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Geographical differences in cancer incidence in the Belgian province of Limburg

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Abstract

Correctly addressing the questions of worried citizens with respect to possible clusters of cancer occurrence requires a risk communication strategy that is informed by a previously established analytical procedure. The aim of this study was to analyse cancer registration data in order to identify municipalities or clusters of municipalities with an increased incidence of one or more cancer types, adjusted for background characteristics at the same level. Ideally, the approach is proactive, straightforward, and easy for untrained citizens to follow and imprecision effects are taken into account. For all municipalities and most cancers, all relevant calculations were performed proactively and all methods and decision thresholds were defined beforehand. For each municipality, standardised incidence ratios (SIRs) were calculated and smoothed using a Poisson-gamma (PG) and a conditional autoregressive (CAR) model. Clusters were confirmed using the Spatial scan statistic of Kulldorff. Identified clusters were tested for possible confounders using all information that was available for each municipality. The Limburg Cancer Registry, serving the population of the Belgian province of Limburg ($n=781\ 759$) was used. We identified a possible cluster of increased prostate cancer incidence (smoothed SIRs around 1.2) and a cluster of increased bladder cancer incidence in males that included seven municipalities with CAR-smoothed SIRs between 1.5 and 2.1. SIRs followed a more or less circular decrease around the centre that was situated in Alken and Hasselt, the provincial capital. Bladder cancer incidence was positively related to an index of socio-economic status (SES) per municipality. No relationship was found with the other indexes that were available. 82% of all bladder cancers were transitional cell carcinomas (TCC). A repeated analysis based on TCCs only resulted in similar results with CAR-smoothed relative risks that tended to be even higher in the cluster zone. A pre-emptive analysis of possible cancer incidence clustering on the municipality level proved to be feasible. A cluster of increased incidence of bladder cancer was identified.

Keywords: Cancer incidence; Geographical differences; Spatial analysis; Bladder cancer

1. Introduction

At regular intervals, both researchers and authorities have to deal with alarmed citizens or health care workers who detect an abnormally high frequency of cancer cases in their region. Alleviating concern tends to be challenging as the required information is not always available. Risk communication may then become difficult. Many times the whole process ends in confusion, with citizens increasingly distrusting a government that was not able to remove or adequately address their worries.

Experience of an increased cancer occurrence can relate to regions of different sizes. The smallest size for which cancer incidences can be calculated by the Limburg Cancer Registry (LIKAR) is the postal number,

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which covers a municipality (sometimes two or three postal numbers relate to one municipality).

In an attempt to provide as much information as possible to both the population and the authorities, we tried to develop and apply a protocol for proactive scrutiny of our data to detect municipalities or groups of municipalities with elevated rates of one or more cancer types. We wanted our protocol to be straightforward and easy for untrained citizens to follow. Imprecision effects should be taken into account. Possible clusters should be adjusted for all background characteristics available at the level of the municipality. In case a real increase should be identified, epidemiological research relating this increase to possible causes was considered to be a subsequent and separate step with a different approach and outside the expertise or the primary responsibilities of the cancer registry.

When dealing with the issue, we had to cope with a number of technical problems [1], such as the following:

(i) The necessary data with respect to disease incidence may be missing or unreliable.
(ii) *Post-hoc* data collection or decisions about the procedures led by a prior suspicion of an increased disease incidence hamper the application of most statistical methods.
(iii) Comparisons between regional groups are subject to ecological fallacy unless both the rate of disease in people that are not exposed to the aetisetiological agent is the same in all populations and the effect of exposure is the same in all populations.
(iv) In relatively small regions or for regions with relatively low numbers of diseases, disease incidence rates tend to differ largely due to random error and may have misleadingly high or low values.

In this paper, we describe the procedures that were developed to deal with these problems and the results of our first analyses.

2. Patients and methods

2.1. Data collection

Data were collected in the framework of the Limburg Cancer Registry [2,3] and include 9989 histologically- or cytologically-confirmed primary cancers that were observed among male and female inhabitants ($n = 781\,759$) of the Belgian province of Limburg within the period of 1996–1998. For each of the 44 municipalities in Limburg (population averaging 18 085 and ranging between 4311 and 67 647 with one outlier Herstappe, having 86 inhabitants), the number of cases of a specific type of cancer was recorded.

2.1.1. The Limburg Cancer Registry

A detailed description of the procedures and results of the Limburg Cancer Registry (LIKAR) has been published before in Refs. [2,3]. 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. Data are provided by all pathological laboratories located in the province and all pathological departments outside the province examines samples from Limburg inhabitants on a fairly regular basis. An unique encrypted code guarantees that all data of the same patient are recognised as such by the registry while it is impossible to identify this individual without consulting the practitioner or the laboratory that provided the data.

All cancers are classified according to the International Classification of Diagnosis Oncology's-2 (ICDO-2) classification. 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). Basal cell carcinomas of the skin and carcinomas *in situ* of the cervix uteri were excluded from this analysis.

For this analysis, histologically- or cytologically-confirmed cases only were included. The likelihood of false-positive diagnoses is therefore expected to be extremely low. Impossible combinations of data are searched for using automated test procedures including the International Agency for Research on Cancer (IARC) check software: 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). Double recording of the same cancer is avoided as all entries are tested with a set of algorithms that were especially developed for this purpose.

2.2. Analysis

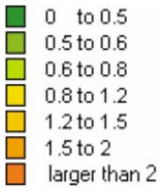
When comparing cancer levels between two areas, or when investigating the pattern of cancer over time for the same area, it is important to adjust for differences in the age and sex structure of those populations. In this study, this was accomplished by sex-stratified age-standardisation. The standardised incidence ratio (SIR) for a certain region was obtained from the ratio of the observed and expected number of cases in that region. We used the indirect method for standardisation. That is, the expected value was calculated by applying the general age-specific reference rates of Limburg to each

municipality. Confidence intervals (CIs) for the SIRs were calculated after log transformation [4].

2.2.1. Cartographic display

A map of a particular disease is a geographical representation of the occurrence of that disease in a well-defined geographical area. It provides instant visual information on the variation of that disease. However, naive use of mapping of health indicators can be misleading. When plotting the maps, the choices of shadings, the scaling of the mapped index quantity, the number of risk classes and their delimitation have to be determined with care. They depend on the range of variation, the precision of the estimates and the need for comparability over multiple maps. Categorisation in classes can be data-dependent, where the proportion of areas in a certain colour is predetermined and expressed in terms of quantiles or fixed percentiles. A data-independent shading system might be more useful for identification of excesses or deficits. However, when the variation is limited, the method can yield oligo-chromic maps.

For all maps of the SIRs we used a bi-chromatic range from red to green. The range was based on a uniform log-scale division similar to the suggestion of Knorr-Held and Raser [5] and subdivided in seven categories with a flexion zone in yellow centered around the median. The cut-offs used are detailed in the legend:



2.2.2. Smoothing methods

As noted earlier, the (observed) raw SIR for region i estimates the true relative risk for that region with standard error equal to $s_i = \sqrt{O_i/E_i}$. Therefore, the SIRs for small areas or sparsely populated regions will have a high sampling variability. When the SIRs are mapped, areas with small populations will often appear to display spuriously elevated risks due to the high variability. These areas are hence attracting the attention of the public simply due to Poisson error. To overcome this problem, Bayesian smoothing methods have been developed in disease mapping.

The Bayesian approach consists of considering, in addition to the observed events in each area, prior information on the variability of mortality rates in the overall map. Each area will receive an estimate of the relative risk that is a compromise between these two types of information (the prior information and the observed data). The Bayesian estimates are close to the standardised rates when based upon a large number of events. However, with fewer events, prior information on the overall map will dominate, thereby shrinking standardised rates towards the overall mean rate. Fluctuations in the estimated relative risks are thus reduced and a smoothed map, which has a better epidemiological interpretation, is obtained. Another advantage of Bayesian methods over the conventional Poisson approach is that the latter does not account for any spatial pattern in disease, i.e. the tendency for geographically close areas to have similar disease rates. Bayesian approaches with prior information on the rates allowing for local geographical dependence are then pertinent. With this prior information, a Bayesian estimate of the rate in an area is shrunk towards a local mean, according to the rates in the neighbouring areas.

2.2.3. Short summary of Bayesian inference for relative risks

Bayesian inference about the unknown relative risks $r = (r_1, ..., r_n)$ is based on the marginal posterior distribution (the product of the likelihood function of the relative risks for the data and a prior distribution of r). In other words, the extra-Poisson variation is incorporated by assuming that the true relative risks follow an *a priori* common statistical distribution on positive values. Several candidate distributions exist, such as the lognormal, Weibull, Gamma, etc.

A convenient choice for the prior distribution of the relative risk is the conjugate with the Poisson likelihood. When the posterior is in the same family as the prior distribution, this prior is called a conjugate prior. The conjugate with the Poisson likelihood is a gamma distribution with parameters α and β. The so-called hyperparameters α and β are unknown. These parameters can be estimated from the data (empirical Bayes approach). Although this method yields acceptable point estimates of the rates, it underestimates their uncertainty. Another method is to express our ignorance or prior knowledge about α and β by assigning them a prior distribution (full Bayesian approach). The latter approach has several computational advantages and leads to estimates that have the best robustness properties in the class of all priors having the same mean and variance. Yet, it is not necessarily a realistic choice. A major drawback with gamma priors lies in the fact that the method does not take into account the geographical location of the region. They do not allow for spatial dependence. Prior knowledge may indicate that geographically close areas tend to have similar relative risks. When using Bayesian methods, it is possible to account for the spatial pattern in disease by using prior information on the rates allowing for local geographical dependence. Besag and colleagues [6] consider a random effects Poisson model allowing for overdispersion and spatial correlation, using a (generalisation of the) conditional autoregressive (CAR) prior.

Their conditional autoregressive prior for r_i is given by: $r_i|r_j \sim N(m_i, v_i)$ where

$$m_i = \frac{1}{n_i}\sum_{j\in\delta_i} r_j$$

δ_i = set of adjacent areas
n_i = number of neighbours

$$v_i = \frac{v^*}{n_i}$$

with v^* the conditional variance of spatial effects. Therefore, r_i is smoothed towards the local average risk in a set of neighbouring areas, with variance inversely proportional to the number of neighbours.

This model can be relatively easily implemented using WINBUGS and has proven effective.

For all cancer groups that were studied, smooth disease maps have been constructed with both a Gamma and a CAR prior. In this report, results are presented only for the most frequent cancers. Clusters were confirmed using the spatial scan statistic of Kulldorff [7].

2.2.4. Spatial scan statistic of Kulldorff

The spatial scan statistic of Kulldorff [7] is a cluster detection test. It locates specific clusters and tests their significance. The statistic is defined by imposing a circular window on the map. The base of the window is in turn centered around each of several possible centroids positioned throughout the study region. For each centroid, the radius of the window varies continuously in size from zero to some upper limit. The window is then moved in space so that it visits every possible location. In this way, the circular window is flexible both in location and size. In total, the method creates a large number of distinct geographical circles, with different sets of neighbouring census areas within them, and each being a possible candidate for a cluster. The scan statistic provides a measure of how unlikely it would be to encounter the observed excess of cases in a larger comparison region. For each window, the number of disease cases inside and outside the window are noted, together with the expected number of cases reflecting the population at risk and relevant covariates. On the basis of these numbers, the likelihood is calculated for each window. The window with the maximum likelihood, and with more than its expected number of cases, is denoted the most likely cluster. If the window size is allowed to expand until it covers most of the geographical region, the likelihood no longer reflects a cluster of increased disease risk inside the window, but rather a decreased risk outside. For this reason, it is recommended (Kulldorff and colleagues, 1998) that the geographical size of the window is limited to half the expected number of cases.

The advantage of the test is that it examines a large range of zone sizes and accounts for the multiple testing inherent in such a procedure. A limitation of the method relates to the use of circular regions, which tends to emphasise compact clusters, and the method has low power against other alternatives such as long and narrow clusters along a river, or against an alternative with a large number of very small clusters at very different locations [8].

2.2.5. Additional analyses

In case of detection of a cluster of increased cancer incidence, the influence of a standard number of basic characteristics on the incidence is tested by simple linear regression analysis. The dependent variable is the standardised incidence rate per municipality for the identified cancer group. The independent variable is each of the basic characteristics respectively. Basic characteristics are the municipality index of socio-economic status (SES), the index of urbanisation, and the percentage of migrants with a southern European, eastern European or Islamic (Turkey and North African countries) nationality. These indexes were provided by the Institute of Social and Economical Geography of the Catholic University of Leuven (Prof. Vanhecke). They are based on data collected in 1991–1999. Additional co-variables can be added according to the specific cancer group under study. If one of these characteristics proved significantly related to the cancer incidence, the full Bayesian approach was repeated using the relevant characteristic as a co-variable in the analysis.

2.3. Procedural and publication policy

Before the start of the analysis, it was decided that crude ratios of cancers per municipality would not be published because of the inherent sensitivity to confounding by age and sex. Age-standardised and sex-stratified SIRs are published. However, SIR differences between municipalities are in itself not considered to be sufficient for the identification of a possible cluster of increased incidence. Poisson-gamma smoothed relative risks and the related displays are available to show possible large scale spatial trends. A cluster of increased incidence is accepted to be identified if CAR smoothed relative risks are found to be larger than 1.5. In cases of a CAR smoothed relative risk of 1.2 or more, a cluster of increased incidence is suspected.

If a cluster is identified or suspected, the spatial scan statistic is used for confirmation. Next, the relationship between basic characteristics per municipality and the incidence rate is examined as described before. If this relationship is found significant, an adjusted Bayesian procedure is performed. The decision to publish the identification of a disease cluster is eventually based on

this analysis. Clusters that are formally accepted are reported to the population by a carefully prepared press release. Intermediary health care professionals (local general practitioners (GPs), consultants of the relevant disciplines, healthcare-related authorities of different levels) are informed in detail the days before the press release in order to avoid them being confronted with questions without a proper briefing. A telephone number, manned by the provincial health inspector, is made available for people requesting additional information.

3. Results

3.1. Patients and data

During the years 1996–1998, 9989 primary cancers were diagnosed and histologically- or cytologically-proven in the inhabitants of the Belgian province of Limburg. 8936 were invasive, 1053 non-invasive tumours. This relates to a crude invasive cancer incidence rate of 440/100 000 person-years for males and 322/100 000 for females. The corresponding standardised rates are 446 and 284 for the European and 303 and 204 for the World standard population.

3.2. Spatial analysis

In this section, disease mapping is used as a way of presenting our results and demonstrating the geographical variation of cancer risk in the province.

Fig. 1 shows the crude and Poisson-Gamma and CAR smoothed SIRs of invasive cancer in males and females. All three arrays of SIRs are compatible with an absence of significant differences in cancer incidence between the municipalities. In separate cancer sites, major differences between municipalities are found in age-SIRs. In most cases, they disappear after Bayesian smoothing. Figs. 2–4 illustrate this with the results for colorectal cancer in both males and females, lung cancer in males and breast cancer in females.

Fig. 5 shows the same three types of SIRs for prostate cancer ($n = 1452$). The Poisson gamma model suggests a gradient with a lower incidence in the east of the province, increasing towards the west. Three non-adjacent municipalities were identified with CAR-smoothed relative risk estimates of 1.2 and 1.3. The presence of a significant cluster was also confirmed by the spatial scan statistic ($P = 0.001$).

Fig. 6 shows the results for bladder cancer among males ($n = 290$) and females ($n = 63$). In males, a clear geographical cluster of municipalities with an increased incidence was identified. Within this cluster, CAR-smoothed SIRs were above 1.5 in all municipalities and reached 2.01 in Alken, the municipality with the highest incidence. In addition, the spatial scan statistic showed a highly significant cluster ($P = 0.0001$). In females, similar or higher age-standardised SIRs were found in the same municipalities. However, these disappeared after smoothing.

The corresponding estimates, together with their CIs can be found in Table 1.

3.3. Detailed analysis of the bladder cancer cluster

We related the SIRs of male bladder cancer of each municipality to an index of the degree of urbanisation (seven ordered categories) by linear regression and found no relationship.

However, incidence rates were significantly related to a municipality-specific index of SES. A higher SIR of bladder cancer was found in municipalities with a higher SES score (the slope of the linear regression line was estimated as 6.7; 95% CI = 0.8–12.6). This index explained 11% of the variance of the incidence rates. There was no relationship between bladder cancer incidence and the per municipality proportion of migrants from the south of Europe, some Islamic states (Turkey and North African countries) and the Eastern European states.

The proportion of 'ever' versus 'never' smokers was available for random samples of the population of two cluster municipalities and seven other municipalities. The odds ratio of ever versus never smokers in the cluster municipalities versus the remaining municipalities was 1.48 (95% CI = 0.90–2.44). Using a simple linear regression analysis, there was no relationship between the proportion of ever-smokers in these municipalities and the standardised bladder cancer rate.

82% of all bladder cancers were transitional cell carcinomas (TCC). We therefore repeated the analysis in males for TCC only. The results were basically similar, with the CAR-smoothed relative risks tending to be higher in the cluster zone (e.g. 2.34 in Alken). There were now five municipalities with a smoothed relative risk above 2.0 and five additional municipalities with a smoothed relative risks above 1.5. The TCC cluster identified using the spatial scan statistic was larger than the bladder cancer clusters, but included all municipalities of the initial cluster. Adjusting for the index of SES while smoothing did not change the picture (e.g. CAR-smoothed RR for Alken = 2.25).

4. Discussion

This report shows a way of dealing with the recurrent cluster alarms in a population. Data are proactively collected and analysed and can be trusted by all parties involved. There is no *post-hoc* bias. Spurious and misleading results are prevented by Bayesian smoothing, while robust effects are identified. This method also

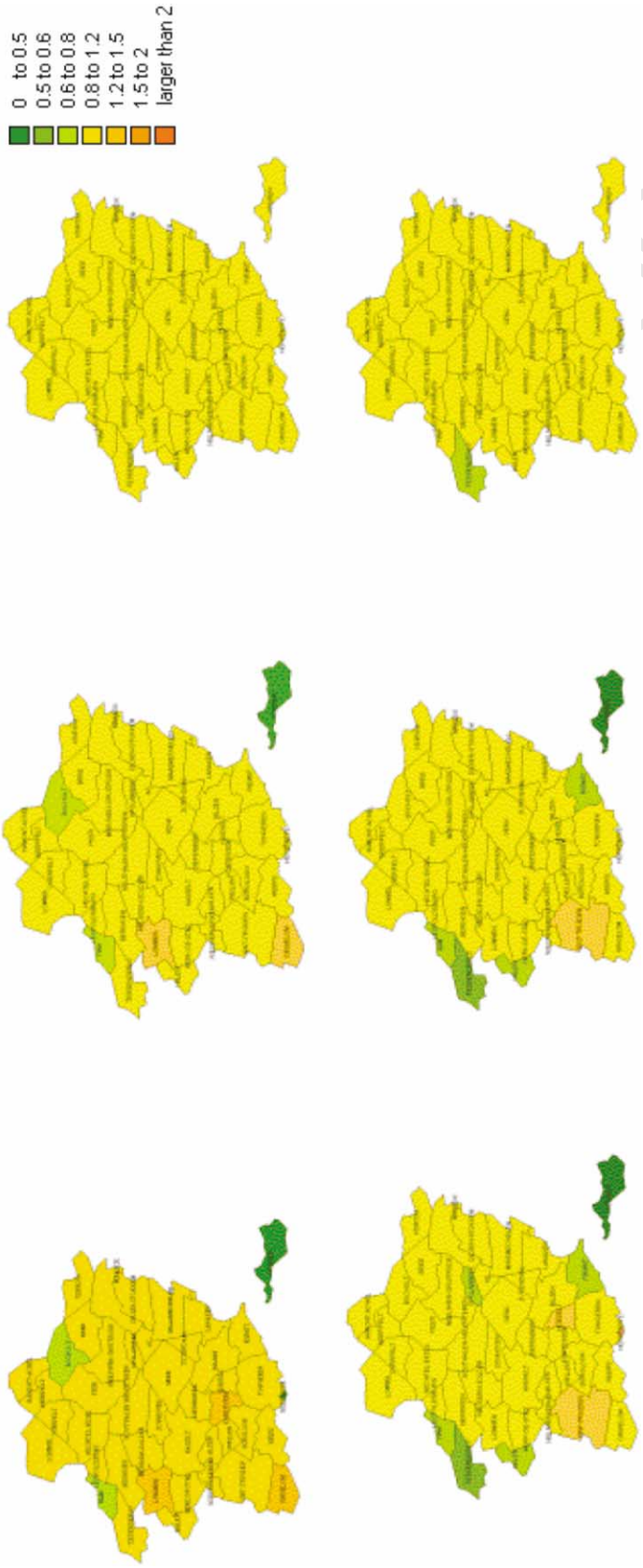


Fig. 1. Crude, PG and CAR smoothed SIRs of invasive cancer for males (top row) and females (bottom row).

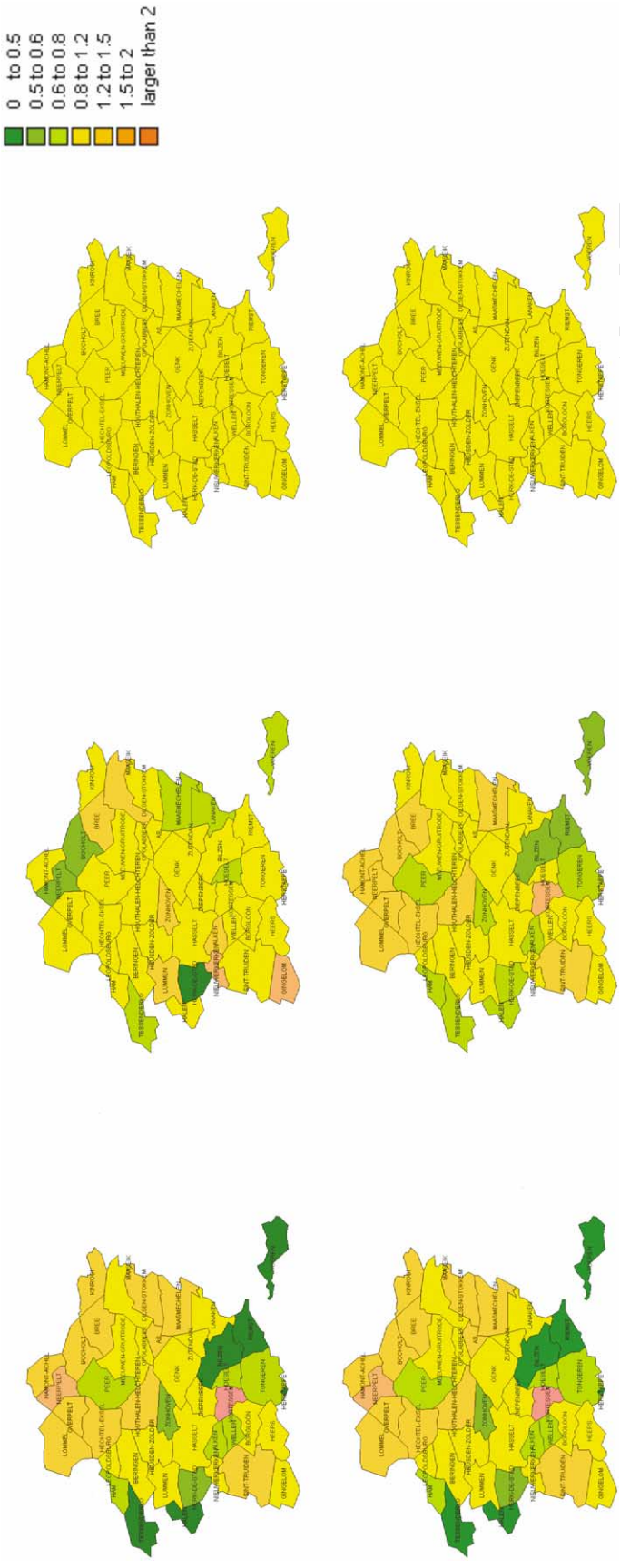


Fig. 2. Crude, PG and CAR smoothed SIRs of colorectal cancer for males (top row) and females (bottom row).

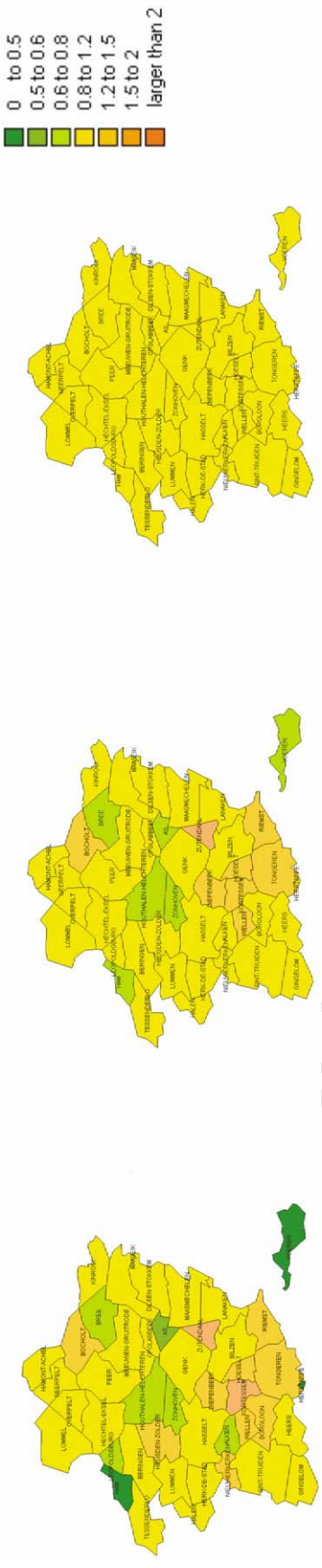


Fig. 3. Crude, PG and CAR smoothed SIRs of lung cancer for males.

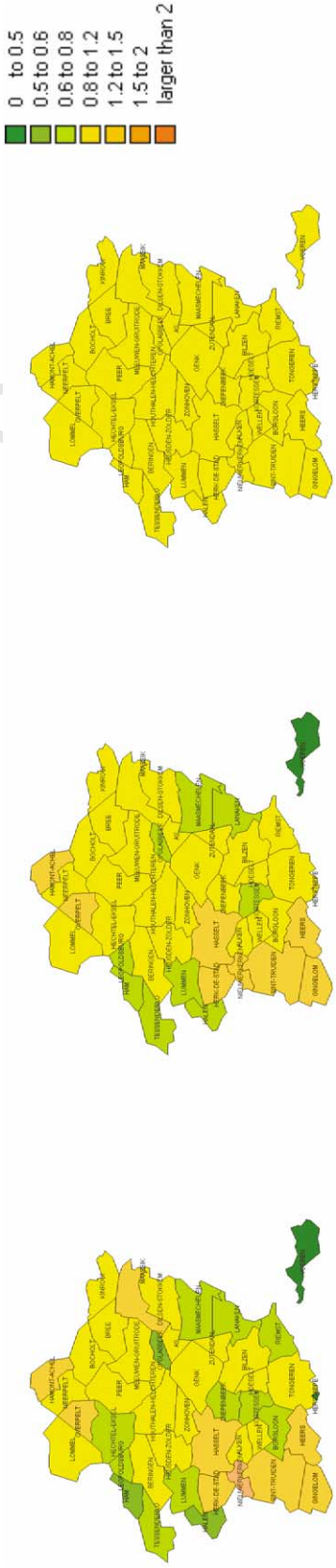


Fig. 4. Crude, PG and CAR smoothed SIRs of breast cancer for females.

Fig. 5. Crude, PG and CAR smoothed SIRs of prostate cancer.

deals with the multiple testing problem. Additional analyses, e.g. for subtypes of cancers are easily performed using exactly the same procedure that has been developed for the main analysis, on condition that the subgroup data are available. If real clusters are detected, an initial epidemiological screening is possible, including the use of municipality-related information. This information can be used either as a co-variable when modelling or as a possible explanation when comparing cluster municipalities with the remaining municipalities of the region. The workload related to the analysis is acceptable if the regional cancer registry has the basic data available. In principle, providing this type of standard analysis is within the possibilities of most cancer registries in the industrialised world.

In principle, a proactive analysis followed by the publication of the results may just as well suggest disease clusters while there was no suggestion before the analysis. This may raise public concerns instead of alleviating them. However, it was our expectation (and our hope) that the implicit message of openness and honesty would also be heard. We expected that this procedure could prevent a lot of questions, concerns and mistrust within the population. The results of this study and the reactions to the press release informing the population about the bladder cancer cluster and the absence of additional clusters supported this view. Radio, TV and newspapers covered the topic, but did so with all the nuances we wanted them to present. The number of questions during subsequent days was low and could easily be addressed. Contrary to previous occasions in this country, there were no signs of mistrust towards the authorities or researchers.

The results of this study essentially do not indicate any presence of geographical differences between the occurrence of cancers in municipalities of the Belgian province of Limburg. As usual in this kind of study, major differences are found in age-standardised incidence rates per municipality. However, they tend to disappear after Bayesian smoothing. There were only two exceptions that deserve a closer look.

Posterior means of the SIR of prostate cancer were increased in three municipalities after full Bayesian smoothing. However, the smoothed relative risks were only 1.2 or 1.3. Additionally, the three municipalities do not really cluster geographically. Finally, we suspect that prostate cancer incidence rates are largely influenced by the prostate specific antigen (PSA) screening policy of the local physicians in patients without symptoms. For all these reasons, no additional analyses are reported with respect to prostate cancer.

Bladder cancer incidence shows a quite different pattern. In males, a clear geographical cluster of municipalities with an increased incidence was identified. Fully Bayesian smoothed SIRs reached 2.01 in Alken, the municipality with the highest incidence, and were above

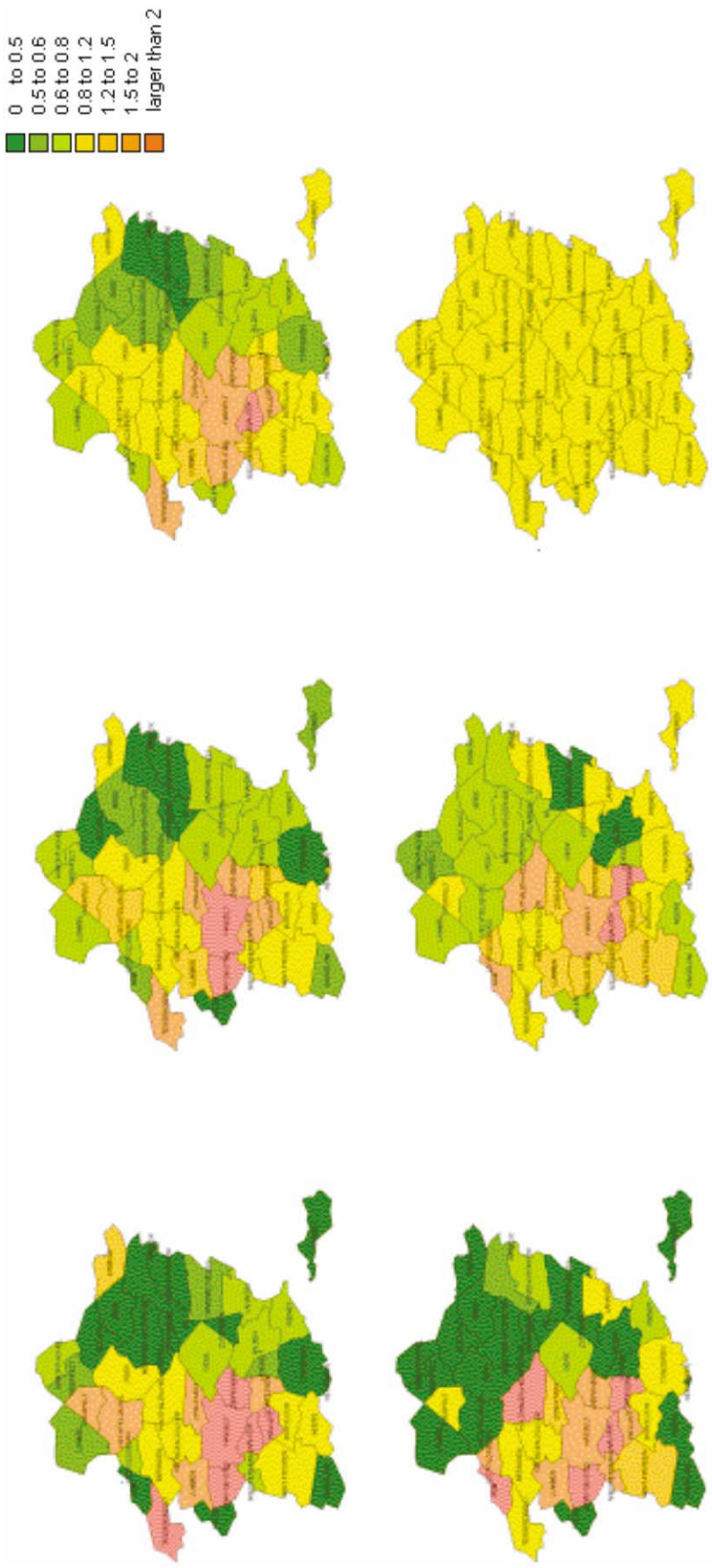


Fig. 6. Crude, PG and CAR smoothed SIRs of bladder bancer in males (top row) and females (bottom row), respectively.

Table 1
Crude, PG and CAR smoothed SIRs for each community

Community	All cancer males	All cancer females	Prostate cancer	Bladder cancer males	Bladder cancer females	Colorectal cancer males	Colorectal cancer females	Lung cancer males	Lung cancer females
Alken	1.1 (0.86, 1.4)	0.93 (0.70, 1.2)	1.1 (0.72, 1.7)	2.6 (1.4, 4.8)	3.6 (1.2, 11.0)	1.4 (0.78, 2.8)	0.66 (0.28, 1.6)	0.71 (0.37, 1.4)	0.88 (0.52, 1.5)
	1.1 (0.85, 1.3)	0.94 (0.70, 1.2)	1.1 (0.71, 1.5)	2.0 (1.0, 3.3)	2.0 (0.56, 4.5)	1.3 (0.72, 1.9)	0.80 (0.37, 1.4)	0.81 (0.44, 1.3)	0.91 (0.55, 1.3)
	1.1 (0.96, 1.2)	1.03 (0.88, 1.2)	1.1 (0.87, 1.4)	2.0 (1.1, 3.3)	1.2 (0.77, 2.7)	1.0 (0.91, 1.2)	0.99 (0.79, 1.2)	1.0 (0.93, 1.1)	1.1 (0.86, 1.3)
As	0.82 (0.59, 1.1)	0.90 (0.62, 1.3)	0.93 (0.52, 1.7)			0.93 (0.39, 2.2)	1.3 (0.58, 2.9)	0.50 (0.19, 1.3)	0.87 (0.45, 1.7)
	0.84 (0.61, 1.1)	0.91 (0.64, 1.2)	0.96 (0.56, 1.5)	0.47 (0.05, 1.3)	0.77 (0.03, 2.3)	0.97 (0.45, 1.7)	1.2 (0.55, 2.0)	0.72 (0.33, 1.2)	0.91 (0.49, 1.4)
	0.94 (0.83, 1.1)	0.96 (0.82, 1.1)	0.93 (0.73, 1.2)	0.49 (0.20, 0.94)	0.93 (0.35, 1.3)	0.99 (0.84, 1.1)	1.0 (0.86, 1.3)	1.0 (0.91, 1.1)	0.94 (0.75, 1.1)
Beringen	1.2 (1.0, 1.3)	1.1 (0.98, 1.3)	1.3 (1.1, 1.7)	1.11 (0.67, 1.8)	1.1 (0.34, 3.3)	1.2 (0.88, 1.7)	0.98 (0.66, 1.5)	0.86 (0.63, 1.2)	1.1 (0.86, 1.4)
	1.1 (1.0, 1.3)	1.1 (0.98, 1.3)	1.3 (1.1, 1.6)	1.09 (0.64, 1.7)	1.0 (0.32, 2.2)	1.2 (0.86, 1.6)	0.98 (0.66, 1.4)	0.88 (0.64, 1.2)	1.1 (0.85, 1.4)
	1.1 (0.96, 1.2)	1.0 (0.90, 1.1)	1.2 (1.0, 1.4)	1.09 (0.68, 1.6)	1.0 (0.69, 1.5)	1.0 (0.91, 1.2)	0.98 (0.80, 1.1)	0.98 (0.87, 1.1)	0.97 (0.82, 1.1)
Bilzen	0.96 (0.83, 1.1)	0.86 (0.72, 1.0)	0.84 (0.63, 1.1)	0.66 (0.32, 1.4)		0.85 (0.55, 1.3)	0.47 (0.26, 0.88)	0.81 (0.56, 1.2)	0.88 (0.64, 1.2)
	0.96 (0.83, 1.1)	0.86 (0.72, 1.0)	0.86 (0.64, 1.1)	0.72 (0.32, 1.3)	0.41 (0.01, 1.3)	0.88 (0.56, 1.2)	0.57 (0.31, 0.90)	0.84 (0.58, 1.1)	0.89 (0.65, 1.2)
	0.96 (0.87, 1.0)	0.90 (0.79, 1.0)	0.87 (0.71, 1.0)	0.72 (0.40, 1.1)	0.95 (0.46, 1.3)	0.98 (0.81, 1.1)	0.93 (0.66, 1.1)	1.0 (0.93, 1.1)	0.83 (0.75, 1.1)
Bocholt	0.76 (0.59, 0.99)	0.85 (0.63, 1.1)	0.78 (0.48, 1.3)	0.25 (0.03, 1.7)		0.32 (0.10, 1.0)	1.3 (0.72, 2.5)	1.3 (0.82, 2.1)	0.85 (0.50, 1.4)
	0.79 (0.61, 0.99)	0.86 (0.64, 1.1)	0.84 (0.53, 1.2)	0.50 (0.03, 2.0)	0.55 (0.22, 1.0)	0.55 (0.22, 1.0)	1.2 (0.67, 1.9)	1.2 (0.79, 1.8)	0.88 (0.54, 1.3)
	0.89 (0.78, 1.0)	0.95 (0.80, 1.1)	0.88 (0.68, 1.1)	0.57 (0.25, 1.0)	0.57 (0.26, 1.3)	0.98 (0.79, 1.1)	1.1 (0.92, 1.4)	0.99 (0.89, 1.1)	1.0 (0.83, 1.2)
Borgloon	0.85 (0.67, 1.1)	0.82 (0.62, 1.1)	0.76 (0.48, 1.2)	0.90 (0.34, 2.4)	0.97 (0.14, 6.9)	0.81 (0.40, 1.60)	0.95 (0.49, 1.8)	1.2 (0.78, 2.0)	0.75 (0.43, 1.3)
	0.87 (0.68, 1.1)	0.84 (0.63, 1.1)	0.82 (0.52, 1.2)	0.93 (0.35, 1.8)	1.0 (0.16, 2.6)	0.88 (0.46, 1.4)	0.97 (0.53, 1.5)	1.2 (0.75, 1.7)	0.81 (0.48, 1.2)
	1.0 (0.87, 1.1)	0.97 (0.82, 1.1)	0.98 (0.77, 1.2)	1.0 (0.49, 1.8)	1.1 (0.71, 1.8)	1.0 (0.89, 1.2)	0.99 (0.79, 1.2)	1.0 (0.94, 1.2)	1.0 (0.81, 1.2)
Bree	0.81 (0.64, 1.0)	0.91 (0.71, 1.2)	0.67 (0.42, 1.1)	0.37 (0.09, 1.5)		1.4 (0.88, 2.3)	1.4 (0.80, 2.3)	0.62 (0.35, 1.1)	1.2 (0.80, 1.8)
	0.82 (0.65, 1.0)	0.92 (0.71, 1.2)	0.74 (0.47, 1.1)	0.55 (0.15, 1.2)	0.60 (0.03, 1.8)	1.3 (0.81, 1.9)	1.3 (0.75, 1.9)	0.72 (0.42, 1.1)	1.1 (0.78, 1.6)
	0.91 (0.79, 1.0)	0.94 (0.79, 1.1)	0.87 (0.66, 1.1)	0.52 (0.21, 0.99)	0.91 (0.24, 1.3)	1.0 (0.89, 1.2)	1.1 (0.91, 1.4)	0.99 (0.87, 1.1)	1.0 (0.84, 1.3)
Diepenbeek	1.2 (0.95, 1.4)	0.91 (0.72, 1.2)	1.1 (0.73, 1.5)	2.2 (1.3, 3.9)	1.7 (0.42, 6.8)	1.1 (0.62, 1.8)	0.86 (0.45, 1.7)	1.3 (0.84, 1.9)	0.77 (0.49, 1.2)
	1.1 (0.94, 1.3)	0.91 (0.72, 1.1)	1.1 (0.74, 14)	1.9 (1.0, 2.9)	1.3 (0.32, 3.1)	1.1 (0.62, 1.6)	0.91 (0.49, 1.5)	1.2 (0.81, 1.7)	0.81 (0.53, 1.2)
	1.0 (0.93, 1.2)	0.96 (0.82, 1.1)	0.98 (0.79, 1.2)	1.6 (0.92, 2.7)	1.0 (0.70, 1.6)	1.0 (0.87, 1.1)	0.97 (0.75, 1.1)	1.0 (0.93, 1.1)	0.95 (0.75, 1.1)
Dilsen-Stokkem	1.0 (0.85, 1.2)	1.2 (0.94, 1.4)	1.1 (0.78, 1.5)	0.32 (0.08, 1.3)	0.75 (0.11, 5.4)	1.1 (0.64, 1.8)	1.3 (0.76, 2.1)	1.1 (0.77, 1.7)	1.0 (0.71, 1.5)
	1.0 (0.84, 1.2)	1.1 (0.92, 1.4)	1.1 (0.78, 1.4)	0.48 (0.13, 1.0)	0.91 (0.15, 2.3)	1.0 (0.64, 1.6)	1.2 (0.73, 1.8)	1.1 (0.75, 1.6)	1.0 (0.71, 1.4)
	0.98 (0.86, 1.1)	1.1 (0.90, 1.2)	0.99 (0.78, 1.3)	0.44 (0.16, 0.86)	0.93 (0.33, 1.3)	0.99 (0.84, 1.1)	1.0 (0.87, 1.4)	1.0 (0.91, 1.10)	0.97 (0.77, 1.2)
Genk	0.99 (0.89, 1.1)	0.94 (0.83, 1.1)	0.85 (0.69, 1.0)	0.69 (0.42, 1.2)	0.62 (0.20, 1.9)	1.0 (0.78, 1.4)	1.0 (0.78, 1.4)	0.90 (0.70, 1.1)	0.84 (0.67, 1.1)
	0.99 (0.89, 1.1)	0.94 (0.83, 1.1)	0.85 (0.70, 1.0)	0.72 (0.42, 1.1)	0.72 (0.22, 1.5)	1.0 (0.77, 1.3)	1.0 (0.77, 1.3)	0.91 (0.71, 1.1)	0.85 (0.67, 1.0)
	0.99 (0.91, 1.1)	0.95 (0.86, 1.0)	0.91 (0.77, 1.0)	0.76 (0.49, 1.1)	0.96 (0.57, 1.3)	1.0 (0.89, 1.1)	1.0 (0.89, 1.1)	1.0 (0.92, 1.1)	0.93 (0.78, 1.1)
Gingelom	1.4 (1.1, 1.7)	1.2 (0.89, 1.5)	1.5 (1.0, 2.2)	0.29 (0.04, 2.1)		2.4 (1.5, 3.7)	0.82 (0.37, 1.8)	0.98 (0.54, 1.8)	1.4 (0.87, 2.2)
	1.3 (1.1, 1.6)	1.2 (0.87, 1.5)	1.4 (0.95, 1.9)	0.56 (0.12, 1.3)	0.68 (0.04, 2.1)	1.9 (1.2, 2.8)	0.89 (0.44, 1.5)	1.0 (0.57, 1.5)	1.3 (0.81, 1.8)
	1.2 (1.0, 1.4)	1.1 (0.91, 1.4)	1.2 (0.92, 1.4)	0.66 (0.20, 1.4)	1.0 (0.44, 1.5)	1.1 (0.92, 1.7)	0.99 (0.73, 1.3)	1.0 (0.92, 1.2)	12 (0.91, 1.6)
Halen	0.92 (0.71, 1.2)	0.68 (0.48, 0.96)	1.2 (0.76, 1.8)			0.83 (0.40, 1.7)	0.40 (0.13, 1.3)	0.82 (0.44, 1.5)	0.59 (0.30, 1.2)
	0.93 (0.71, 1.2)	0.72 (0.51, 0.96)	1.1 (0.76, 1.6)	0.36 (0.04, 0.97)	0.66 (0.02, 2.1)	0.91 (0.46, 1.5)	0.63 (0.26, 1.2)	0.88 (0.51, 1.4)	0.71 (0.37, 1.1)
	1.0 (0.86, 1.2)	0.86 (0.67, 1.1)	1.2 (0.88, 1.6)	1.0 (0.20, 1.43)	1.0 (0.48, 1.7)	1.0 (0.81, 1.2)	0.93 (0.58, 1.1)	1.0 (0.88, 1.1)	0.94 (0.65, 1.2)
Ham	0.73 (0.55, 0.97)	0.68 (0.48, 0.98)	1.1. (0.74, 1.7)	0.27 (0.04, 1.91)	2.8 (0.69, 11.0)	0.96 (0.48, 1.9)	0.62 (0.23, 1.7)	0.41 (0.17, 0.98)	0.50 (0.24, 1.1)
	0.76 (0.58, 0.98)	0.72 (0.51, 0.98)	1.1 (0.73, 1.6)	0.54 (0.10, 1.28)	1.6 (0.40, 4.0)	0.99 (0.51, 1.6)	0.78 (0.33, 1.4)	0.61 (0.30, 1.0)	0.64 (0.33, 1.1)
	0.91 (0.76, 1.0)	0.82 (0.65, 0.99)	1.1 (0.85, 1.4)	0.76 (0.28, 1.49)	1.1 (0.69, 2.2)	1.0 (0.84, 1.2)	0.95 (0.65, 1.1)	0.97 (0.81, 1.1)	0.84 (0.58, 1.1)
Hamont-Achel	0.87 (0.70, 1.1)	1.1 (0.85, 1.4)	0.72 (0.47, 1.1)	0.69 (0.26, 1.84)		1.1 (0.64, 1.8)	1.4 (0.83, 2.4)	0.84 (0.51, 1.4)	1.4 (0.94, 2.0)
	0.87 (0.71, 1.1)	1.1 (0.84, 1.3)	0.77 (0.51, 1.1)	0.78 (0.28, 1.52)	0.59 (0.03, 1.9)	1.1 (0.64, 1.6)	1.3 (0.76, 2.0)	0.88 (0.55, 1.3)	1.3 (0.89, 1.8)
	0.88 (0.75, 1.0)	1.0 (0.85, 1.2)	0.82 (0.60, 1.1)	0.67 (0.26, 1.32)	0.90 (0.18, 1.3)	0.99 (0.80, 1.1)	1.1 (0.91, 1.6)	0.98 (0.84, 1.1)	1.1 (0.90, 1.5)
Hasselt	1.2 (1.09, 1.3)	1.2 (1.1, 1.3)	1.1 (0.96, 1.3)	2.1 (1.7, 2.75)	1.8 (1.8, 3.2)	1.1 (0.83, 1.4)	1.1 (0.86, 1.4)	1.1 (0.85, 1.3)	1.3 (1.1, 1.6)
	1.2 (1.08, 1.3)	1.2 (1.1, 1.3)	1.1 (0.95, 1.3)	2.0 (1.6, 2.59)	1.6 (0.89, 2.6)	1.1 (0.82, 1.3)	1.1 (0.85, 1.3)	1.1 (0.85, 1.3)	1.3 (1.1, 1.5)
	1.1 (1.04, 1.2)	1.1 (1.0, 1.2)	1.1 (0.96, 1.3)	1.9 (1.4, 2.57)	1.1 (0.78, 1.9)	1.0 (0.92, 1.1)	0.99 (0.87, 1.1)	1.0 (0.94, 1.1)	1.1 (0.97, 1.3)
Hechtel-Eksel	1.0 (0.81, 1.3)	0.86 (0.63, 1.2)	1.0 (0.67, 1.6)	1.6 (0.71, 3.51)		0.69 (0.31, 1.6)	1.4 (0.72, 2.6)	1.1 (0.63, 1.8)	0.78 (0.45, 1.4)
	1.0 (0.81, 1.3)	0.87 (0.64, 1.2)	1.0 (0.69, 1.5)	1.4 (0.60, 2.46)	0.71 (0.03, 2.2)	0.81 (0.39, 1.4)	1.2 (0.66, 1.6)	1.1 (0.65, 1.6)	0.84 (0.50, 1.3)
	0.98 (0.86, 1.1)	0.96 (0.81, 1.1)	1.0 (0.81, 1.2)	1.1 (0.59, 2.00)	0.96 (0.48, 1.3)	1.0 (0.86, 1.1)	1.0 (0.89, 1.3)	0.98 (0.87, 1.1)	0.97 (0.77, 1.1)

(*continued on next page*)

Table 1 (*continued*)

Community	All cancer males	All cancer females	Prostate cancer	Bladder cancer males	Bladder cancer females	Colorectal cancer males	Colorectal cancer females	Lung cancer males	Lung cancer females
Heers	1.1 (0.88, 1.5)	0.97 (0.70, 1.3)	1.1 (0.71, 1.8)	0.95 (0.31, 2.95)		1.3 (0.67, 2.5)	0.96 (0.43, 2.1)	1.2 (0.65, 2.0)	1.4 (0.87, 2.3)
	1.1 (0.87, 1.4)	0.97 (0.70, 1.3)	1.1 (0.71, 1.6)	0.98 (0.32, 2.04)	0.71 (0.04, 2.2)	1.2 (0.65, 1.9)	0.97 (0.47, 1.7)	1.1 (0.66, 1.7)	1.3 (0.80, 1.9)
	1.1 (0.93, 1.2)	1.0 (0.85, 1.2)	1.1 (0.83, 1.4)	0.88 (0.38, 1.66)	1.0 (0.55, 1.5)	1.0 (0.91, 1.3)	0.98 (0.77, 1.2)	1.0 (0.93, 1.2)	1.0 (0.90, 1.4)
Herk-De-Stad	1.1 (0.87, 1.3)	1.1 (0.82, 1.4)	1.2 (0.82, 1.8)	2.5 (1.4, 4.57)	2.1 (0.52, 8.3)	0.20 (0.05, 8.2)	0.58 (0.24, 1.4)	1.1 (0.63, 1.7)	1.4 (0.92, 2.1)
	1.1 (0.86, 1.3)	1.1 (0.81, 1.3)	1.2 (0.78, 1.6)	2.0 (1.1, 3.32)	1.4 (0.34, 3.3)	0.46 (0.17, 0.87)	0.73 (0.34, 1.2)	1.1 (0.64, 1.6)	1.3 (0.86, 1.8)
	1.1 (0.95, 1.2)	1.0 (0.86, 1.2)	1.2 (0.92, 1.5)	2.0 (1.1, 3.28)	1.1 (0.74, 2.2)	0.99 (0.81, 1.1)	0.95 (0.68, 1.1)	1.0 (0.92, 1.1)	1.1 (0.89, 1.4)
Herstappe		2.0 (0.28, 14.0)						1.2 (0.88, 1.6)	
	0.9 (0.36, 1.7)	1.1 (0.43, 2.0)	1 (0.34, 2.0)	1.0 (0.11, 2.87)	1.0 (0.05, 3.2)	1.0 (0.27, 2.2)	0.99 (0.27, 2.1)	1.0 (0.35, 2.0)	0.95 (0.32, 1.9)
	0.96 (0.69, 1.3)	0.98 (0.64, 1.4)	0.91 (0.49, 1.5)	0.83 (0.08, 3.16)	1.1 (0.38, 2.4)	1 (0.74, 1.2)	0.95 (0.54, 1.3)	1.0 (0.9, 1.2)	1.0 (0.61, 1.6)
Heusden-Zolder	1.1 (1, 1.3)	1.1 (0.95, 1.3)	1.3 (0.98, 1.6)	0.8 (0.4, 1.6)	0.98 (0.25, 3,9)	1.2 (0.81, 1.7)	1.0 (0.63, 1.6)	1.3 (0.79, 2.2)	1.1 (0.82, 1.5)
	1.1 (0.99, 1.3)	1.1 (0.94, 1.3)	1.2 (0.95, 1.5)	0.83 (0.4, 1.43)	1.0 (0.24, 2.3)	1.2 (0.8, 1.6)	1.0 (0.63, 1.5)	1.2 (0.86, 1.5)	1.1 (0.8, 1.4)
	1.1 (0.99, 1.2)	1.1 (0.94, 1.2)	1.2 (0.98, 1.4)	1.0 (0.56, 1.56)	1.0 (0.7, 1.6)	1.0 (0.91, 1.2)	0.99 (0.81, 1.2)	1 (0.91, 1.1)	1.0 (0.86, 1.2)
Hoeselt	0.82 (0.62, 1.1)	1.2 (0.91, 1.6)	0.59 (0.32, 1.1)	0.59 (0.15, 2.34)		0.52 (0.19, 1.4)	0.76 (0.32, 1.8)	0.7 (0.46, 1.1)	1.0 (0.61, 1.7)
	0.84 (0.64, 1.1)	1.2 (0.89, 1.5)	0.7 (0.4, 1.1)	0.75 (0.19, 1.63)	0.7 (0.3, 2.1)	0.7 (0.3, 1.2)	0.87 (0.4, 1.5)	1.2 (0.75, 1.8)	1.0 (0.62, 1.5)
	0.95 (0.83, 1.1)	1.0 (0.84, 1.2)	0.86 (0.66, 1.1)	0.81 (0.37, 1.48)	1 (0.58, 1.4)	0.99 (0.81, 1.1)	0.94 (0.68, 1.1)	1.0 (0.94, 1,2)	0.96 (0.76, 1.2)
Houthalen-Helchteren	0.98 (0.84, 1.2)	1.2 (0.97, 1.4)	1.1 (0.81, 1.4)	1.1 (0.61, 2.12)	2.8 (1.2, 6.7)	1.1 (0.73, 1.7)	1.3 (0.82, 2.0)	1.1 (0.63, 1.8)	0.97 (0.71, 1.4)
	0.98 (0.84, 1.1)	1.1 (0.96, 1.3)	1.1 (0.8, 1.4)	1.1 (0.57, 1.85)	2.0 (0.74, 3.9)	1.1 (0.71, 1.6)	1.2 (0.78, 1.7)	0.76 (0.49, 1.1)	0.98 (0.71, 1.3)
	1 (0.91, 1.1)	1.0 (0.93, 1.2)	1.0 (0.88, 1.2)	0.99 0.59, 1.53)	1.0 (0.7, 1.5)	1.0 (0.9, 1.1)	1.0 (0.89, 1.2)	0.99 (0.89, 1.1)	0.97 (0.82, 1.1)
Kinrooi	0.98 (0.77, 1.2)	1 (0.75, 1.3)	0.72 (0.43, 1.2)	1.3 (0.53, 3.1)		1.1 (0.61, 2.1)	1.3 (0.67, 2.5)	1.5 (0.88, 2.6)	1.0 (0.62, 1.6)
	0.98 (0.77, 1.2)	1 (0.75, 1.3)	0.8 (0.49, 1.2)	1.2 (0.48, 2.2)	0.67 (0.03, 2.1)	1.1 (0.6, 1.7)	1.2 (0.64, 1.9)	1.1 (0.64, 1.6)	1.0 (0.62, 1.5)
	0.95 (0.82, 1.1)	0.97 (0.81, 1.2)	0.88 (0.64, 1.1)	0.82 (0.35 1.6)	0.91 (0.23, 1.3)	1.0 (0.86, 1.2)	1.1 (0.89, 1.1)	0.99 (0.88, 1.1)	1.0 (0.8, 1.3)
Kortessem	1.2 (0.93, 1.6)	1.1 (0.83, 1.5)	1.7 (1.2, 2.6)	1.5 (0.58, 4.1)	6.7 (2.52, 17.9)	1.2 (0.57, 2.5)	22 (1.3, 3.9)	1.2 (0.86, 1.6)	0.69 (0.35,1.4)
	1.2 (0.91, 1.5)	1.1 (0.82, 1.5)	1.5 (1.0, 2.1)	1.3 (0.49, 2.6)	2.7 (0.88, 5.9)	1.1 (0.57, 1.9)	1.7 (0.96, 2.6)	13 (0.8, 2.0)	0.79 (0.43, 1.2)
	1.1 (0.94, 1.2)	1.0 (0.89, 1.2)	1.1 (0.89, 1.4)	1.3 (0.72, 2.3)	12 (0.77, 2.5)	1.0 (0.89, 1.1)	1 (0.84, 1.2)	1.0 (0.94, 1.1)	0.99 (0.98, 1.2)
Lanaken	0.87 (0.73, 1.0)	1.0 (0.84, 1.2)	0.92 (0.69, 1.3)	0.75 (0.36, 1.6)	1.1 (0.26, 4.2)	0.53 (0.29, 0.95)	0.82 (0.48, 1.4)	0.74 (0.44, 1.3)	0.72 (0.49, 1.1)
	0.87 (0.74, 1.0)	1.0 (0.84, 1.2)	0.93 (0.7, 1.2)	0.8 (0.37, 1.4)	1.0 (0.24, 2.4)	0.61 (0.34, 0.95)	0.86 (0.51, 1.3)	1.2 (0.84, 1.5)	0.76 (0.52, 1.0)
	0.9 (0.8, 1.0)	0.95 (0.83, 1.1)	0.87 (0.69, 1.1)	0.7 (0.36, 1.2)	0.96 (0.46, 1.3)	0.96 (0.69, 1.1)	0.95 (0.71, 1.1)	1.0 (0.93, 1.1)	0.87 (0.66, 1.0
Leopoldsburg	0.96 (0.79, 1.2)	0.89 (0.69, 1.1)	1.1 (0.73, 1.5)	0.71 (0.27, 1.9)	1.7 (0.42, 6.6)	1.2 (0.71, 2.0)	0.92 (0.49, 1.7)	0.93 (0.66, 1.3)	0.7 (0.42, 1.2)
	0.97 (0.79, 1.2)	0.89 (0.69, 1.1)	1.0 (0.73, 1.4)	0.78 (0.29, 1.5)	1.3 (0.31, 3.0)	1.1 (0.69, 1.7)	0.95 (0.52, 1.5)	0.81 (0.49, 1.2)	0.76 (0.47, 1.1)
	0.97 (0.85, 1.1)	0.91 (0.75, 1.1)	1.1 (0.84, 1.4)	0.84 (0.37, 1.5)	1.0 (0.66, 1.8)	1.0 (0.88, 1.2)	0.99 (0.75, 1.2)	0.98 (0.83, 1.1)	0.88 (0.64, 1.1)
Lommel	0.88 (0.75, 1.0)	0.96 (0.81, 1.1)	0.81 (0.6, 1.1)	0.58 (0.26, 1.3)	0.46 (0.06, 3.3)	1.2 (0.79, 1.7)	1.3 (0.86, 1.9)	1.1 (0.69, 1.7)	1.0 (0.76, 1.4)
	0.88 (0.75, 1.0)	0.96 (0.8, 1.1)	0.83 (0.61, 1.1)	0.65 (0.28, 1.2)	0.7 (1.0, 1.8)	1.1 (0.77, 1.6)	1.2 (0.83, 1.7)	0.95 (0.67, 1.3)	1.0 (0.75, 1.30
	0.9 (0.8, 1.0)	0.97 (0.84, 1.1)	0.88 (0.69, 1.1)	0.7 (0.35, 1.2)	0.93 (0.33, 1.3)	1.0 (0.86, 1.1)	1.1 (0.86, 1.1)	0.98 (0.86, 1.1)	1.0 (0.84, 1.2)
Lummen	1.2 (1.0, 1.5)	0.96 (0.75, 1.2)	1.5 (1.1, 2.1)	1.5 (0.75, 3.0)	1.9 (0.46, 1.8)	1.5 (0.95, 2.4)	1.0 (0.55, 1.9)	1.0 (0.7, 1.5)	0.69 (0.41, 1.2)
	1.2 (1.0, 1.4)	0.96 (0.75, 1.2)	1.4 (1.0, 1.8)	1.4 (0.66, 2.3)	1.4 (0.33, 3.3)	1.4 (0.86, 2.0)	1.0 (0.56, 1.6)	1.1 (0.7, 1.5)	0.76 (0.46, 1.1)
	1.1 (1, 1.3)	0.99 (0.85, 1.1)	1.3 (1.0, 1.6)	1.4 (0.76, 2.2)	1.1 (0.73, 1.8)	1.0 (0.91, 1.2)	0.98 (0.76, 1.1)	1 (0.91, 1.1)	0.97 (0.77, 1.2)
Maaseik	1.1 (0.96, 1.3)	1.0 (0.85, 1.2)	1.4 (1.1, 1.8)	0.37 (0.12, 1.1)	0.57 (0.08, 4.0)	1.3 (0.83, 1.9)	1.0 (0.62, 1.7)	0.99 (0.73, 1.4)	1.2 (0.89, 1.7)
	1.1 (0.95, 1.3)	1.0 (0.84, 1.2)	1.4 (1.1, 1.7)	0.5 (0.17, 1.0)	0.77 (0.12, 2.0)	1.2 (0.8, 1.7)	1.0 (0.62, 1.5)	1.0 (0.71, 1.4)	1.2 (0.86, 1.6)
	1.0 (0.91, 1.1)	0.99 (0.86, 1.1)	1.1 (0.89, 1.3)	0.48 (0.23, 0.83)	0.92 (0.33, 1.3)	1.0 (0.9, 1.1)	1.0 (0.9, 1.3)	0.99 (0.9, 1.1)	1.0 (0.86, 1.2)
Maasmechelen	0.9 (0.78, 1.0)	0.96 (0.82, 1.1)	0.61 (0.44, 0.84)	0.58 (0.27, 1.2)		0.66 (0.41, 1.0)	1.2 (0.86, 1.8)	1.2 (0.7, 1.9)	0.77 (0.56, 1.1)
	0.91 (0.78, 1.0)	0.96 (0.82, 1.1)	0.64 (0.46, 0.86)	0.64 (0.29, 1.1)	0.39 (0.01, 1.2)	0.71 (0.45, 1.0)	1.2 (0.84, 1.7)	1.0 (0.73, 1.3)	0.79 (0.57, 1.0)
	0.93 (0.84, 1.0)	0.97 (0.85, 1.1)	0.79 (0.63, 0.97)	0.58 (0.3, 0.96)	0.92 (0.32, 1.3)	0.97 (0.75, 1.3)	1.0 (0.88, 1.3)	1.0 (0.92, 1.1)	0.89 (0.7, 1.0)
Meeuwen-Gruitrode	1.1 (0.9, 1.4)	0.94 (0.7, 1.3)	1.0 (0.65, 1.6)	0.27 (0.04, 1.9)		1.2 (0.62, 2.2)	1.1 (0.5, 2.2)	0.82 (0.5, 1.4)	0.92 (0.55, 1.5)
	1.1 (0.88, 1.4)	0.94 (0.7, 1.2)	1.0 (0.67, 1.5)	0.53 (0.11, 13.)	0.66 (0.03, 2.0)	1.1 (0.62, 1.8)	1.0 (0.54, 1.7)	1.1 (0.7, 1.7)	0.94 (0.58, 1.4)
	0.98 (0.87, 1.1)	0.96 (0.83, 1.1)	0.97 (0.78, 1.2)	0.55 (0.25, 1.0)	0.92 (0.33, 1.3)	1.0 (0.88, 1.1)	1.0 (0.89, 1.3)	0.99 (0.89, 1.1)	0.99 (0.81, 1.2)
Neerpelt	0.85 (0.69, 1.1)	1.0 (0.81, 1.3)	1.0 (0.71, 1.5)	0.55 (0.18, 1.7)		0.41 (0.17, 0.98)	1.7 (1.0, 2.7)	1.3 (0.72, 2.3)	1.2 (0.8, 1.7)
	0.86 (0.69, 1.0)	1.0 (0.81, 1.3)	1.0 (0.71, 1.4)	0.67 (0.22, 1.3)	0.59 (0.03, 1.8)	0.57 (0.26, 0.99)	1.5 (0.92, 2.2)	0.88 (0.54, 1.3)	1.1 (0.78, 1.6)
	0.89 (0.79, 1.0)	1 (0.86, 1.2)	0.92 (0.73, 1.1)	0.69 (0.32, 1.2)	0.91 (0.26, 1.3)	0.98 (0.75, 1.1)	1.1 (0.93, 1.5)	0.98 (0.87, 1.1)	1.1 (0.89, 1.3)

(*continued on next page*)

Table 1 (*continued*)

Community	All cancer males	All cancer females	Prostate cancer	Bladder cancer males	Bladder cancer females	Colorectal cancer males	Colorectal cancer females	Lung cancer males	Lung cancer females
Nieuwerkerken	1.1 (0.86, 1.5)	1.2 (0.83, 1.6)	0.79 (0.42, 1.5)	0.79 (0.2, 3.2)	1.9 (0.26, 13.2)	2.1 (1.2, 3.7)	0.9 (0.38, 1.6)	0.93 (0.46, 1.9)	1.7 (1.1,2.7)
	1.1 (0.85, 1.5)	1.1 (0.81, 1.5)	0.86 (0.49, 1.3)	0.89 (0.24, 1.9)	1.3 (0.21, 3.3)	1.6 (0.93, 2.5)	1.2 (0.69, 1.8)	1.2 (0.69, 1.8)	1.4 (0.89, 2.1)
	1.1 (0.95, 1.3)	1.1 (0.92, 1.3)	1.1 (0.81, 1.3)	1.4 (0.61, 2.5)	1.1 (0.76, 2.3)	1.0 (0.92, 1.3)	0.98 (0.77, 1.2)	1.0 (0.93, 1.1)	1.2 (0.94, 1.6)
Opglabbeek	0.82 (0.6, 1.1)	0.77 (0.53, 1.1)	0.98 (0.56, 1.7)			0.7 (0.26, 1.9)	0.89 (0.33, 2.4)	0.89 (0.52, 1.5)	0.5 (0.23, 1.1)
	0.85 (0.62, 1.1)	0.8 (0.55, 1.1)	1 (0.59, 1.5)	0.45 (0.05, 1.2)	0.77 (0.03, 2.4)	0.84 (0.36, 1.5)	0.95 (0.41, 1.7)	0.97 (0.53, 1.6)	0.66 (0.34, 1.1)
	0.96 (0.83, 1.1)	0.94 (0.78, 1.1)	0.98 (0.77, 1.2)	0.53 (0.21, 1.0)	0.94 (0.5, 1.3)	1 (0.86, 1.1)	1.0 (0.85, 1.3)	0.99 (0.9, 1.1)	0.93 (0.71, 1.1)
Overpelt	0.96 (0.77, 1.2)	1.2 (0.9, 1.5)	0.9 (0.59, 1.4)	1.5 (0.72, 3.2)	1.1 (0.15, 7.5)	0.96 (0.52, 1.8)	1.4 (0.8, 2.5)	0.89 (0.53, 1.5)	1.3 (0.89, 2.0)
	0.97 (0.77, 1.2)	1.1 (0.89, 1.4)	0.92 (0.61, 1.3)	1.3 (0.61, 2.4)	1.0 (0.15, 2.7)	0.99 (0.54, 1.6)	1.3 (0.74, 2.0)	0.93 (0.57, 1.4)	1.2 (0.83, 1.8)
	0.94 (0.82, 1.1)	1.0 (0.88, 1.2)	0.93 (0.72, 1.2)	1.1 (0.57, 2.1)	0.94 (0.36, 1.3)	0.99 (0.82, 1.1)	1.1 (0.91, 1.5)	0.98 (0.86, 1.1)	1.1 (0.87, 1.4)
Peer	0.9 (0.72, 1.1)	1 (0.78, 1.3)	0.81 (0.52, 1.3)	1.1 (0.44, 2.5)		0.75 (0.37, 1.5)	0.67 (0.3, 1.5)	1.4 (0.98, 2.0)	1.1 (0.7, 1.6)
	0.91 (0.73, 1.1)	1 (0.78, 1.3)	0.86 (0.55, 1.2)	1.0 (0.41, 1.9)	0.61 (0.03, 1.8)	0.83 (0.43, 1.3)	0.78 (0.38, 1.3)	0.93 (0.56, 1.4)	1.0 (0.68, 1.5)
	0.94 (0.83, 1.0)	0.99 (0.85, 1.1)	0.93 (0.74, 1.1)	0.88 (0.46, 1.5)	0.93 (0.35, 1.3)	0.99 (0.83, 1.1)	1.0 (0.89, 1.3)	0.99 (0.88, 1.1)	1.0 (0.84, 1.2)
Riemst	0.85 (0.7, 1.0)	0.63 (0.48, 0.83)	0.62 (0.4, 0.96)	0.61 (0.23, 1.6)	0.72 (0.1, 5.1)	0.96 (0.57, 1.6)	0.32 (0.12, 0.9)	1.1 (0.85, 1.4)	0.77 (0.49, 1.2)
	0.86 (0.71, 1.0)	0.66 (0.5, 0.84)	0.68 (0.45, 0.97)	0.71 (0.26, 1.4)	0.89 (0.13, 2.3)	0.98 (0.58, 1.5)	0.5 (0.22, 0.9)	1.3 (0.93, 1.8)	0.81 (0.52, 1.1)
	0.91 (0.8, 1.0)	0.82 (0.68, 0.97)	0.8 (0.6, 0.99)	0.67 (0.31, 1.2)	0.98 (0.49, 1.4)	0.98 (0.81, 1.1)	0.91 (0.58, 1.1)	1.0 (0.94, 1.2)	0.91 (0.7, 1.1)
Sint-Truiden	1.1 (0.94, 1.2)	1.2 (1.1, 1.4)	1.1 (0.91, 1.4)	1.1 (0.71, 1.8)	1.3 (0.56, 3.2)	1.1 (0.8, 1.5)	1.3 (0.99, 1.8)	1.0 (0.64, 1.5)	1.3 (1.0, 1.6)
	1.1 (0.94, 1.2)	1.2 (1.1, 1.4)	1.1 (0.91, 1.3)	1.1 (0.69, 1.7)	1.2 (0.48, 2.4)	1.1 (0.79, 1.4)	1.3 (0.96, 1.7)	1.1 (0.84, 1.4)	1.2 (1, 1.5)
	1.1 (0.98, 1.2)	1.1 (1.0, 1.3)	1.1 (0.94, 1.3)	1.1 (0.72, 1.7)	1.1 (0.75, 1.8)	1.0 (0.92, 1.2)	1.0 (0.88, 1.3)	1.0 (0.94, 1.1)	1.1 (0.96, 1.4)
Tessenderlo	0.87 (0.71, 1.1)	0.55 (0.41, 0.75)	0.9 (0.62, 1.3)	2.0 (1.2, 3.6)	0.85 (0.12, 6.0)	0.59 (0.3, 1.2)	0.47 (0.2, 1.1)	1.2 (0.93, 1.6)	0.61 (0.36, 1.0)
	0.88 (0.71, 1.1)	0.59 (0.43, 0.77)	0.92 (0.64, 1.3)	1.8 (0.96, 2.8)	0.92 (0.15, 2.4)	0.7 (0.37, 1.1)	0.63 (0.29, 1.1)	1.0 (0.65, 1.4)	0.69 (0.41, 1.0)
	0.92 (0.79, 1.1)	0.73 (0.56, 0.91)	1.0 (0.77, 1.3)	1.7 (0.92, 2.9)	1.0 (0.56, 1.8)	0.98 (0.75, 1.1)	0.93 (0.58, 1.1)	0.98 (0.84, 1.1)	0.83 (0.57, 1.1)
Tongeren	0.94 (0.82, 1.1)	0.95 (0.81, 1.1)	0.82 (0.63, 1.1)	0.31 (0.11, 0.81)	0.98 (0.32, 3.1)	0.88 (0.6, 1.3)	0.72 (0.46, 1.1)	0.32 (0.08, 1.3)	1.0 (0.79, 1.4)
	0.94 (0.82, 1.1)	0.95 (0.81, 1.1)	0.83 (0.63, 1.1)	0.4 (0.63, 1.1)	1.01 (0.31, 2.2)	0.9 (0.61, 1.2)	0.76 (0.48, 1.1)	1.2 (0.92, 1.5)	1.0 (0.78, 1.3)
	0.79 (0.87, 1.1)	0.95 (0.84, 1.1)	0.89 (0.84, 1.1	0.57 (0.3, 0.93)	1.0 (0.67, 1.4)	0.99 (0.86, 1.1)	0.94 (0.71, 1.1)	1.0 (0.94, 1.2)	1 (0.84, 1.2)
Voeren	0.21 (0.1, 0.44)		0.21 (0.05, 0.83)			0.24 (0.03, 1.7)		1.3 (0.73, 2.4)	
	0.36 (0.19, 0.57)	0.22 (0.07, 0.44)	0.51 (0.2, 0.92)	0.53 (0.05, 1.5)	0.81 (0.04, 2.5)	0.64 (0.2, 1.3)	0.58 (0.15, 1.2)	0.65, 0.27, 1.2)	0.45 (0.14, 0.91)
	0.99 (0.96, 1.0)	0.97 (0.94, 1.0)	0.99 (0.93, 1.0)	0.83 (0.7, 0.96)	0.97 (0.69, 1.3)	1 (0.92, 1.1)	1 (0.91, 1.1)	1 (0.94, 1.1)	0.99 (0.93, 1.1)
Wellen	1.2 (0.9, 1.5)	1.1 (7.5, 1.5)	1.5 (0.98 2.4)	2.4 (1.1, 5.4)	2.0 (0.28, 13.9)	0.89 (0.37, 2.1)	0.65 (0.21, 2.0)	0.72 (0.43, 1.2)	0.81 (0.4, 1.60
	1.2 (0.88, 1.5)	1.0 (0.75, 1.4)	1.4 (0.89, 2.0)	1.7 (0.76, 3.2)	1.3 (0.2, 3.3)	0.96 (0.44, 1.7)	0.82 (0.33, 1.5)	1.2 (0.7, 1.9)	0.87 (0.47, 1.4)
	1.1 (0.96, 1.2)	1.1 (0.91, 1.5)	1.1 (0.91, 1.5)	1.8 (0.92, 3.2)	1.1 (0.76, 2.2)	1.0 (0.9, 1.2)	0.99 (0.79, 1.2)	1.0 (0.93, 1.1)	1.0 (0.83, 1.3)
Zonhoven	1.0 (0.87, 1.3)	1.1 (0.89, 1.3)	1.2 (0.82, 1.6)	1.8 (0.99, 3.2)	1.5 (0.37, 5.9)	1.3 (0.82, 2.1)	0.58 (0.27, 1.2)	1.9 (1.1, 3.2)	0.92 (0.62, 1.4)
	1.0 (0.87, 1.2)	1.1 (0.89, 1.3)	1.1 (0.81, 1.5)	1.6 (0.85, 2.6)	1.2 (0.3, 2.8)	1.2 (0.77, 1.8)	0.7 (0.35, 1.2)	0.79 (0.49, 1.2)	0.94 (0.64, 1.3)
	1.0 (0.93, 1.2)	1.1 (0.92, 1.2)	1.1 (0.87, 1.3)	1.5 (0.86, 2.5)	1.0 (0.7, 1.7)	1.0 (0.91, 1.2)	0.97 (0.75, 1.1)	0.99 (0.89, 1.1)	0.99 (0.81, 1.2)
Zutendaal	0.87 (0.61, 1.2)	1.1 (0.75, 1.5)	0.71 (0.34, 1.5)	0.49 (0.07, 3.5)		0.66 (0.21, 2.0)	1.1 (0.4, 2.8)		1.1 (0.58, 2.0)
	0.89 (0.63, 1.2)	1.1 (0.75, 1.4)	0.82 (0.43, 1.3)	0.75 (0.15, 1.8)	0.81 (0.03, 2.6)	0.83 (0.34, 1.5)	1.0 (0.46, 1.9)	1.5 (0.9, 2.3)	1.0 (0.6, 1.6)
	0.93 (0.81, 1.1)	0.97 (0.82, 1.1)	0.86 (0.65, 1.1)	0.64 (0.26, 1.2)	0.94 (0.39, 1.3)	0.98 (0.78, 1.1)	0.99 (0.78, 1.2)	1.0 (0.93, 1.1)	0.93 (0.73, 1.1)

1.5 in all of the municipalities of the cluster. The cluster was confirmed when using the spatial scan statistic of Kulldorff. When focusing on TCCs only, the results were confirmed and the CAR-smoothed relative risks tended to be even higher. In the female population, similar or even higher age-SIRs were found in all, but one of the municipalities of the male cluster. However, these were not significant and disappeared after smoothing, probably as a result of the much lower numbers ($n = 63$ for females versus 290 for males).

We checked if this result could be explained by weaknesses within our registration process. The incidence rate of invasive bladder cancer, standardised according to the European standard population (EST) for the whole of the province is 25.7/100 000 person-years for males and 4.4 for females. These figures are similar to the SIRs in the Dutch population, for example. We received the standardised mortality rates per municipality for bladder cancer (P. Hooft, Flemish government administration, data not shown) and found no increased cause-specific mortality in our cluster region. However, these numbers are small and the CIs large. Additionally, the input of cause of death for the Belgian mortality statistics is known to be unreliable at this detailed level. We therefore are not prepared to base any conclusions upon them.

Some considerable discussion exists among pathologists with respect to the coding of invasive and non-invasive papillomas. It can be imagined that one pathological laboratory could classify these differently compared another. If such a laboratory worked selectively (more or less) for people from the cluster municipalities, this might have a confounding influence on our results. We therefore compared the number of invasive bladder cancers diagnosed by each laboratory in inhabitants of the cluster municipalities to the remaining part of the province and found no differences. We also examined the possible influence of new urologists that recently started working in the cluster region. We therefore identified all urologists working in the cluster region and found seven of them who started their practice between 1989 and 1998. However, they were evenly spread geographically throughout the province and were not more frequently present within the hospitals of the cluster region.

We related the SIRs of each municipality to an index of the degree of urbanisation by linear regression and found no relationship. However, they were significantly related to a municipality-specific index of SES. A higher SIR of bladder cancer was found in municipalities with a higher SES score, which was unexpected. This score explained 11% of the variance of the incidence rates. However, this finding might result from an ecological bias. A similar result was found in Finland where cervical cancer incidence rates per municipality were found to be related to the higher SES status per municipality while individuals with a SES status had the lowest cervical cancer incidence [10]. The province of Limburg is characterised by the presence of a large number of migrants from the south of Europe, some Islamic states (Turkey and North African countries) and recently the Eastern European states. One could argue that one of these groups may have an increased or decreased risk of bladder cancer compared with other populations. We therefore also tested the presence of a relationship between bladder cancer incidence and the proportion of inhabitants of each of these groups per municipality. We found no relationship whatsoever.

In both males and females, bladder cancer has been related to slow acetylation polymorphism [11,12], smoking [12–15] and occupational exposure in the dye, rubber and tyre industries [12–20]. Interactions between these exposure factors have also been identified [12–15]. We compared the proportion of ever versus never smokers in random samples of the population of two cluster municipalities and seven other municipalities [21] and found no differences ($P = 0.12$). In the cluster region, both rubber and asphalt-related industries have been active during the last 30 years. If any of these factories are related to the increased incidence of bladder cancer in the cluster municipalities, either by environmental or by professional influences, cannot be determined without an additional full-scale epidemiological survey with the individual as the unit of analysis. Actually the main professions in the region are service industries or farming. In two studies, mining and the metal industry have also been related to an increased risk of bladder cancer [13,22]. Both have been major industries within the province, but outside of the cluster region. Although a certain number of cluster region inhabitants may have worked as miners or later as metal industry workers, the proportion will be much lower compared with the remaining part of the province. Therefore, this cannot explain our findings.

In summary, our results support the hypothesis of an absence of geographical differences between municipalities with respect to the incidence of cancer, including the most frequent cancer sites separately. For male bladder cancer, a clear cluster with an increased incidence was identified. We were not able to explain the presence of the increased incidences by the data that were available. All these data, however, were municipality-related. They may therefore be vulnerable to ecological bias and this part of the analysis can only be considered to be of a preliminary nature. Final conclusions about possible explanations can only be based on epidemiological research using a retrospective cohort or case–control design with the individual as the unit of analysis.

Uncited references

Ref. [9] is not cited.

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