belgian province of Limburg (n = 777644) were identified based on test results provided by the pathologists. For each case patient characteristics, doctor characteristics and diagnostic results, classified according to the International Classification of Diseases for Oncology were registered.*

Results: *During 1996, 3195 primary cancers were identified .This relates to a crude invasive cancer incidence rate of 454/100000 person-year for males and 329/100000 for females. This corresponds with a European standardised rate of 471 and 293 respectively and a World standardised rate of 339 and 170. Additionally, 451 metastases, 345 borderline malignancies and 530 basal cell carcinoma of the skin were identified. The top five cancers in males were prostate, lung, urinary bladder, colon and non-melanoma skin cancer. In females they were breast, colon, urinary bladder, non-melanoma skin cancer and non-Hodgkin lymphoma.*

Our results have been compared with a number of neighbouring Belgian and Dutch cancer registries: the Belgian National Cancer Registry (NKR), the Netherlands Cancer Registry (NCR), the registry of the Comprehensive Cancer Centre Antwerp (IKSA) and the Comprehensive Cancer Centre Limburg – the Netherlands (IKL).

Apart from a clear first year effect, our results are largely similar to the Dutch results.

Key-words

Cancer, epidemiology, cancer registry, Belgium.

Introduction

Epidemiological research with respect to occurrence and determinants of cancer has never been very popular in Belgium.A rather comprehensive cancer incidence registry, providing basic data for epidemiological research never succeeded (1). Such information however, is very important for those who have to determine a policy with respect to prevention, diagnosis or treatment of cancer. The wish to have an ongoing cancer

registry in the Belgian province of Limburg has been existing for many years. With the help of the provincial authorities and sponsored by the Flemish Community Government, the LIKAR (Limburgs Kanker Register – Limburg Cancer Registry) working party was charged with the preparation and production of a cancer incidence registry for the population of the province of Limburg, based on collaboration with all relevant pathological laboratories.This paper is based on its first report covering the results of the year 1996 (2).

Methods

1. Design

Of all cytological and pathological tests resulting in a cancer diagnosis and related to somebody belonging to the population at risk, patient characteristics, doctor characteristics, and diagnostic results are centrally registered. Denominator of all calculations is the "inhabitants of the Belgian province of Limburg" or age and gender related subgroups.

Data are provided by all pathological laboratories located in the province and all pathological departments outside the province which more than occasionally examine samples from Limburg inhabitants.

Data collection

For each patient and each test result indicating malignancy, a record is made by the laboratory and stored centrally at the university campus of the Limburgs Universitair Centrum at Diepenbeek -Expertisecentrum Digitale Media (EDM). For each test, a number of data are registered: an encrypted, but unique identification code for each person, the identification of the pathologist and the laboratory, the month and the year of the examination, the identification of the referring clinician, some patient related data such as gender, month and year of birth and postal code, and the test result, including site and morphology. The identification code for each person is delivered to the registry in an encrypted form. Therefore, the participating laboratories and practitioners are equipped with especially developed software. This software applies a "hashing algorithm". This algorithm generates a unique code for each individual, but it is impossible to identify this individual without consulting the practitioner or the laboratory that provided the data. The unique encrypted code guarantees that all data of the same patient are recognised as such by the registry.

Records entering the registry are extensively tested. Records related to people outside the province of Limburg, as well as non-cancer results are identified and discarded. Next, the records are tested in order to be defined as a metastasis, a borderline malignancy or a cytologically or histologically proven primary cancer.

A lot of tests are implemented to enable the computer to decide whether or not a record is a new primary cancer (2). There are however, a number of cases where a pathologist has to intervene manually.

Data exchange

The agreement between NKR and LIKAR includes the mutual exchange of data. This is made possible by the use of a common hashing algorithm. In this way, we will be able to yearly examine which cases were missed by each of the registries and to continuously improve our coverage. A similar agreement exists with the hospital based registry of the province of Antwerp that recently published its 1995 results (3).

Coding and classification rules

To ensure compatibility with other international cancer registries, all cancers are classified according to the ICD-O classification.

Because most of the collaborating pathologists use the "Codap" classification (Code voor histopathologische diagnosen – Department of Pathology, University Hospital Leuven) for their clinical work (each with their own adaptations), software was produced converting the CODAP to ICDO codes. A thesaurus-committee of pathologists ensures the update of the conversion algorithm as new codes show up

If two tumours of the same histological type occur simultaneously at the same site (or subsite for tumours of colon, rectum, skin, bone and soft tissue) one tumour is registered (e.g. two adenocarcinomas in the stomach result in one registration).

Ovarian tumours of borderline malignancy and the serous, papillary, mucinous and pseudomucinous cystadenomata are included in the general report. In urinary bladder tumours, only in-situ cancers were considered as non-invasive and registered separately. All others, including the non-infiltrating papillary bladder cancers, have been coded as invasive.

Basal cell carcinomas of the skin and carcinomas in situ of the cervix uteri are excluded from the basic report, but registered separately in the database.

2. Quality control

Completeness of coverage

Our purpose is to register every case of cancer within our population. Sources of underregistration may be incomplete medical cover (never diagnosed cancers) and missing of known cancers because of the registration procedure.

Underestimation certainly happens in very old patients, where biopsies are rarely performed or impossible because of a poor general condition, or the site of the tumour (CNS, pancreas). There is no way to correct for this deficit, although its frequency is decreased by the fact that also cancers found in patients that are not hospitalised are included in the registry. Moreover, in this initial phase, only pathological laboratories are involved. As haematological cancers are often diagnosed by haematologists and not by pathologists, also in this field underregistration can be expected. In the future, special efforts will be made to integrate data from the haematological laboratories as well. Linking our results with the national Cancer registry and exchange of information between the registries of the Euregio (Belgium, The Netherlands and Germany) provides data on Limburg inhabitants that are not examined by our pathologists' network or that are cared for in nearby Dutch or German centres.

Validity

Validity of a cancer registry is defined as the proportion of cases in the registry with a given characteristic (e.g. cancer site, age, and gender) which truly has that attribute (4). This depends upon the accuracy of the data source documents and the level of skill in processing this information. The LIKAR procedure allows the inclusion of histologically/cytologically confirmed cases only. The likelihood of false positive diagnoses therefore is expected to be extremely low on the level that is reported here.

Impossible combinations of data are searched using automated test procedures including the IARC check software (5): illegal codes are not allowed (for example neutral as gender, or a city outside the catchment area) and a logical consistency between data is necessary (for example: between sex or age and site or type of cancer.

We compared our results to neighbouring cancer registry results: the Belgian national cancer registry (NKR), the Dutch national cancer registry (NCR) and the IKL-registry of the Dutch province of Limburg,our neighbours.

Multiple recording

Multiple recording of a patient by the hashing procedure is possible, but uniform coding and hashing of all identification data reduces this possible source of error. The hashing algorithm (including the soundex) has been tested for the generation of double output in three databases and resulted in an unique result in 99.11% (n = 8599), 99.98% (n = 35866) and 99.93% (n = 466429) respectively (6). Only in twins of the same gender or in people of the same gender with a very similar name that are born on the same date, problems may arise.

An additional source of error may be the inaccuracy in recording the personal data of the patient: aberrant given names, inconsistency between spoken and written (legal) sources, etc.

All collaborating laboratories have been questioned about their method of patient identification registration. For biopsies, mostly taken from patients seen in hospitals, patient identification data are entered in the local computer from the official medical insurance documents. This method guarantees a high degree of uniformity. In one laboratory which receives a lot of specimens from general practitioners and extern specialists, patients are partly registered based on hand-written documents.

As we accept that a certain degree of initial double-recording resulting from multiple test results of the same cancer in one patient is inevitable, all cancer inputs are additionally tested for the possibility of being related to the same patient, using a set of algorithms that were especially developed for this purpose. If two records complied with one of these algorithms, they are considered to be related to the same cancer in the same patient or to two different cancers in the same patient respectively.

Completeness of data

Incoming data are checked on the completeness of the included information, with respect to both demographic and clinical aspects. Incomplete data errors are rectified by a feedback system, elaborated at the Expertisecentrum Digitale Media (EDM) of the University of Diepenbeek.

According to international publications, missing information is most frequent in cases with "primary site unknown" (PSU). The percentage of PSU consequently is an indicator of the quality of diagnostic information (7). In our data, this relates to 5 cases or less than 0.2% of all

primary invasive tumours. Adding these PSU cases to the sum of the Not Other Specified (NOS) categories for all organs, results in a total of 120 or 3.94% of all primary tumours. Missing data concerning demographic information should constitute less than 1%. In our registry, this relates to 3 cases with missing information on age and they were excluded.

Results

Population at risk

The area of the Limburg Cancer Registry consists of the province of Limburg, situated in the north-east of Belgium. The territory covers 2422 square km or 7,9% of Belgium territory.

The population at risk was calculated as the average of the population figures for the beginning and the end of the year as published by the National Institute of Statistics. For the year 1996, this results in 389454 males and 388190 females, totalling 777644 inhabitants. This means: 7,6% of the Belgian population and 13,2% of the Flemish. Remarkably is the restricted degree of urbanisation: the only two major cities Hasselt (n = 67504) and Genk (n = 62239) constitute 17% of the population. Both are situated in Middle Limburg. The rural character of this province also shows from the following data: 44% of the population lives in 32 municipalities with 20000 inhabitants or less, and 39% in 10 municipalities with 20000 to 40000 inhabitants.

From an economical point of view, there are some differences between the regions. North and Middle Limburg developed industrial activities especially related to petrochemical industry, electronics and the automobile industry. The industrial zone is gradually spreading into West Limburg and the Maasland (eastern region). South Limburg essentially remained a rural area with fruit farming as its major activity.

Limburg has a relatively young population: 25% is younger than 20 and 17% is older than 60. Limburg tends towards the end of its demographic wealth. The percentage of inhabitants of age 20 or less decreases, the active population increases and the number of people aged 60 or older is growing rapidly.

The tendency is towards a proportional increase of ageing population and is similar to the general Flemish profile.

People not possessing the Belgian nationality constitute 8,7% of the total population of Limburg. 56% of the 66386 non-Belgian inhabitants lives in 5 agglomerations: Genk, Maasmechelen, Houthalen-Helchteren, Beringen and Heusden-Zolder. From 1918 until 1992, this was the coalmining region.

The majority of the non-Belgian population (28%) is of Dutch nationality, living in the border communities of the Maasland region and North Limburg. Turks, Italians, Moroccans, Spaniards and Greeks follow in degressive order. 4/5 of them is situated in the former mining regions.

Incidence rates

During the year 1996, 3195 primary cancers were diagnosed and histologically/cytologically confirmed in inhabitants of the Belgian province of Limburg. Of all these malignancies 96% had been histologically verified, 4% only cytologically. 3045 were invasive, 150 non-invasive tumours. This relates to a crude invasive cancer incidence rate of 454/100 000 person-years for males (95% CI = 433-475) and 329 /100 000 for females (95% CI = 311-348). The corresponding standardised rates are 471 and 293 for the ESR and 339 and 170 for the WSR. Additionally 451 metastases without known primary tumour were identified, 530 basal cell carcinomata of the skin and 345 borderline malignancies. For 3 records, the information with respect to age was incomplete. These cases were excluded.

As expected, cancer incidence sharply rises with age (Figure 1).

The top five cancers in males are: prostate, lung, urinary bladder, colon and non-melanoma tumours of the skin (basal cell carcinomas are not included). In females, they are: breast, colon, urinary bladder, non-melanoma tumours of the skin and non-Hodgkin lymphomas.

Figure 2 shows the age-adjusted incidence rates per 100000 inhabitants (standardised according to the world standard population) for major cancer sites in males and females.

The mortality – incidence ratio based on the overall cancer mortality data of 1996 was 0,57 for males and 0,47 for females. Only for lung cancer in males the ratio was larger than 1.

The age, sex and organ specific mortality figures were provided by the Ministry of Flanders, Preventive and Social Health Care Division.

There were only 8 cases of cancer in childhood (0-14 years). Therefore a specific analysis is inappropriate.

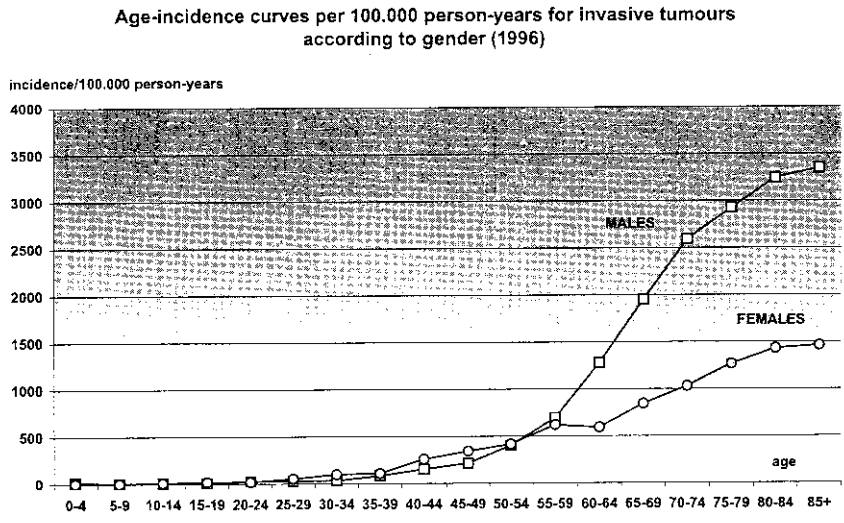

Fig. 1: Age-incidence curves per 100.000 person-years for invasive tumours according to gender (1996)

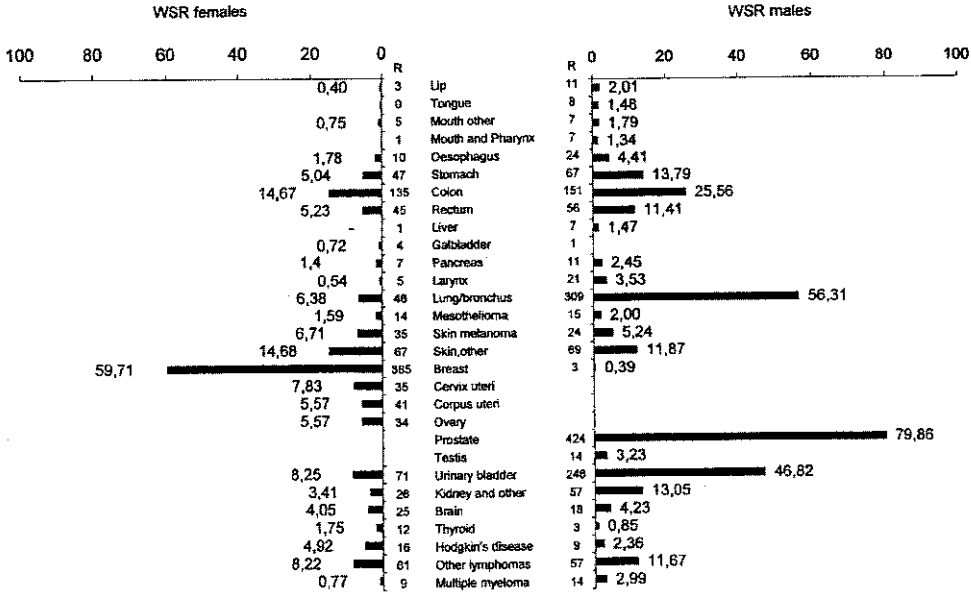

Fig. 2: Age-adjusted incidence rates per 100 000 inhabitants (Standardised according to the world standard population) for major cancer sites in males and females in 1996)

Discussion

The overall cancer ESR estimated by LIKAR for the male Belgian – Limburg population is slightly higher than the estimates of both the national Dutch registry (8) and the IKL registry (9). For females, the

LIKAR rate is lower compared to Dutch results, but very near to the Dutch – Limburg numbers (table 1). For a new registry reporting its first results, it is of course encouraging that the results are so near to the results of the more experienced neighbour. It is temping to conclude that, from the very beginning, our data are as trustworthy as the Dutch. More probably however, this similarity is the result of a number of biases in different directions, with a first year effect compensating for all kinds of small missings that are characteristic for a new registry.

During the first registration year, a number of cancers, classified as primary tumours, are expected to be prevalent cases. There is no way to directly estimate the amount of the resulting bias, but the problem will resolve itself the coming years. It should be mentioned that LIKAR only includes histologically or cytologically confirmed cancers, while both Dutch registries also include cancer diagnoses based on clinical tests only. For most cancers the proportion of only clinically determined cases in the Dutch registry is less than 5% (8).

The most recent data available of the Belgian NKR for the Limburg population are those of the year 1994 (personal communication by Dr. M. Haelterman). The NKR identified 1225 malignant tumours in males and 1048 in females.

The LIKAR registry resulted in 63% (basal cell carcinoma included) more inclusions compared to the NKR's own collection.

Also the mortality – incidence ratio tends to confirm absence of substantial underreporting of cancers.

Specific analysis for the most prevalent cancer sites

TABLE 1

Comparison of the ESR 1996 with the ESR 1995 of the NCR and the ESR 1996 of the IKL (invasive tumors)

ESR: Incidence rates per 100000 person-years standardised for the European Population

	ESR **Likar** 1996	ESR **NCR** 1995	ESR **IKL** 1996
Males	471	453	437
Females	293	329	296

LIKAR: Limburg Cancer Registry (Belgium)
NCR: Netherlands Cancer Registry
IKL: Comprehensive Cancer Centre Limburg – The Netherlands

The similarity between the LIKAR and IKL results is striking for stomach and colorectal cancer, especially in females.

LIKAR is relatively low in lung cancers. For males the ESR = 80, 94.1 and 103 for LIKAR, NCR and IKL respectively.Also the mortality – incidence ratio for lung cancer in males is the only one to exceed 1. It is not sure if this results from a really lower, probably even decreasing incidence, from random error and differences between the incidence years studied, from underregistration, from underdiagnosis or from a large proportion of cancer diagnoses that are only clinically determined (6.1% in the Dutch registry (8). A combination of these explanations is perhaps the most probable.

Grouping all cancers of the pelvic female genital organs results in a slightly higher incidence rate in the LIKAR registry. In this group however, the category of "female genital organs. other/NOS" is 7.5% against about 1% in both Dutch registries. It is a challenge for the Belgian pathologists to explore the reasons for the high number of non-specific diagnoses in this category, especially because in most other organs the number of "other/NOS" tends to be lower in the LIKAR registry. Also pancreatic cancers are relatively seldom in our registry. This however could be a random error effect due to small numbers.

With respect to breast cancer incidence, our results are almost identical to the IKL results (ESR 94 and 91.5 respectively), but lower than the results for the entire Netherlands (ESR 112.1). This difference also probably results from the absence of larger inner cities with their own specific life style problems or from a different screening history.

Strikingly high are the LIKAR incidence rates for bladder and prostate cancer. Most patients with prostate cancer survive many years without even knowing they have a cancer as long as they have not specifically been examined. The availability of PSA tests increased the number of diagnoses and so the number of labelled and treated patients. At this moment, incidence rates for prostate cancer in Europe are probably more descriptive for regional screening and diagnostic policies than for differences in "real" incidence.

For bladder cancer, the reason is not that clear. Differences in coding habits have been mentioned as a possible reason for differences between cancer registries (9). Follow-up after treatment is done by cystoscopy and biopsy of new polyps. This may go on for many years. In such situation the first year effect on cancer registration can be expected

to be higher compared to most other cancers. Additionally one gets the impression that this tumour is getting increasingly frequent, also in some other countries with long standing and stable registries, e.g Denmark (10). It will not be easy to entangle the exact influence of all these determinants.

To make the comparison of bladder cancer incidence between LIKAR and IKL more accurate, the IKL figures have been elaborated in an attempt to make the two different methods of registration more similar: only cyto-histologically confirmed malignancies were included, the non-infiltrating papillary bladder cancers were added, as were the relapses of 1995 to simulate a first year bias.After this simulation the recalculated ESR for LIKAR and IKL were 62.8 and 51.5 respectively in males and 13.75 and 6.6 in females (personal communication by Dr. L. Schouten).

What can go wrong with cancer registration?

In cancer incidence estimation, a number of possible biases related to both numerator and denominator are possible.

The inhabitants of the province of Limburg are the *denominator* when calculating incidence rates. They are a dynamic population, changing continuously. Therefore a mid-year population is used as the best estimate for the denominator. However the incidence rates based on this denominator would differ only slightly from pooled daily incidences using the population of each day as the denominator. There is no reason to expect selection towards either increased or decreased incidence of any of the cancers.

The Belgian privacy law prohibits the registration of any information about ethnical origin. Considering the heterogenic character of the population, epidemiologically extremely valuable information is lost by this restriction. This should be kept in mind when performing in depth investigation of our results. Additional efforts, including retrospective searches, will be necessary to retrieve these data.

The estimate of the numerator may be false high as a result of the use of multiple names for one patient, identification writing errors at the site of sample taking, or problems with the hashing algorithm.

In preventing duplicate coding of the same patient, the hashing algorithm (including the soundex) has been tested repeatedly and was found very reliable in preventing duplicate coding of the same patient. The

problem actually only emerges in twins of the same gender with a similar Christian name or in people of the same gender that are born on the same day and have similar names as well as Christian names.

At this moment however, it is not possible to quantify both first sources of error. Hopefully, the use of official medical insurance documents by all but one laboratory keeps the problem within limits. Only one measure could resolve this problem: the use of the official national registration number by all medical facilities as well as, after encryption, by epidemiological research centres. It should be desirable that this number would be automatically read from some kind of credit card as it is planned in hospitals and social security services for the near future. At this moment the privacy law forbids the use of this number in research. Future government plans do not include the use of the card by private working clinicians. It is our hope, as the hope of most epidemiologists in this country, that Belgian authorities will follow the lead of most of their European colleagues and change these regulations.

The estimate of the numerator may be false low if the hashing algorithm relates different cancer patients to the same identification string, if samples are examined in pathology departments outside our collaborators' group or if cancers are diagnosed without cytological/ histological confirmation.

The likelihood of the first error has been tested and estimated at less than 1 in 100 million (6).

Our list of collaborating pathologists includes all departments that handle samples from Limburg inhabitants more than incidentally. Although it is sure that some cases are missed, we expect the number to be low. As soon as the NKR data for 1996 are available, it will be possible to compare both data files and to estimate the number of missings related to such laboratories.

In the border regions, some people are examined and cared for in neighbouring countries, especially the Netherlands. The IKL provided us with a listing of all Belgian Limburg inhabitants that were included in their registry. It concerns 15 patients. No site was strikingly more prevalent. It is quite possible that part of these are also examined in Belgium and thus included in the LIKAR registry as well. For the future, the possibility will be examined to exchange records between both registries.

To estimate the influence of the number of cancers that are not histologically or cytologically confirmed, we have to fall back on the NCR publications. Following the 1995 report, this relates to 4,7% of all can-

cers (8). From the start of the LIKAR planning, we accepted that some cancers would be missed in the highly aged in which detailed exploration is considered irrelevant or even damaging. The exact number of these cancers cannot be estimated, but we realise our results may lose accuracy in the highest age-groups. Additionally samples of the lymph nodes or the bone marrow that are the basis for diagnosing cancers of the haematolymphopoetic system are partly examined by haematologists instead of pathologists. Our registry now misses such cancers. It is part of our planning to contact the haematologists concerned and to include their results in our databases the same way pathological test results are included now.

Conclusion

This report is the result of intensive collaboration between pathologists, clinicians, epidemiologists, informaticians and politicians around and within the LIKAR working party. It was worth the effort. For the first time, cancer incidence data that may claim any degree of completeness are available for part of the Belgian population.

As could be expected, these results are not perfect. Some possible errors partly relate to the simple fact of being the first report. Others were incalculated from the start. Partly they are intrinsically related to our design (tumours of the aged), partly they will be resolved in the future (tumours of the haematolymphopoetic system), partly they are due to a less than optimal privacy law (identification coding errors). We have reasons however, to believe that most important sources of possible error have been identified and accounted for. We invite anybody to comment on this report and to turn our attention to possible additional sources of bias.

In the mean time, the numbers and rates that are reported are the best estimate available of cancer incidence in Limburg. We intend to continuously improve their quality, to make them more precise and to analyse them as thoroughly as possible.

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Appendix

Definitions

Cancer: Are considered as cancer: the Morphology codes beginning with "M", and with the following figure greater than or equal to 80001 and smaller than or equal to 99999. The last figure is not "0".

Group of cance: all records related to the diagnosis and evolution of one and the same cancer. Primary cancers, metastases and cytology results belonging to the same group of cancer, get the same group number.

e.g.	data	topo-graphy	mor-phology	type	status	group of cancer	patient no
30/12/96	T-01000	173.9	M-80703	" "	"N"	1090	1202
15/04/96	T-08000	196.9	M-96633	" "	"N"	1091	1202
21/04/97	T-02010	173.4	M-80812	" "	"D"	1090	1202
03/01/97	T-01000	173.9	M-80812	" "	"D"	1090	1202
06/06/97	T-08220	196.0	M-80706	"M"	"N"	1090	1202
12/04/96	T-0Y800	196.9	M-96633	"C"	"N"	1091	1202

This results in 1 primary cancer (M-80703 squamous cell carcinoma) at site 173 (skin) and a second primary cancer (M-96663 Hodgkin's disease) at site 201 (hematolymphopoietic system).

Primary cancer: a record that is not classified as borderline, metastasis, basal cell carcinoma of the skin, carcinoma in situ of the cervix uteri, or duplicate test result. For each cancer group, only one primary cancer is possible.

Borderline malignancy: The Morphology codes M-..... ending in 1. If these codes occur in combination with the same Morphology code M-.... ending in 2 or 3 at the same anatomic site, they belong to one and the same group of cancer. Only unique registrations of /1 are excluded from the general registry report and registered separately.

Metastasis: If at different anatomic sites, the Morphology codes ending in 6 (metastasis) occur in combination with the same Morphology code ending in 2 or 3 they belong to one and the same group of cancer. The first record gets the status of new primary cancer, the other gets the

status "duplicate". Only unique registrations of /6 are excluded from the general registry report and separately registered as "metastasis" within the LIKAR database.

Duplicate: Records with the same morphology code and topography code or identified as duplicate by the appropriate algorithm.

Multiple cancer: more than one group of cancer is related to the same patient.