CANCER MAPPING IN ALPINE REGIONS

ATLANTE DEL CANCRO NELLE REGIONI ALPINE

KREBSATLAS ALPENRAUM

ZEMLJEVIDI BREMENA RAKA V ALPSKI REGIJI

2001-2005

Austria, Italy, Slovenia, Switzerland
Austria, Italia, Slovenia, Svizzera
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1 INTRODUCTION

Cancer mapping has a long tradition in cancer epidemiology. Maps have been produced for decades and some of them have been regarded as milestones, see for example the Cancer Mapping of Scotland [1]. Both layout and methods have changed since then. Layout has mostly changed due to progress in IT-technology and methods ever since programmes for sophisticated smoothing methods have become widely available [2,3].

Our main goal is to show a stable estimate of the regional distribution in our study area. The study area covers fourteen registries in the eastern part of Switzerland, the western part of Austria, Northern Italy and the Alpine parts of Slovenia. The study area covers about 6.2 million people, hence more than half of the Alpine population. The entire study area is located in Alpine regions, where we are confronted with sparse populations. Regional units are small with an average population size of 20,000 inhabitants, the smallest units not having less than 10,000. There are only few larger cities with more than 100,000 people. We present incidence and mortality data for the years 2001 to 2005, but shorter periods for some registries due to the availability of incidence data. Incidence data are collected by cancer registries that are part of Cancer Incidence in Five Continents [4]. Mortality data are official data in the whole area, with the exception of South Tyrol where a local procedure for collecting mortality data was implemented.

We present information for main cancer sites and omit rarer cancer sites in order to provide more stable estimates. Also, for main cancer sites we are confronted with small numbers per unit, and thus need to apply smoothing methods. We show only smoothed maps, which should give a more stable estimate of the underlying pattern. In addition to maps, we also present additional material for those readers interested in details.

Cancer registries require funding, and some people ask whether it is still necessary to run cancer registries. Regional distribution of cancer incidence and mortality is one of the important public health questions, where cancer registries can play a major role. Maps are very easy to read, which means the importance of cancer registries can be demonstrated to a broad audience.

We hope that our material will be widely discussed and will lead to in-depth investigations of those sites where we see clear risk gradients in regional distribution. The material is presented in such a way that not only specialists should be able to read the maps. This of course entails some danger, because the interpretation of cancer maps requires great skill. Higher rates in some regions can be due to a) risk factors, b) screening activities (which can directly influence rates namely low incidence, for example for cervical cancer, and at least temporarily high incidence, for example for prostate cancer), c) differences in outcome if we see high risk in mortality and not in incidence, d) documentation or registration bias, and finally e) random variation.

As mentioned above, it was not our aim to detect cancer clusters. We strongly urge our readers not to use the material presented here to search for cancer clusters. For this task, other methods based on statistical testing are more suitable. We also would like to stress that some readers will be interested only in maps with regional effects. However, the analysis of cancer sites with no high risks in certain

geographical units is important, because this information is relevant for the public. In addition, one must also bear in mind that for some cancer sites like the stomach, incidence and mortality in the study region are high as compared to the European countries.

One of the very important side-effects of this project was the deepening of collaboration between all participating cancer registries. We would like to thank all participating registries for their willingness to collaborate and for their very stimulating discussion. We hope this collaboration leads to interesting investigations beyond cancer mapping.

As compared to former publications, where we already observed various levels of risk, this version shows a still clearer picture. We very carefully discussed the results before going to publication. Now, it is our task, and the responsibility of public agencies to draw the conclusions needed to diminish the gaps we observe.

Finally, we would like to express our gratitude to all the companies who sponsored this publication. It is very important to emphasize that none of the companies had influenced this publication. We can state with certainty that there was no conflict of interest.

Willi Oberaigner, Innsbruck Fabio Vittadello, Padua

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2 MATERIAL & METHODS

Fabio Vittadello, Willi Oberaigner

It is the aim of this publication to show the geographical distribution of cancer incidence and mortality in Alpine regions, based on stable estimates of the geographic distribution for the main cancer sites.

2.1 Which sites and why these sites

Due to the small populations in the chosen geographic units considered (range from 10,000 to 326,000) and thus due to the limited number of incident cases registered in these areas during the period (2001-2005), some cancer sites (like kidney, melanoma, pancreas, thyroid) were not investigated in our study. In two cases, in order to reach the numerical consistency necessary for the analysis, the only solution was to proceed to an aggregation of various sites: Head & neck and oesophagus and larynx (ICD 10: C00-15 plus C32) and the haematopoietic system (including leukaemias and lymphomas, ICD 10: C81-85, C88-95, C96). Since the incidence of non-melanotic skin cancer (NMSC, ICD 10: C44) is difficult to assess and completeness of registration varies among cancer registries, this site was not included in the analysis comparing all cancer cases (All – NMSC). Moreover, since in Austria and also to some extent in Switzerland PSA testing heavily influenced prostate cancer incidence rates, resulting in an "extremely large increase" in incident cases for this cancer, we decided for men to show only the aggregation of all malignant cancers excluding NMSC and also excluding prostate cancer.
The complete list of cancer sites analyzed in the study is illustrated below:

Tab. 1: List of Cancer sites analyzed

ICD 10 Codes	Description	Sex
C00-15, C32	Head & Neck and Oesophagus and Larynx	M, F
C16	Stomach	M, F
C18–21	Colon/Rectum	M, F
C22	Liver	M, F
C33-34	Bronchus, Lung	M, F
C50	Breast	F
C53	Cervix uteri	F
C54	Corpus uteri	F
C56	Ovary	F
C61	Prostate	M
C67	Bladder	M, F
C81-85, C88-95, C96	Hematopoietic / Lymphatic System	M, F
C00-96 except C44	All sites except NMSC (All – NMSC)	M, F
C00-96 except C44, C61	All sites except NMSC and prostate (All – NMSC – Prostate)	M, F

Some considerations are needed:

a) for some cancer sites (especially liver, bladder and head&neck), the maps showing female cases must be interpreted with caution, because the numbers observed in the area for this sex and for these sites are small;

b) the group Hematopoietic / Lymphatic System (C81-85, C88-95, C96) was initially split into leukaemias and lymphomas and myelomas, in order to analyse them separately; however, the low numerical consistency suggested that the data be aggregated for the final analysis.

2.2 Geographical units

In accordance with the study's objectives, and because municipalities in Alpine regions are characterized by small numbers of inhabitants (except for a small number of larger towns), we decided to subdivide each country area into wider geographical units, defined by agreed upon criteria: the population should be at least 10,000 inhabitants; moreover, each geographical unit should be morphologically homogeneous, meaning cities or "natural" units should not be split up. For all but Slovenia and Austrian registries, official administration units were used. For Austria, NUTS2-regions were not already defined, and therefore in Austria the boundaries of units were defined by experts at the local level. It should be noted that in most areas the specific geographical situation made this a very straightforward task.

Tab. 2: Geographical units

Registry	Geographical units		
	Number	Names	Type
Varese	4	Valcuvia, Valganna e Valmarchirolo, Valceresio, Valli del Luinese	Alpine communities
Graubünden-Glarus	15	Albula, Glenner, Heinzenberg, Hinterrhein, Imboden, Inn, Maloja, Oberlandquart, Plessur, Unterlandquart, Val Müstair, Vorderrhein, Bernina, Moësa, Glarus	administrative districts
St. Gallen - Appenzell	18	Appenzell I.Rh., Alttoggenburg, Gaster, Gossau, Hinterland, Mittelland, Neutoggenburg, Oberrheintal, Obertoggenburg, Rorschach, Sargans, See, St. Gallen, Unterrheintal, Untertoggenburg, Vorderland, Werdenberg, Will	
Ticino	8	Bellinzona, Blenio, Leventina, Locarno, Lugano, Mendrisio, Riviera, Vallemaggia	
Carinthia	29	Bad Kleinkirchheim, Ebene Reichenau - Ob. Gurktal, Feldkirchen-Glantal, Gailtal und Lesachtal, Gegendtal, Glantal-Wimitz, Görtschitztal, Gurktal, Jauntal, Klagenfurt Land - Ost, Klagenfurt Stadt, Lieser- und Maltatal, Metnitztal, Oberes Drautal, Oberes Mölltal, Rosental Ost, Rosental West, Sattnitz West, Spittal - Millstättersee, St. Veit an der Glan-Krappfeld-Zollfeld, Unteres Drautal, Unteres Gailtal, Unteres Lavanttal, Unteres Mölltal, Villach Stadt, Völkermarkt-Unteres Drautal, Wolfsberg - Oberes Lavanttal, Wörthersee Ost, Wörthersee West	morphologically homogeneous units
Salzburg	12	Bischofshofen und Pongau Nord, Flachgau Nord/West, Flachgau Süd/Ost, Hallein Umgebung, Lungau, Oberpinzgau, Saalfelden Umgebung, Schwarzach und Pongau Süd, St.Johann und Pongau Ost, Stadt Salzburg, Tennengau ohne Hallein Umgebung, Zell am See und Pinzgau Süd/Ost	
Slovenia	38	Ajdovščina, Celje, Domžale, Dravograd, Grosuplje, Hrastnik, Idrija, Jesenice, Kamnik, Kranj, Laško, Lenart, Litija, Ljubljana, Logatec, Maribor, Mozirje, Nova Gorica, Ormož, Pesnica, Ptuj, Radlje ob Dravi, Radovljica, Ravne na Koroškem, Ruše, Šentjur pri Celju, Škofja Loka, Slovenj Gradec, Slovenska Bistrica, Slovenske Konjice, Šmarje pri Jelšah, Tolmin, Trbovlje, Tržic, Velenje, Vrhnika, Zagorje ob Savi, Žalec	
Tyrol	32	Brixental, Brixlegg und Umgebung, Hall und Umgebung, Hinteres Zillertal, Imst Umgebung und Pitztal, Jenbach und Umgebung, Kematen und Sellrain, Kitzbühel und Umgebung, Kufstein und Umgebung, Landeck und Umgebung, Landeshauptstadt Innsbruck, Lechtal, Tannheimertal, Lienz und Umgebung, Matrei i.O., Kals, Defereggen, Oberes/Oberstes Gericht, Sonnenterrasse, Ötztal, Reutte und Umgebung, Rietz bis Roppen, Salzstraße und Seefeld, Schwaz und Umgebung, Sillian und Umgebung, St. Johann, Pillersee, Söll, Stanzertal, Paznaun, Stubaital, Südöstliches Mittelgebirge, Telfs und Mieminger Plateau, Untere Schranne und Kössen, Vorderes Zillertal, Wattens und Umgebung, Westliches Mittelgebirge, Wipptal, Wörgl und Wildschönau	
Vorarlberg	18	Bregenz, Dornbirn, Feldkirch, Grosses Walsertal Umgebung, Hinterer Bregenzerwald /Kleines Walsertal, Hofsteig, Hohenems, Klostertal/Bludenz, Leiblachtal, Lustenems, Mittlerer Bregenzerwald, Montafon, Rheindelta, Rheintal Oberland, Rheintal Unterland, Vorderer Bregenzer Wald, Walgau SüdOst, Walgau West	

	Geographical units		
Friuli Venezia Giulia	4	Carnia, Gemonese & Sandanielese, Pordenone Nord, Tarcentino & Cividalese	health districts (or their aggregation)
Sondrio	5	Bormio, Chiavenna, Morbegno, Sondrio, Tirano	
South Tyrol	20	Bozen/Bolzano, Brixen-Umgebung/Bressanone-circondario, Bruneck-Umgebung/Brunico-circondario, Eggental-Schlern/Val d'Ega-Sciliar, Gadertal/Val Badia, Gröden/Val Gardena, Hochpustertal/Alta Val Pusteria, Klausen-Umgebung/Chiusa-circondario, Lana-Umgebung/Lana-circondario, Leifers-Branzoll-Pfatten/Laives-Bronzolo-Vadena, Meran-Umgebung/Merano-circondario, Mittelvinschgau/Media Val Venosta, Naturns-Umgebung/Naturno-circondario, Obervinschgau/Alta Val Venosta, Passeiertal/Val Passiria, Salten-Sarntal-Ritten/Salto-Val Sarentino-Renon, Tauferer-Ahrntal/Tures-Aurina, Überetsch/Oltradige, Unterland/Bassa Atesina, Wipptal/Alta Valle Isarco	
Trentino	11	Alta Valsugana, Alto Garda e Ledro, Bassa Valsugana e Tesino, Fiemme, Giudicarie e Rendena, Ladino di Fassa, Primiero, Vallagarina, Valle dell'Adige, Valle di Non, Valle di Sole	
Veneto	5	Agordo, Belluno, Cadore, Feltre, Sette Comuni	
Total	***219***		

2.3 Incidence and mortality data

The cancer incidence and mortality data presented in this study were collected by fourteen registries in the eastern part of Switzerland, the western part of Austria, Northern Italy and the Alpine parts of Slovenia. All of these are population-based cancer registries: incidence data were published in "Cancer Incidence in Five Continents – Vol. IX" (Salzburg and Carinthia as part of the Austrian nationwide registry, South Tyrol, Trentino and Friuli Venezia Giulia as the Northeast Italy Cancer Surveillance Network). All data were checked using IARC tools, and multiple cancers were accepted in accordance with IARC rules. Urinary cancers included only malignant invasive tumours (not in-situ or of uncertain malignity), while cases judged to be "borderline" for cancer of the ovary were not considered. Intraductal carcinoma NOS were included in breast cancer cases collected by two registries.

The following table shows the participating registries and the years covered by every registry: our focus was on years 2001-2005. However, some registries had not yet finished their data and therefore included the most recent five-year period available at time of data collection.

Tab. 3: Availability of Incidence and Mortality data by Registry

Cancer Registry	**Data period**		Population data by sex, 5-year class, geographical unit - availability
	Incidence	**Mortality**	
Carinthia	2001 - 2005	2001 - 2005	2001-2005
Friuli Venezia Giulia	2001 - 2005	2001 - 2005	2000-2005
Graubünden-Glarus	2001 - 2005	2001 - 2005	Census 2000
Salzburg	2001 - 2005	2001 - 2005	2001 - 2005
Slovenia	2001 - 2005	2001 - 2005	2001-2005
Sondrio	2001 - 2005	2001 - 2005	2000-2005
South Tyrol	1999 - 2003	1999 - 2003	1998-2003
St. Gallen/Appenzell	2001 - 2005	2001 - 2005	Census 2000

Cancer Registry	Data period		Population data by sex, 5-year class, geographical unit - availability
	Incidence	Mortality	
Ticino	2001 - 2005	2001 - 2005	2000-2005
Trentino	2000 - 2004	2000 - 2004	1999-2004
Tyrol	2001 - 2005	2001 - 2005	2001-2005
Varese	1998 - 2001	1998 - 2001	1998-2001
Veneto	1999 - 2003	1999 - 2003	1998-2003
Vorarlberg	2001 - 2005	2001 - 2005	Census 2001

Cancer mortality data were extracted from national mortality files, with the exception of South Tyrol where a local procedure for collecting mortality data was implemented in 2001. During the study period, the coding of mortality causes was changed from ICD9 to ICD10. For conversion, a program based on IARC rules was used. The mortality data did not include the deaths registered as C97 (multiple cancers at independent multiple sites), because different coding practices prevailed among the registries. At any rate, the weight of these cases on all deaths is very small (< 0.05%). Consequently their exclusion from the analysis should have a neglectable effect on the final maps.

2.4 Data quality

Completeness of registration is the proportion of all incident cases in the registry population that are included in the registry database. Completeness should be as close to 100% as possible, so that comparison between regions reflects true differences in cancer risk. In order to evaluate completeness of registration some indices have been used.

Death certificates are an important supplementary source of information for cancer registries and help capture information that escaped the registration process during life. Death certificate only (DCO) cases show the proportion of cases remaining after various follow-back procedures. Because the diagnostic information in death certificates is well known to suffer from lack of accuracy and / or precision, a high proportion of DCO cases implies low accuracy and, to some degree, incompleteness of registration [1].
The ratio Mortality: Incidence (RMI) is an important indicator of completeness, because as the information on mortality is provided from the national vital statistics office and thus constitutes an independent data source. When the quality of the mortality data is good and we observe stable incidence and survival, then RMI is expected to be approximately 1 – survival probability.

Histological or cytological verification (%HV) is an indicator of the validity of diagnostic information. However, a very high proportion of cases diagnosed by histology or cytology suggests an over reliance on the pathology laboratory as a source of information and a failure to find cases by other means.

2.5 Population data

Availability of population data, needed to calculate the population at risk (person-years) for each geographical unit, differed slightly among the registries. In fact, while most of the registries can access population registers that are updated every year at the municipal level, in three cases (Graubünden-Glarus, St. Gallen and Vorarlberg) population at the municipal level is gathered only at 10-year intervals, namely by census. The availability of population data for the study period is presented in Tab. 3.

As population data corresponded to the number of inhabitants by geographical unit, sex and age-class with reference to the end (31st of December) of every year, the estimate of person-years for the whole period was calculated as the sum of the average population of each year, namely as follows:

$$P^{2001-2005} = \frac{P^{2000} + P^{2001}}{2} + \ldots + \frac{P^{2002} + P^{2003}}{2} + \ldots + \frac{P^{2004} + P^{2005}}{2}$$

where P^{year} = population at 31st of December, age x, (x+5), by sex

In cases where population data were not available at the municipal level at the end of every year, person-years were estimated by multiplying the census population times 5.

2.6 Epidemiological rates

Annual crude incidence and mortality rates, obtained by division of the total number of cancer cases by the corresponding estimated person-years, were computed. In order to compare cancer levels among the areas considered in the study, annual age-standardized rates were calculated using the direct method. The standard used was the theoretical World Standard Population which was modified by Doll et al. (1966) from that proposed by Segi (1960) [1] – and the European Standard Population [2]. The standard errors of directly age-adjusted rates were computed in accordance with binomial approximation [2].

For each cancer site, the expected number of cases and deaths was calculated via the indirect age-standardization method, by applying the age-specific rates obtained for the whole area to the population of each geographical unit population. Standardized incidence ratios (SIR) and standardized mortality ratios (SMR) were calculated with the indirect method [3]. Their 95% confidence intervals were estimated using Byar's method [3]. It should be noted that Slovenia accounts for about one-quarter of cases. Therefore, Slovenia has a larger influence on the rates observed in the area and, consequently, on the SIR and SMR estimated for each geographical unit.

2.7 Smoothing procedure

Disease mapping based on small geographical units is known to be less susceptible to ecological bias, because within-area heterogeneity will be smaller. However, data are usually much sparser, which can produce unstable estimates and over-dispersion with respect to the Poisson model. Hence, it is common practice to apply modelling to overcome some of these problems. The main goal is to

achieve a more stable estimate of the underlying pattern and to approach the true underlying risk pattern [4].

We therefore decided to apply a Bayesian hierarchical model and thus chose the well known BYM model proposed by Besag, York and Mollié [5]. This model takes adjacency of regions into account and is defined by the following set of equations:

$y_i \approx \text{Poisson}(e_i\theta_i)$

$$\log(\theta_i) = \alpha + u_i + v_i$$

α … overall level of relative risk
u_i … correlated heterogeneity
v_i … uncorrelated heterogeneity

where y_i denotes number of cases
$\approx \text{Poisson}(e_i\theta_i)$

Uncorrelated heterogeneity is modelled using the following formula

$$v_i \approx N(0,\tau_v^2)$$

Correlated heterogeneity or adjacency is modelled as follows

$$\left[u_i \middle| u_j, i \neq j, \tau_u^2\right] \approx N(\bar{u}_i, \tau_i^2)$$

$$\bar{u}_i = \frac{1}{\sum_j \omega_{ij}} \sum_j u_j \omega_{ij}$$

$$\tau_i^2 = \frac{\tau_u^2}{\sum_j \omega_{ij}}$$

$\omega_{ij} = 1$ if i and j are adjacent and 0 otherwise

It is known that this model is improper, so it is necessary to define a constraint to ensure that the model is identifiable. This is done by assigning a uniform prior distribution to α.
For every site and sex combination, we fitted a separate model for incidence and for mortality. Firstly, two chains were defined as starting from different initial values chosen a priori, using the same initial values for every model. Afterwards, 10000 samples were run in a burn in step. Secondly, convergence was checked visually. According to the literature, there are no formal procedures for checking convergence, but at least a lack of convergence is clearly known. We looked at the Gelman Rubin statistics, inspected history plots and density plots and finally checked the condition MCError/SD <= 5% [6]. After assuring convergence, we finally ran another 10000 samples in order to obtain the final estimates. For every combination of site, sex and incidence/mortality, we were able to achieve reasonable convergence. Analysis was performed using WinBUGS Version 1.4 [6].

2.8 Scaling, colour scheme

For mapping purposes, we chose to apply absolute scaling, especially because this approach allows the reader to directly compare cancer maps across sites and sexes throughout the whole report, using a common colour scale: regions shown in the same colour have the same meaning or interpretation for every site. In order to best illustrate the distribution of geographical units by risk in smoothed maps, 11 breakpoints were defined around 1:5 intervals, and we used green to indicate SMR/SIR smaller than 1, yellow for the central category and red to brown for SMR/SIR greater than one.

Tab. 4: Definition of colors and breakpoints for the maps

Color	Minimum SIR/SMR	Maximum SIR/SMR	Legend label
Green	0.000	0.533	≤ 0.53
Medium green	0.534	0.612	≤ 0.61
Light green	0.613	0.704	≤ 0.70
Yellow	0.705	0.810	≤ 0.81
Light yellow	0.811	0.932	≤ 0.93
Very light yellow	0.933	1.071	≤ 1.07
Light orange	1.072	1.232	≤ 1.23
Medium orange	1.233	1.417	≤ 1.42
Orange	1.418	1.630	≤ 1.63
Red	1.631	1.876	≤ 1.88
Brown	1.877	∞	> 1.88

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3 GLOBAL SUMMARY & CALL FOR ACTION

Willi Oberaigner

Global Summary and Call for Action

It was the aim of this publication to show the geographic distribution of cancer incidence and mortality in Alpine regions, based on stable estimates of the geographic distribution for the main cancer sites.

Fourteen cancer registries covering Alpine regions in Austria, Italy, Switzerland and the national registry for Slovenia participated in this project. The study area covers a population of more than 6 million inhabitants. The study area consists of 219 geographical units, having a median population of 19,383 persons. The 12 most important tumour sites or groups of sites were examined. This study is the continuation to a previous cancer atlas of Alpine regions for the years 1996-2000.

Data quality seems to be rather high, although we should mention that some bias could exist in diagnostics procedures for bladder cancer, in the definitions and/or registration of lymphoma/myeloma/leukaemia and in coding the precise cause of death for cervical and corpus cancer which could have a substantial influence on mortality data for cervical and corpus cancer.

Results for males: As prostate cancer incidence is heavily influenced by PSA testing in Austria, which caused prostate cancer rates to double, for the aggregation of all cancer sites for men we also excluded prostate cancer. For all cancer sites except NMSC and prostate cancers we observe a gradient from low incidence in Austria and Switzerland to high incidence in Italy (except Trentino and South Tyrol) and Slovenia. This gradient is more pronounced for mortality and less marked for incidence, for which we observe only small excess risk in Slovenia. For head & neck cancer, there is excess risk in the Italian regions and slightly higher risk in the eastern part of Slovenia; for stomach cancer there is excess risk in Slovenia and some parts of Tyrol, South Tyrol, Trentino and Sondrio and lower risk in the Swiss regions; for colorectal cancer there is excess risk in Slovenia (especially for mortality); for liver cancer there is excess risk in the Italian regions and also in Ticino; for lung cancer there is excess risk in the Italian regions (except South Tyrol and Trentino) and (more marked) in Slovenia. For prostate cancer, we observe high incidence rates in the Austrian registries and excess risk for mortality in Slovenia; for bladder cancer mortality, there is excess risk in the Italian regions (except South Tyrol) and Slovenia and for lymphoma/myeloma/leukaemia, the excess risk is rather small and there is no consistent picture between incidence and mortality.

Results for Females: Aside from a small excess risk in cancer mortality in Slovenia, no strong variation is seen for all cancer sites combined. The size of excess risk in incidence is generally lower as compared to males. For head & neck cancer, there is excess risk in Veneto, Sondrio and Friuli Venezia Giulia (especially mortality); for stomach cancer there is excess risk in Tyrol, South Tyrol, Veneto and Friuli Venezia Giulia and the eastern parts of Slovenia; for colorectal cancer there is excess risk in Slovenia (mortality only); for liver cancer there is excess risk in the Italian regions (especially high risk in Trentino, Veneto and Friuli Venezia Giulia); for lung cancer we see some excess risk in the central parts of Tyrol, Veneto and some regions of Slovenia; for breast cancer we see some small excess risk

in incidence without corresponding risk in mortality (therefore, the excess risk in incidence could be attributed to differences in mammography screening attendance rates), for cervical cancer there is excess risk in the eastern parts of Tyrol, Carinthia and Slovenia, with a consistent picture between incidence and mortality; for corpus cancer we see excess risk in Slovenia and the Swiss regions (mainly mortality); for ovarian cancer there is some small excess risk only in some regions of Salzburg; for bladder cancer we see some excess risk in incidence in Veneto, the eastern part of Trentino and Carinthia but no excess risk in mortality (therefore the excess risk in incidence could be attributed to differences in diagnostics and/or registration procedures for bladder cancer); and for lymphoma/myeloma/leukaemia there is some excess risk in incidence in some Swiss regions but no corresponding risk in mortality (therefore, the excess risk could be attributed to differences in diagnostic and/or registration procedures).

We observe elevated risk in different parts of the study region. However, the affected cancer sites are different. Therefore, our recommendations also take these differences into consideration. In **Italy**, we observe high risk mainly for head&neck, liver and bladder cancer. All three cancer sites are correlated with smoking and drinking, and our call for action is thus to intensify already established campaigns to reduce smoking and alcohol consumption in the Alpine regions. In **Slovenia**, the main problem is high risk for mortality and therefore improvements in screening, diagnostics and therapeutic procedures should reduce the elevated risk. In **Austria**, higher risk is seen for cervical cancer and stomach cancer: for cervical cancer, it is well known that well organised screening programs can effectively reduce incidence and mortality; for stomach cancer, primary prevention campaigns towards healthy diet seem to be the best choice. In **Switzerland**, we observe a rather favourable situation for most sites and only some small additional risk in corpus cancer.

Sintesi e proposte operative

Scopo di questa pubblicazione è quello di analizzare la distribuzione geografica dell'incidenza e della mortalità per le principali sedi tumorali nelle regioni Alpine, attraverso stime stabili.

Al progetto hanno partecipato 14 Registri Tumori in Austria, Italia, Svizzera e Slovenia (quest'ultima ha un unico Registro nazionale). L'area in studio comprende una popolazione di più di 6 milioni di abitanti suddivisa in 219 unità geografiche, con una popolazione mediana di 19.383 persone. Sono state considerate le 12 sedi tumorali, o gruppi di sedi, più importanti. Questo studio rappresenta la continuazione di un precedente Atlante del cancro nelle regioni Alpine, relativo agli anni 1996-2000.

La qualità dei dati appare abbastanza elevata, anche se va segnalata la possibilità di alcune distorsioni, legate alle procedure diagnostiche del tumore vescicale, alla definizione e/o registrazione dei linfomi, mielomi e leucemie ed alla codifica esatta della causa di morte per i cancri della cervice e del corpo dell'utero. Quest'ultimo aspetto può influenzare sensibilmente i dati di mortalità delle due sedi uterine.

Risultati per i Maschi.
Per i maschi, l'aggregato dei tumori maligni viene analizzato escludendo i tumori prostatici, perché l'incidenza di questi ultimi è fortemente influenzata dall'uso intensivo del test PSA (es.: in Austria), che comporta un raddoppio dei relativi tassi d'incidenza.
Considerando il complesso delle sedi tumorali, esclusi i tumori cutanei non melanotici e quelli della prostata, si osserva un gradiente di aumento dell'incidenza che, da bassi valori in Austria e Svizzera, passa a valori elevati in Italia (tranne Trentino e Alto Adige) e Slovenia. Tale gradiente è più marcato per la mortalità che per l'incidenza, per la quale si nota solo un contenuto eccesso di rischio in Slovenia.
Per i tumori di testa e collo, laringe ed esofago, si osservano rischi elevati nelle regioni italiane e, meno pronunciati, nelle zone orientali della Slovenia. Per il cancro dello stomaco, si riscontra un eccesso di rischio in Slovenia ed in alcune parti del Tirolo, Alto Adige, Trentino e Sondrio, ed un rischio inferiore nelle aree svizzere. Per i tumori colo-rettali, l'eccesso di rischio si presenta in Slovenia e riguarda soprattutto la mortalità. Il rischio per i tumori del fegato è eccedente nelle aree italiane e nel Canton Ticino; per bronchi e polmone, il rischio di cancro è superiore nelle zone italiane (esclusi Alto Adige e Trentino) e, in misura più marcata, in Slovenia.
Per i tumori della prostata, si notano alti tassi d'incidenza in Austria ed un eccesso di mortalità in Slovenia; per il cancro della vescica, si riscontra un eccedenza di mortalità nelle aree italiane (tranne il Alto Adige) ed in Slovenia.
Per linfomi, mielome e leucemie, gli eccessi di rischio sono modesti, ed il confronto tra incidenza e mortalità fornisce un quadro non coerente.

Risultati per le Femmine.

A parte un lieve eccesso di mortalità per tutti i tumori che si registra in Slovenia, non si notano complessivamente forti variazioni geografiche. In generale, l'entità dell'eccesso di rischio per l'incidenza è inferiore rispetto ai maschi. Per i tumori della testa e collo, laringe ed esofago, si osservano rischi eccedenti a Sondrio, in Veneto ed in Friuli Venezia Giulia (specialmente per la mortalità); per il cancro dello stomaco, i rischi maggiori si riscontrano in Tirolo, Alto Adige, Veneto, Friuli Venezia Giulia e nelle zone orientali della Slovenia. I tumori colo-rettali mostrano mortalità più elevata in Slovenia, mentre rischi eccedenti si riscontrano per il cancro del fegato in Italia, soprattutto in Trentino, Veneto e Friuli Venezia Giulia; il tumore del polmone presenta alcuni eccessi di rischio in Tirolo, Veneto ed alcune zone della Slovenia. Si osservano contenuti eccessi di rischio per l'incidenza dei tumori mammari, senza corrispondenza nella mortalità, attribuibili, probabilmente a differenze nella diffusione ed adesione allo "screening" mammografico. Per il cancro del collo dell'utero, si nota un rischio superiore in aree del Tirolo orientale, Carinzia e Slovenia, in un quadro coerente tra incidenza e mortalità; per il corpo dell'utero, l'eccesso di rischio di cancro riguarda la Slovenia e la Svizzera (principalmente la mortalità), mentre per il cancro dell'ovaio si osserva qualche lieve eccesso solo in alcune zone del Salisburghese. Per i tumori della vescica l'incidenza è elevata in Veneto, in alcune zone orientali del Trentino ed in Carinzia, ma non vi è eccedenza di mortalità; perciò le differenze potrebbero essere dovute a differenze nelle pratiche diagnostiche e/o di registrazione. Analoga spiegazione potrebbe valere per gli eccessi d'incidenza tra i linfomi, mielome e leucemie, riscontrabili in alcune aree svizzere, per i quali non si notano corrispondenti eccedenze di mortalità.
Rischi elevati si osservano in diverse parti della regione in studio, tuttavia le sedi tumorali coinvolte sono differenti: di questa circostanza si è tenuto conto anche nelle successive raccomandazioni.

In **Italia**, si osservano rischi elevati principalmente per i tumori delle prime vie aero-digestive ed esofago, del fegato e della vescica. I tumori di tutte queste sedi sono correlati con l'abitudine al fumo ed alle bevande alcoliche, per cui la nostra indicazione è di intensificare le azioni, già adottate, per ridurre il fumo ed il consumo di alcolici, nelle regioni alpine.
In **Slovenia**, il problema principale è l'alta mortalità, che si dovrebbe poter ridurre con miglioramenti negli "screening" e nelle procedure diagnostiche e terapeutiche.
In **Austria**, i rischi elevati riguardano il tumori della cervice uterina e dello stomaco. Per i primi, è risaputo che tanto l'incidenza quanto la mortalità possono essere efficacemente ridotti da programmi di "screening" ben organizzati; per i secondi, la scelta migliore appare quella di svolgere azioni di prevenzione primaria, per la promozione di una dieta sana.
In **Svizzera**, per la maggior parte delle sedi la situazione appare abbastanza positiva, e si riscontra solo un rischio moderatamente superiore per il cancro del corpo dell'utero.

Gesamtzusammenfassung und Aktionsplan

Ziel dieser Publikation war es, die geographische Verteilung von Krebsinzidenz und Mortalität in der Alpenregion, basierend auf exakten Berechnungen der geographischen Verteilung der wichtigsten Krebslokalisationen zu zeigen.

14 Krebsregister aus Österreich, Italien der Schweiz und Slowenien nahmen an diesem Projekt teil. Ausgewertet wurden Daten von mehr als 6 Millionen Einwohnern in 219 geographischen Einheiten mit einer medianen Population von 19383 Personen. Untersucht wurden die 12 häufigsten Lokalisationen bzw. Lokalisationsgruppen. Die vorliegende Arbeit stellt die Fortsetzung des Krebsatlas der Jahre 1996-2000 dar.

Die Datenqualität ist sehr hoch, dennoch sollte erwähnt werden, dass eine gewisse Fehlermöglichkeit besteht, z.B. in der Diagnostik des Blasenkarzinoms, in den Definitionen bzw. in der Registrierung von Lymphom/Myelom/Leukämie und in der Codierung der exakten Todesursache für Zervix- und Korpuskarzinome, welche für beide Tumorentitäten einen substanziellen Einfluss auf die Mortalität haben könnte.

Ergebnisse für männliche Patienten:
Die Inzidenz des Prostatakarzinoms ist in Österreich stark beeinflusst durch die PSA-Testung, die zu einer Verdoppelung der Prostatakarzinomraten führte. Bei der Zusammenfassung aller Tumorlokalisationen für Männer schlossen wir daher das Prostatakarzinom aus. Für alle Krebslokalisationen außer dem NMSC und dem Prostatakarzinom zeigte sich eine geringe Inzidenz in Österreich und der Schweiz, eine hohe Inzidenz in Italien (außer in Trentino und in Südtirol), sowie in Slowenien. Dieser geographische Verlauf ist klar erkennbar für die Mortalität und weniger stark ausgeprägt für die Inzidenz, bei der wir nur in Slowenien eine geringe Erhöhung beobachten konnten. Für HNO Tumoren besteht ein erhöhtes Risiko in Italien, sowie ein gering erhöhtes Risiko im westlichen Teil Sloweniens. Für Magenkarzinome besteht ein erhöhtes Risiko in Slowenien und Teilen Tirols, Südtirols, Trentino, sowie in Sondrio und ein geringeres Risiko in der Schweiz. Für das kolorektale Karzinom besteht in Slowenien ein erhöhtes Mortalitätsrisiko. Das Risiko für Leberkarzinome ist besonders hoch in Ticino, sowie in den italienischen Regionen, wo auch ein erhöhtes Risiko für das Lungenkarzinom besteht (mit Ausnahme von Südtirol und Trentino). Ein besonders hohes Lungenkarzinom-Risiko besteht auch in Slowenien. Für das Prostatakarzinom wurden hohe Inzidenzraten in den österreichischen Regionen beobachtet und ein erhöhtes Mortalitätsrisiko in Slowenien. Das Risiko an einem Blasenkarzinom zu versterben, ist besonders hoch in den italienischen Regionen (mit Ausnahme von Trentino) und in Slowenien. Für die Tumorentitäten Lymphom/Myelom/Leukämie beobachten wir geringe Risikounterschiede und es gibt keine klare Konsistenz zwischen Inzidenz und Mortalität.

Ergebnisse für Frauen:
Abgesehen von einer geringen Erhöhung der Krebssterblichkeit in Slowenien konnten keine Risikounterschiede für alle Karzinome gefunden werden. Für HNO-Tumoren besteht eine Risikoerhöhung in Veneto, Sondrio und Friaul Julisch Venezien (besonders bezüglich der Mortalität); für Magenkarzinome weisen die Raten in Tirol, Südtirol, Veneto und in Friaul Julisch Venezien auf eine Erhöhung hin. Die Mortalität des kolorektalen Karzinoms ist in Slowenien erhöht. Leberkarzinome sind am häufigsten in italienischen Regionen zu finden, ein besonders hohes Risiko besteht in Trentino, in Venetien und in Friaul Julisch Venezien. Für Lungenkarzinome gibt es eine Risikoerhöhung in den zentralen Teilen Tirols, Veneto und in einigen Regionen Sloweniens. Für Mammakarzinome finden wie eine geringe Inzidenzerhöhung ohne gleichzeitige Mortalitätserhöhung. Eine Ursache könnte in der unterschiedlichen Teilnahmerate an Mammographieprogrammen gesehen werden. Für Zervixkarzinome besteht erhöhtes Krebsrisiko in den östlichen Teilen Tirols, Kärnten und Sloweniens, wobei die Daten für Mortalität und Inzidenz konsistent sind. Für das Korpuskarzinom können Risikoerhöhungen in Slowenien und in den Schweizer Regionen festgestellt werden (insbesondere die Mortalität). Für das Ovarialkarzinom besteht nur eine geringe Risikoerhöhung in wenigen Regionen Salzburgs. Für das Harnblasenkarzinom ist das Inzidenzrisiko in Venetien und in den östlichen Teilen von Trentino und in Kärnten erhöht. Es besteht keine Erhöhung des Risikos betreffend der Sterblichkeit (Verantwortlich für diese Diskrepanz könnten diagnostische Maßnahmen und Unterschiede in der Registrierung des Harnblasenkarzinoms sein). Für die Gruppe Lymphom, Myelom und Leukämie besteht eine Inzidenzerhöhung in einigen Schweizer Regionen, aber keine konsistente Mortalitäterhöhung (auch hier könnten diagnostische Maßnahmen oder Registrierungsprozeduren ursächlich sein).

Wir beobachten ein erhöhtes Risiko in verschiedenen Gebieten, sie unterscheiden sich jedoch bezüglich der betroffenen Tumorlokalisationen. Unsere Empfehlungen berücksichtigen diese Unterschiede. In **Italien** kann man ein hohes Risiko für HNO-, Leber- und Harnblasenkarzinome feststellen. Alle 3 Karzinomarten korrelieren streng mit Rauchen und Alkoholkonsum, sodass wir empfehlen bestehende Gesundheitsprogramme (Reduktion von Rauchen und Alkohol) zu forcieren. In **Slowenien** ist das Hauptproblem das hohe Mortalitätsrisiko, weshalb Verbesserungen in Screening, Diagnostik und Therapie zu einer Risikoreduktion führen sollten. In **Österreich** wurde ein höheres Risiko für Zervix- und Magenkarzinome festgestellt. Für Zervixkarzinome ist bekannt, dass gut organisierte Screening-Programme Inzidenz und Mortalität effektiv reduzieren können. Für Magenkarzinome scheinen primäre Präventionsmaßnahmen (Aufklärungsprogramme über gesunde Ernährung) das Mittel der Wahl zu sein.
In der **Schweiz** können wir eine besonders günstige Situation für die meisten Tumorentitäten feststellen, lediglich beim Korpuskarzinom wurde ein geringes zusätzliches Risiko festgestellt.

Pregled najpomembnejših ugotovitev in poziv k ukrepanju

Glavni namen raziskave je bil predstaviti geografsko porazdelitev incidence in umrljivosti pri najpogostejših vrstah raka v alpski regiji.

Pri projektu je sodelovalo 14 registrov raka iz Avstrije, Italije in Švice ter Register raka Republike Slovenije. V obravnavanem področju prebiva šest milijonov ljudi. Za potrebe analize je bila alpska regija razdeljena v 219 geografskih enot s povprečno 19.383 prebivalci. V raziskavi je bilo obravnavanih 12 najpogostejših lokacij raka. Raziskava je nadaljevanje že objavljenega atlasa bremena raka v alpski regiji za obdobje 1996 – 2000.

Kakovost zbranih podatkov je v splošnem ustrezna, nekaj pristranosti v analize pa bi lahko prinesle znane razlike pri diagnostičnih postopkih z01a ugotavljanje raka mehurja, pri definiciji in registraciji limfomov, mieloma in levkemij ter pri kodiranju vzroka smrti pri bolnicah z rakom na maternicnem vratu in maternicnem telesu.

Rezultati pri moških: Pri pripravi podatkov za vse rake skupaj smo pri moških poleg bolnikov z nemelanomskim kožnim rakom izključili tudi bolnike z rakom prostate, saj na incidenco tega raka močno vplivajo razlike v intenzivnosti določanja PSA – v Avstriji so se incidenčne stopnje raka prostate ob uvedbi množičnega testiranja podvojile. Rezultati za vse rake skupaj kažejo geografski gradient incidenčnih stopenj; nižje incidenčne stopnje so v Avstriji in Švici, visoke pa v Italiji (razen v pokrajinah Trention in Južna Tirolska) in v Sloveniji. Opisani gradient je še bolj kot pri incidenčnih očiten pri umrljivostnih stopnjah. Največja ogroženost z raki glave in vratu je bilo ugotovljena v italijanskih območjih, nekoliko večja pa je bila ogroženost tudi v vzhodnem delu Slovenije. Z želodčnim rakom so najbolj ogroženi prebivalci Slovenije in nekaterih predelov Tirolske, Južne Tirolske, Trentina in Sondria, manjše tveganje za nastanek te vrste raka pa imajo prebivalci v švicarskih pokrajinah. Največje breme raka debelega črevesa in danke je bilo ugotovljeno v Sloveniji (še zlasti visoka tam je umrljivost). Z jetrnim rakom so najbolj ogroženi prebivalci v italijanskih območjih in v pokrajini Ticino. V Italiji (razen Južne Tirolske in pokrajine Trentino) opažamo tudi večje breme pljučnega raka, je pa bilo breme tega raka še nekoliko večje v Sloveniji. Pri raku prostate so bile visoke incidenčne stopnje zabeležene v avstrijskih registrih, v Sloveniji pa je bilo ugotovljen relativen presežek smrti zaradi tega raka. Presežek smrti zaradi raka mehurja je bilo ugotovljen na italijanskih območjih (z izjemo pokrajine Trentino) in v Sloveniji. Bistvenih presežkov v bremenu limfomov, mieloma in levkemij ne ugotavljamo, prav tako pa pri teh rakih ni prisotne pričakovane odvisnosti med incidenco in umrljivostjo.

Rezultati pri ženskah: Razen nekoliko večje umrljivosti zaradi raka v Sloveniji, bistvenih odstopanj v bremenu vseh rakov skupaj med pokrajinami ne opažamo. Razlike v pojavljanju raka med pokrajinami so pri ženskah na splošno nižje kot pri moških. Breme rakov glave in vratu je povečano v Benečiji,

Sondriu in v Furlaniji-Julijski krajini (tu je povečano le tveganje smrti). Ogroženost z želodčnim rakom je povečana na Tirolskem, Južnem Tirolskem, Benečiji, Furlaniji-Julijski krajini in vzhodnih predelih Slovenije. Umrljivost za rakom debelega črevesa in danke je povečana v Sloveniji. Posebej visoka ogroženost z jetrnim rakom je v italijanskih pokrajinah Trentino, Benečija in Furlanija-Julijska krajina. Breme pljučnega raka je povečano v centralnem delu Tirolske, v Benečiji in v nekaterih predelih Slovenije. Ponekod opažamo nekoliko večjo ogroženost z rakom dojke, vendar tveganja smrti v teh predelih ni večje, zato lahko večjo ogroženost pripišemo različni udeležbi v presejanjih z mamografijo. Večja ogroženost z rakom maternicnega vratu je bilo ugotovljena v vzhodnih predelih Tirolske, na Koroškem in v Sloveniji, pri čemer obstaja medsebojna odvisnost med incidenco in umrljivostjo. Breme raka maternicnega telesa je povečano v Sloveniji in švicarskih pokrajinah (predvsem umrljivost). Pri raku jajčnika opažamo nekaj presežka v okolici Salzburga. Ogroženost z rakom mehurja je povečana v Benečiji, vzhodnih predelih pokrajine Trentino in na Koroškem, vendar tveganje smrti ni povišano, zato lahko večjo ogroženost pripišemo razlikam v diagnostičnih postopkih in/ali registraciji raka mehurja. Ogroženost z limfomom, mielomom ali levkemijo je nekoliko višja v nekaterih švicarskih pokrajinah, vendar tveganje smrti zaradi teh rakov ni povišano, zato lahko večjo ogroženost tudi tu pripišemo razlikam v diagnostičnih postopkih in/ali registraciji.

Ugotovili smo razlike v bremenu raka tako v posameznih področjih alpske regije, kot tudi med posameznimi vrstami raka. V svojih priporočilih smo te razlike upoštevali. V **Italiji** smo opazili povišano breme rakov glave in vratu, jetrnega raka in raka mehurja. Vsi trije našteti raki so povezani s kajenjem in pretiranim uživanjem alkohola, zato je naš poziv k boju proti vsem trem rakom usmerjen k spodbujanju večje dejavnosti za omejevanje kajenja in uživanja alkohola. V **Sloveniji** je najbolj problematično povečano tveganje smrti za rakom, kar nas opozarja, da je treba posodobiti presejanje, diagnostiko in postopke zdravljenja, s čimer bo mogoče to tveganje znižati. V **Avstriji** je povišano breme raka maternicnega vratu in želodčnega raka. Znano je, da je z dobro organiziranimi presejalnimi programi mogoče učinkovito znižati incidenco in umrljivost raka maternicnega vratu, za preprečevanje zbolevanja za želodčnim rakom pa je najučinkovitejši ukrep zdravo prehranjevanje. V **Švici** so razmere na področju zbolevanja in umiranja za rakom precej ugodne; ugotovljena je bila le nekoliko večja ogroženost z rakom maternicnega telesa.

4 COUNTRY-SPECIFIC DESCRIPTION

4.1 Italy Sandro Tognazzo

4.1.1 Incidence data

Among the six Italian Cancer Registries participating in the present Atlas:

- South Tyrol, Trentino and Sondrio are established within the respective Local Health Units;
- Varese, Veneto and Friuli Venezia Giulia are established in Cancer Research Institutions - Istituto Nazionale Tumori (INT) Milano, Istituto Oncologico Veneto (IOV) Padova, Centro di Riferimento Oncologico (CRO) Aviano – and supported by the regional governments (Regione Lombardia - Direzione Generale Sanità, Regione Veneto - Assessorato alle Politiche Sanitarie, Agenzia Regionale Sanità Friuli Venezia Giulia, respectively).

Although each registry covers the population of a single province, except Friuli Venezia Giulia and Veneto, this publication considers only cancer cases resident in Alpine areas.
The entire population of Sondrio (176,856 inhabitants), Trentino (477,017 inhabitants) and South Tyrol (462,999 inhabitants) resides in Alpine areas, whereas in Varese (812,477 inhabitants) the Alpine population makes up 18% of the total.
In Friuli Venezia Giulia (four provinces) the entire population is registered (1,183,764 inhabitants), of whom 6.4% reside in the Alpine areas, characterised as municipalities with medium/high economic disadvantage [1]. The municipality of Tolmezzo, located at the centre of the mountain area, was excluded because of its low economic disadvantage.
In Veneto (seven provinces), 49% of the regional population is registered (2,213,673 inhabitants), of whom 10% live in the Alpine area, mainly in Belluno Province.
As to the time period of availability of data, Sondrio and Friuli Venezia Giulia reported for 2001-2005, Trentino for 2000-2004, South Tyrol and Veneto for 1999-2003, Varese for 1998-2001.

4.1.2 Registration system

Three main diagnostic sources are used by all Registries: hospital discharge (HD) records, pathology reports (P) and death notifications (DC). HD are collected from Local Health Units or Regional Information Systems, depending on each registry's coverage and organization; P records are collected from Pathology Departments in the registration area and from other main centres of attraction. DC are extracted from the Nominal Registry of Causes of Death (RENCAM). In the case of Trentino and South Tyrol, this registry is managed by the Provincial Bureaus of Statistics. In all other cases, notifications are coded by the Local Health Unit of residence and collected from the latter and/or at the regional level.
The use of automated procedures for case definition is a distinctive feature of all the registries participating in the present Atlas [2-7] except South Tyrol. Concordance among collected diagnoses, coded in a standard nomenclature (ICD 9, ICD-O, SNOMED), is assessed by computer program. A relevant share of cases is automatically accepted, ranging from 50% to 59% of the total number of registered cancers; only rejected cases are manually evaluated. The diagnostic sources processed are previously linked with population files, to exclude patients resident outside the study areas.
The South Tyrol Cancer Registry uses a passive notification system, based on a form completed by all care units in that province. Such notifications are checked and integrated in an active procedure using

the three mentioned diagnostic sources and a further flow deriving from the procedure of reimbursement for care received at Innsbruck Medical University (Austria).
When manually defining cases, all registries exploit available auxiliary sources such as radiotherapy records, radiology and laboratory analysis reports, and clinical notes.

4.1.3 Mortality data

As far as possible, the official mortality data published by the National Institute of Statistics (ISTAT) is used. Because of the particular administrative autonomy of the provinces of Trentino and South Tyrol, the corresponding mortality data substantially coincide with those used in case registration. The same does not hold true for the other areas where, furthermore, the official figures were not available for the years 2003-2005. Local data, deriving from the above-mentioned RENCAM flow, were used for such periods; comparison of the two sources in the preceding years showed no relevant differences from official data.

4.1.4 Data quality

Incidence data are checked according to the criteria established by the International Agency for Cancer Research (IARC), using standard software tools provided by that agency.
Synthetic indications about overall data quality may be drawn from three standard indicators: proportion of cases with histological verification (HV), proportion of cases referred only by death certification (DCO), ratio of mortality to incidence (RMI). For all sites analyzed, these indicators are rather similar to the expected and to those calculated in the pool of the participating registries.
We observed that for all cancers aggregated, only HV values are lower than those of the pool (males 86%-91% versus 93%, females 84%-91% versus 92%), but are far from being abnormally low. A relevant contribution is made by lung cancer, for which the range of difference in HV figures is wider (females 68%-83% versus 88%, males 72%-89% versus 90%).
A further note concerns mortality for cervix and corpus uteri. In Italy, a trend exists to use the code corresponding to "Uterus, unspecified" as cancer site when coding the cause of death; this induces under-reporting for the two sub-sites, and low RMI ratios can be observed.

4.1.5 Use of data, reporting

All participating Registries have their data reported by the International Agency for Research on Cancer (IARC), in the publication "Cancer Incidence in Five Continents – Vol. IX."
They also contribute to the Italian national database, kept by Associazione Italiana dei Registri Tumori (AIRTUM), from which some important reports on incidence and survival have derived [8-10].
They are participating in the EUROCARE study, coordinated by the above-mentioned INT in Milano and by Istituto Superiore di Sanità (ISS) in Rome, and are involved in a number of studies, including a national study on the impact of mammographic screening, coordinated by the Centre of Diseases Control - Ministry of Health.
Each registry distributes its data in the form of local reports and on its own web site, or that of the Institution of affiliation [11].

4.1.6 Population

The main socio-demographic indicators [11,12] are summarized in the following table

Tab. 5: Socio-demografic indicators by registry

INDICATOR		REGISTRY					
		Varese	Sondrio	South Tyrol	Trentino	Veneto	Friuli Venezia Giulia
Resident population in Alpine areas (Census 2001)		144,304	176,856	462,999	477,017	230,612	76,146
Females (%)		51.5%	51.2%	50.8%	51.3%	52.0%	51.3%
Population density (inhabitants/km^2) (Census 2001)		316.9	55.0	63.0	77.0	55.6	21.6
Ageing index (Census 2001) (+)		137.6	124.3	92.0	120.7	168.4	226.6
Life expectancy at birth 2001 (*)	Males	*77.5*	75.0	77.2	77.3	75.0	*76.5*
	Females	*83.6*	83.3	84.1	84.2	83.2	*83.0*
Birth rates/1000 - 2001 (*)		*9.0*	8.9	11.8	10.4	7.9	*8.1*
Mortality rates/1000 - 2001 (*)		*9.2*	9.7	7.8	9.4	11.9	*11.8*
% Foreign residents of total residents	Census 2001	3.3%	1.4%	3.1%	3.4%	2.3%	2.1%
	January 2005	n.a.	2.3%	4.6%	5.5%	4.1%	n.a.
Employment by economic sector (Census 2001)	Agriculture	2.0%	3.6%	9.9%	5.0%	2.4%	4.4%
	Industry	46.1%	35.4%	26.4%	30.7%	44.7%	44.8%
	Other activities	51.9%	60.9%	63.7%	64.3%	52.9%	50.8%
Unemployment rate (Census 2001)		5.5%	5.3%	2.3%	3.9%	3.7%	5.1%

Source: National Institute of Statistics (ISTAT), General Population Census 2001, Current demographic indicators.
(+) Per cent ratio of the oldest population (65 years or more) to the youngest population (0-14 years).
(*) For Varese and Friuli Venezia Giulia, the indicator refers to the whole province and region, respectively.

With the exception of South Tyrol, all populations are rather aged, particularly in Veneto and Friuli Venezia Giulia, and exhibit a relatively low density, except in Varese. Life expectancy is similar, especially among women, while natural demographic balance is positive in South Tyrol and Trentino, negative or null elsewhere. Immigration from foreign countries has notably increased during the study period, but the proportion out of total residents is lower when compared to regional figures (in January, 2005: 6.3% Lombardy, 6.1% Veneto, 4.9% Friuli Venezia Giulia).

Most employed persons work in the tertiary sector, particularly in Trentino, South Tyrol and Sondrio, but industrial employment holds prominent importance in Varese, Veneto and Friuli Venezia Giulia mountain areas. The occupational role of agriculture is merely residual, only South Tyrol represents a possible exception. Unemployment at Census date was not dramatic; while quite low in South Tyrol, Trentino and Veneto, it was a bit higher than the corresponding regional levels (Lombardy 4.7%, Friuli Venezia Giulia 4.9%) in the other areas.

Figures on financial resources per capita [7] are available at the province level only for Trentino and South Tyrol; Gross Domestic Product (GDP) and Public Expenditure for Health (PEH) in 2003 for the two provinces, expressed in Euros, were, respectively, 27,929 and 1,476 (GDP); 29,521 and 1,921 (PEH).

The corresponding figures for Lombardy (including Varese and Sondrio), Veneto and Friuli Venezia Giulia were, respectively: 30,449, 26,957, 25,428 (GDP); 1,340, 1,375, 1,746 (PEH).
In 2003, the share of the total expenditure for health over GDP was: Lombardy 6.2%, Veneto 6.9%, Friuli Venezia Giulia 8.1%, Trentino and South Tyrol (aggregated) 7.5%.

4.1.7 Health system

In the Alpine areas considered, 13 local health units (LHU) are responsible for all public health-related matters; there are 39 public hospitals in the territory, seven of which are managed autonomously.
In the majority of cases, comprehensive services for cancer diagnosis, surgery and chemotherapy are provided locally. Radiotherapy is available within the province of residence, with the exception of South Tyrol, where patients had to be referred elsewhere during the study period; the nearest centres were in Trentino and Innsbruck.
The Cancer Institute (CRO) located in Aviano, near the border between Friuli Venezia Giulia and Veneto, attracts a consistent number of patients from both regions.
Relevant health migration outside the province occurs in Varese and Sondrio, to the above-mentioned INT in Milano and other referral centres for cancer treatment, and in South Tyrol, to the University Hospital in Innsbruck. Less consistent flows of patients exist, with local relevance, from some Trentino areas to the hospitals of Verona and Feltre, in Veneto.

4.1.8 Screening activities

During the period of analysis, organized mammographic screenings programmes were activated in all areas, except Friuli Venezia Giulia. In Varese and South Tyrol, the first round of screening started during the last year considered (2000 and 2003, respectively), while elsewhere it started in the first years (Sondrio 2001, Trentino 2000, Veneto 1999).
Organized cervical cancer screening has been under way in Trentino since 1993; similar programs started later in Friuli Venezia Giulia, Veneto and South Tyrol (1999, 1998-2001 and 2001, respectively). In Sondrio and Varese, there are presently no organized screenings, but a specific sample survey [13,14] indicates that about 80% of women, aged 25-65 years, have a smear taken at least every three years.
No colon-rectum screenings were conducted during the study period, except in Veneto (where the starting date varies between 1998 and 2001, depending on the sub-area).
There are no organized screenings on prostate cancer, but PSA testing is very diffuse, with a widely variable intensity among the different areas.

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4.2 Switzerland Alessandra Spitale

4.2.1 Registry structure and incidence data

Swiss data included in the present project derive from three Cancer Registries of the southern, eastern and northeastern parts of the country.

The Cancer Registry of Canton Ticino (www.ti.ch/cancer/), located in the south of Switzerland (total area 2,812 km2), was instituted in 1995 by the local government through a cantonal law, based on a popular initiative, and began data collection in 1996. It is located within the Cantonal Institute of Pathology and is staffed by a full-time medical doctor (epidemiology specialist and Registry head), two data managers (1 full-time and 1 part-time), responsible for data collection and coding, and a full-time statistician, responsible for quality control and data analysis. About 80% of cases are reported by the Cantonal Institute of Pathology and Cytology. Additional cases come from main public and private hospitals, radiotherapy and oncology centres, haematology laboratory, oncologists, general practitioners and from the Cancer Registries in Geneva, Vaud, Basel, Zürich and St. Gallen (mostly skin cancers).

The Cancer Registry of Graubünden – Glarus (www.krebsregister-gr.ch/), covering the population of the two corresponding cantons in the eastern part of Switzerland (total area 7,785 km2), is located within the Department of Pathology at the main hospital at Chur and started its activity in 1990. The staff includes a part-time pathologist and part-time registrars. About 85% of the new cases are directly reported through the pathology network, the remainder being found by scrutinizing medical documents in about 30 departments of the 12 hospitals of the two cantons. Information about patients hospitalized outside the registration area is provided by the Cancer Registries in Zürich, St. Gallen and Ticino.

The Cancer Registry of St. Gallen – Appenzell (www.krebsliga-sg.ch/de/krebsregister/) covers a total area of 2,430 km2 in the northeastern Switzerland (cantons of St. Gallen, Appenzell AR and Appenzell IR). It was founded in 1960 at the Department of Pathology in St. Gallen Central Hospital. It was hospital-based until 1980, when it became population-based. At present the Registry has 4.8 full-time positions. All possible data sources in the catchment area are systematically exploited. Active case finding includes search in the central pathology laboratory, the departments of oncology, haematology, radiotherapy, neurosurgery, paediatrics and the geriatric clinic of the central hospital and in all other acute hospitals and laboratories in the region. Cancer Registries of the two neighbouring cantons of Zürich and Graubünden - Glarus as well as other Cancer Registries in Switzerland report cases diagnosed or treated in their respective catchment area. The three Registries routinely collect and record all invasive and in situ tumours according to the IARC/IACR and ENCR guidelines. Topography and morphology coding are performed by trained personal on the basis of the third version of the International Classification of Diseases for Oncology (ICD-O-3). In all Cancer Registries, cases are identified by active and/or passive search under a voluntary agreement between the Registry and the medical institutions (private and public hospitals, laboratories) or general / specialist medical practitioners.

4.2.2 Mortality data

The official nationwide mortality data collected by the Swiss Federal Office of Statistics were used to analyse cancer mortality in the Swiss cantons involved in the study (Ticino, Graubünden - Glarus and St. Gallen - Appenzell).

4.2.3 Data quality

All information are actively collected, checked and manually coded (ICD-O-3) by the Registry Staff before being entered in the database. The first quality inspection and plausibility tests are automatically performed by the computer system during the data entry phase. In addition, IARC checks and multiple primary programs together with several other plausibility, validity and consistency checks, such as logical sequences of dates, validity of codes, morphology by topography, by sex and age, are established and applied by each Cancer Registry on a periodic basis. Quality indicators (i.e. DCO, HV and RMI) are reported in the Results Section of the present Atlas, according to tumour site and sex.

4.2.4 Use of data, reporting

Data are used by the registries to produce estimates of cancer incidence, survival and mortality in Switzerland, and by the International Agency for Research on Cancer (IARC) for publication in Cancer Incidence in Five Continents (www-dep.iarc.fr/). Policy makers more and more often use Cancer Registry data to plan and evaluate health services. Registries are also currently involved in epidemiological research at the local, national and international level, such as bio-molecular epidemiology, incidence and survival analysis (e.g. ACCIS, EUROCARE, HAEMACARE, CONCORD, EUROCIM).

4.2.5 Population

The Swiss population covered by the three Registries amounts on average to 1,062,455 inhabitants (520,100 males and 542,355 females) for the period 2001-2005: 29.8% (316,255) in Ticino, 21.2% (225,241) in Graubünden - Glarus and 49% (520,959) in St. Gallen – Appenzell. The percentage of foreigners varies across the cantons: about 27% in Ticino, 17% in St. Gallen – Appenzell, 20% in Graubünden - Glarus.

The official language is Italian in Ticino and German in St. Gallen, Appenzell and Glarus.

Graubünden is the only canton of Switzerland with three official languages: Italian (spoken by 10% of the population), German (68%) and Romanish (15%). A further 7% of the population speaks other languages.

The Ticino economy is mainly based on the services sector; trade and restaurants, financial, insurance and real estate activities, health and social care, education, transport and communication, public administration employ 80% of the population, followed by industry and manufacturing (18%) and farming and forestry (2%).

Agriculture, forests and mountain pasturage in summer, as well as tourism, concentrated in the mountains, are the pillars of the Graubünden economy. Glarus is one of the most industrialized cantons and 80% of its generated output is exported around the world; cotton printing, hydroelectric plants, metal and machinery factories, paper mills, together with dairy farming and cattle breeding in the mountains represent the most important activities.

The St. Gallen - Appenzell economy is characterized by important industries, metal machines and construction, which are broadly distributed over much of the region. Cattle breeding and dairy farming are the main activities in mountains areas.

4.2.6 Health system, especially screening programs

The political system in Switzerland is characterized by both liberalism and federalism. This is also reflected by the organization of the Swiss health care system at three different levels of government: the federal government, the cantons and the communes. It is a liberal and decentralized system: public and private medical institutions co-exist, health providers are free to choose where to locate and patients are free to choose providers within a canton.

In Canton Ticino there are four public hospitals (Ente Ospedaliero Cantonale, ECO) and six private facilities. There is only one radiotherapy department for the whole region, namely at the hospital in Bellinzona.

General healthcare in Graubünden and Glarus is provided mostly in the two main hospitals in the capital Chur and in Glarus. Radiotherapy is available only at the centre in Chur.

In St. Gallen most cancer patients are treated at the central hospital in the city of St. Gallen or in one of the peripheral acute hospitals within the region. Some people living in areas adjacent to the urbanised Canton of Zürich seek care there.

The areas covered by the Cancer Registries of Canton Ticino and of St. Gallen - Appenzell presently have no cancer screening programmes. In Ticino, spontaneous screening is well accepted by the population for either breast or cervical cancer, and opportunistic PSA testing is common. In St. Gallen – Appenzell, opportunistic screening is well established for cervical cancer; but early detection of breast cancer should be improved.

In the cantons Graubünden and Glarus, spontaneous breast cancer screening and PSA-screening for prostate cancer are widely accepted and performed, whereas screening for cervix cancer is not thoroughly established and needs further awareness on the part of rural population at the periphery.

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4.3 Slovenia Maja Primic-Žakelj

4.3.1 Population

The Republic of Slovenia covers about 20,000 km2, with its northwestern third being Alpine territory, included in this publication. The population at the most recent census in 2002 was 1,964,036, making the population density approximately 100 inhabitants per km2. About half of the population lives in urban areas (>3000 inhabitants). Main ethnic group is Slovene (83%). The prevailing religion is Roman Catholic; 15% of the population is younger than 15 years and the same percentage of the population is older than 65 years. In 2005, life expectancy was 74.1 years for men and 81.3 years for women. The birth rate was 9.1 per 1,000 inhabitants, the mortality rate 9.4 per 1,000 with major causes of death being cardiovascular diseases (40%) and cancer (28%). Slovenia GDP equals 14,000 € per capita, where industry makes up 40% of the GDP, with agriculture contributing only 3.2%. The main industries include manufacturing of food and beverages, electronics, electrical machinery, metal processing and metallurgy and motor vehicles. The agricultural sector is dominated by dairy farming and stock breeding. The main crops are corn, barley and wheat.

4.3.2 Cancer incidence data

The cancer incidence data in Slovenia is collected by the Cancer Registry of the Republic of Slovenia (CRS). CRS is one of the oldest population-based registries in Europe; it was founded in 1950 at the Institute of Oncology Ljubljana (IOL). Notification of cancer has been compulsory since the beginning and prescribed by law. CRS is staffed by two full-time medical doctors, specialized in epidemiology and public health, a junior researcher studying statistics, four registrars, a computer operator and a part-time system analyst.

4.3.3 Registration procedure

The main sources of data are notifications gathered from all hospitals and diagnostic centers in Slovenia, and exceptionally from primary health care centers in cases in which the patient was not referred for further diagnostic investigations and/or treatment. Death certificates and autopsy protocols stating cancer diagnosis complete this information. When needed, requests are sent to notifiers to ensure accurate information as well as to the hospitals or doctors who signed the death certificates if the patient was not yet registered. Case identification is based on a personal identification number that also enables accurate follow-up of patients' vital status by regular linkage of our data to the Central Population Register. Data protection regulations are strictly respected.

Trained registrars code the notification information. Since 1997, cancer sites have been coded according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). For morphology registration, since 1983 the morphology part of International Classification of Diseases for Oncology has been used, since 2001 its third edition. The IARC rules are respected for coding multiple primary tumors.

4.3.4 Data quality

The reliability and completeness quality measures are regularly monitored and published in CRS annual reports. The small and stable proportion of cases registered after publication of annual reports (about 4%) shows that the majority of cases are reported to CRS. Similarly, the ratio between mortality and incidence is stable over years, too. The percentage of DCO cases is small as it has recently not exceeded two. More than 90% of registered cases are microscopically confirmed. However, we are aware of incomplete registration of patients treated in the outpatient departments only (e.g. non-melanoma skin cancer, multiple myeloma, chronic lymphatic leukaemia, as well as prostate cancer).

4.3.5 Use of data, reporting

Annual reports on cancer incidence have been published since 1951, since 1965 in Slovenian and English. Annual reports for the years 2001–2006 are available on IOL website: www.onko-i.si/crs. The data collected and processed serve as the basis for assessing the national cancer burden, for planning and evaluation of primary prevention, diagnosis, treatment and rehabilitation programs, for planning facilities and funding needed for cancer control (personnel, equipment and hospital capacities) as well as for clinical and epidemiological studies in Slovenia. Our data are also included in international databases and are often used in international studies. The results of our studies are published in national and foreign medical literature and as publications for the general public. CRS data have been published in all eight volumes of Cancer Incidence in Five Continents. The data on cancer incidence and mortality were also included in the international databases EUROCIM, GLOBOCAN, ACCIS. The survival of Slovenian cancer patients is included in and analyzed by the international studies EUROCARE II, EUROCARE III and EUROCARE IV.

4.3.6 Cancer mortality data

Data on the deceased and on the cause of death are routinely collected for the entire territory of Slovenia by the Institute of Public Health of the Republic of Slovenia, where the database of the Register of Deceased Persons is kept. Determination of death and cause of death are the responsibility of the physician. Following confirmation of death, the physician issues a death certificate and completes the cause-of-death section in accordance with WHO guidelines. For statistical purposes, physicians at the regional institutes of public health specify the underlying cause of death using the coding system of the ICD-10. In Slovenia, only the underlying cause of death and external cause of death by violence are coded for routine data processing.

4.3.7 Health system

Cancer screening

Opportunistic cervical cancer screening was introduced in regular gynaecological practice in 1960 in Slovenia. The proportion of the population screened was unknown, and there were no standards for quality assurance and control; the cervical cancer incidence rose until 1997. As a public health response, a nationwide organized screening program was introduced in 2003. A pilot study of organized screening began in the central and costal parts of the country three years earlier, in 1999. Coverage of population aged 20-64 in the period 2003–2005 was 65%.

No population-based breast cancer screening was implemented in Slovenia until 2008, but in the period 2001–2005 women could have "preventive", opportunistic screening mammography in diagnostic settings. Furthermore, preventive clinical breast examination was offered to women who attended gynaecology clinics in primary health care. This opportunistic screening, lacking quality control, has not achieved satisfactory results. The number of screened women is not known, but from the findings of several studies, it seems that the proportion of women in the age group 50-69, where screening is most effective, is low, that screening intervals are too short, and that many women who attend the opportunistic screening are too young to benefit from it.

Screening for colorectal cancer was not introduced in Slovenia until 2008. In the period 2001–2005, colonoscopy screening was offered to patients in some diagnostic settings, but the volume of this activity is unknown.

There is no explicit policy on prostate cancer screening using the prostate-specific antigen test (PSA), but this test is becoming more popular on an opportunistic basis despite the continuing controversy about its value.

Diagnosis and treatment of cancer

In Slovenia cancer treatment is fully covered by health insurance. Healthcare centers and private practitioners provide primary and outpatient secondary health care; most of them are included in the public healthcare network, which has a contract with the Health Insurance Fund. There are 12 general hospitals across the country as well as clinical centers in Ljubljana and Maribor, acting as tertiary healthcare facilities. The majority of cancer patients receive their initial diagnosis from specialists in one of the general hospitals or clinical centers, with only about 15% being diagnosed at the Institute of Oncology Ljubljana. However, about 50% of patients diagnosed elsewhere are subsequently referred to the IOL.

The Institute of Oncology, founded in Ljubljana in 1938, is the only national cancer center in Slovenia. Besides patient care, it is involved in research and education. Working closely with specialists from several other secondary and tertiary clinical departments treating cancer patients it is the only comprehensive cancer center in Slovenia. While common cancers are also treated in general hospitals, the IOL is the only referral center for rare cancers. Except for skin cancer, radiotherapy is provided only at this institute.

Palliative care

Palliative care is an important part of the management of cancer patients. It is provided in hospital settings or by general practitioners. The IOL has recently established a special team for palliative care but, at present, palliative care and specialist rehabilitation of cancer patients are the least well developed component of cancer control in Slovenia.

4.4 Austria Zorica Jukić

Four of Austria's existing regional cancer registries, the cancer registries of Carinthia, Salzburg, Tyrol and Vorarlberg, are participating in this project. All these registries are population-based and are members of the International Association of Cancer Registries (IACR). Cancer registration in Austria is required by law going back to 1969; hospitals, pathology institutes as well as institutes for forensic medicine, but not private institutes, are required to report every cancer case to the Austrian National Institute of Statistics – *Statistik Austria*. Regional cancer registries also report their data to *Statistik Austria,* who runs Austria's nationwide cancer registry.

4.4.1 Population

The following table describes some key facts of the population.

Tab. 6: Population in Austria

	Carinthia	Salzburg	Tyrol	Vorarlberg
Area	9538 km²	7156 km²	12 640 km²	2601 km²
Habitable area - 2008	25.7 %	20.3 %	11.9 %	21.8 %
GDP in € per capita in year 2005	25 400	33 000	30 800	31 200 €
Inhabitans – Census 2001	559 404	515 327	673 504	351 095
Foreigners 01.01.2008	6.5 %	12.5 %	10.4 %	12.7 %
% of population aged between 25 and 64 with university degree	8.7 %	10.9 %	9.5 %	8.2 %
Unemployed rate 2007	3.9 %	3.0 %	2.8 %	3.6 %
Life expectancy at birth in 2007	77.74 males 83.44 females	78.43 males 83.68 females	78.83 males 83.72 females	78.3 males 83.76 females

4.4.2 Registry structure

The **Cancer Registry of Carinthia** was established in 1987 and is under the general management of the *Landessanitätsdirektion.* It is a part of the Department of Radiotherapy and Radioncology at Klagenfurt General Hospital and is managed by a medical oncologist. The two existing pathology departments in Carinthia, the Department of Pathology at Klagenfurt General Hospital and the Pathology Department at Villach General Hospital, report all the newly diagnosed malignant cancer cases, precancerous and in-situ lesions (CIS) to the cancer registry. Part of the histological diagnosis is performed by institutes outside Carinthia. However, due to the good cooperation between hospitals, the cancer registry is advised of the main cases. Malignant cases diagnosed without histological diagnosis are reported directly by clinics to the cancer registry.

The population in the western part of Carinthia generally attends the Lienz County Hospital, given easy road access to the hospital from that part of Carinthia. Lienz County Hospital does not report cancer cases to the Carinthian Cancer Registry.
The registry is staffed by a registry manager and 1.5 administration officers. IT support is provided by an external company (the company that produced the cancer registry program).
Data coding, check of staging, comparison with existing data are carried out by the registry manager (a medical doctor).
The **Salzburg Cancer Registry** was established in 1983. It is located within the *SALK* (Salzburg University Clinic) - Department of Internal Medicine III and is managed by a medical oncologist. The two existing pathology departments in the state of Salzburg, the *SALK* Department of Pathology and the Pathology Department at Schwarzach County Hospital, as well as the private pathology institutes report all the newly diagnosed malignant cancer cases, precancerous and in-situ lesions (CIS) to the cancer registry. Hospitals and medical doctors reported all new diagnosed cancer cases to the cancer registry via an official report form. Data from the oncological documentation system at the Department of Internal Medicine III at SALK was also included.
The registry is staffed by 1.5 administration officers.
Data are coded by trained staff.
The **Cancer Registry of Tyrol** commenced operations at the end of 1986 and has been population-based since 1988. The Cancer Registry of Tyrol is a department within the *TILAK,* the organisation responsible for managing Innsbruck Medical University Hospital and other smaller hospitals in Tyrol. All hospitals are required to report cancer cases. In addition, a second database manages information about cancer patients found in various sources: pathology reports (the main source), from radiotherapy units and other specialised cancer care units, department-specific systems and the diagnosis upon discharge from hospital.
The registry is staffed by an epidemiologist, a registrar and data entry clerks.
Data coding, check of staging and comparison with existing data is carried out by trained staff.
The **Cancer Registry of Vorarlberg** was established in 1978 by the head of Pathology at Feldkirch Hospital. It has been managed since 1981 by the *Arbeitskreis für Vorsorge und Sozialmedizin (AKS)* - the agency for preventive and social medicine.
The diagnostic finding of the Department of Pathology at Feldkirch Regional Hospital, Vorarlberg's only pathology facility, forms the starting point for recording malignant tumours cases. Cases without histological diagnosis are reported directly by clinics. Part of the pathology diagnosis is also undertaken by institutes outside Vorarlberg.
On the staff of the cancer registry are a scientific manager, the registry manager (a medical doctor), the administrative officer and staff members of the IT department of the *AKS* as required.
The administrative officer and registry manager subsequently process the data (coding, comparison of existing data, data entry).

4.4.3 Data quality

All four of the above-mentioned cancer registries used IARC check programs, and multiple cancer cases are registered according to the IARC rules.

Data were coded according to the International Classification of Diseases for Oncology (Carinthia ICD-O-1 until the end of 2002 and ICD-O-3 since 2003, Salzburg ICD-O-2, Tyrol ICD-O-3, Vorarlberg ICD-O-1 until 2003 and ICD-O-3 since 2004).
All four registries set up a DCN database, and finally a DCO database.
Data from the cancer registries in Tyrol and Vorarlberg have appeared separately in a publication entitled "Cancer Incidence in Five Continents Volume IX" issued by the International Association for Research on Cancer (IARC), data from the cancer registries of Carinthia and Salzburg are included in data from Austria (all registries report data to the Austrian National Cancer Registry).

4.4.4 Mortality

The official data collected by Statistik Austria were used to analyse cancer mortality.

4.4.5 Health system

Expenditure on health in the year 2006 in Austria was 10.2% of gross domestic product.
Access to therapy for all cancer patients is in Austria free of charge.
In the majority of cases cancer therapy is provided regionally. Special and complicated cases are treated at university hospitals in Innsbruck and Salzburg and at central hospitals in Feldkirch and Klagenfurt.
Indisputable oncological principles of the interdisciplinary approach are applied today.
Radiotherapy is available at university hospitals in Innsbruck and Salzburg and at central hospitals in Feldkirch and Klagenfurt.

4.4.6 Screening activities

During the study period no organised screening programs were established.
Opportunistic mammographic screening for breast cancer, cervical smear screening for cervical cancer, and PSA testing are available throughout Austria. Most screening activities are free of charge and are paid by insurance carriers.
Well organised and well used preventive care and/or early detection programmes organised by the AKS have been available in Vorarlberg for many years. A mammography screening program in Vorarlberg has been running since 1989.
Intensive PSA testing has been performed in Tyrol since 1992 and Vorarlberg since 1999/2000.
Carinthia has conducted some regional activities relating to colorectal cancer and melanoma.
In Salzburg and Tyrol, intensive melanoma precaution measures are carried out by dermatologists.

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5 RESULTS

5.1 All except for NMSC Vesna Zadnik

Tutte le sedi, esclusi tumori cutanei non melanotici e prostata
Alle Lokalisationen außer NMSC
Vsi raki razen nemelanomskega kožnega raka

5.1.1 Summary and Call for Action

Summery and Call for Action

There is an excess risk of cancer in the Veneto and Sondrio regions in both sexes. In males, there is also an excess risk in Friuli Venezia Giulia and Varese regions. In Slovenia, the mortality rates in males and females exceed the rates expected according to incidence rates. The last can also be noticed in the Trentino male population.

Cancer burden would be reduced if people made appropriate choices about their health and lifestyle habits [9]. Activities in the areas of health promotion and prevention (non-smoking, healthy diet, reducing alcohol consumption, physical exercise…) should be incorporated in national/regional cancer control strategies and organized population-based screening programs for cervical, breast and colorectal cancers should be offered to the target population. In regions where cancer mortality remains high, rapid access to diagnosis and multidisciplinary clinical care is needed, using the full range of appropriate treatments, as well as rehabilitation of cancer patients or appropriate palliative care.

Sintesi e proposte operative

Un eccesso di rischio neoplastico si osserva, in entrambi i sessi, nel Veneto ed in provincia di Sondrio. Nei maschi, un eccesso di rischio si riscontra anche in Friuli Venezia Giulia e nel Varesino. In Slovenia, per entrambi i sessi i tassi di mortalità sono superiori a quelli attesi in base ai tassi d'incidenza. Quest'ultima osservazione vale anche per la mortalità maschile del Trentino.

L'impatto del cancro potrebbe ridursi attraverso appropriate scelte individuali (abitudini e stili di vita). Le strategie regionali e nazionali per il controllo delle neoplasie dovrebbero includere attività di promozione alla salute e prevenzione primaria (astensione dal fumo, dieta sana, riduzione del consumo di alcolici, esercizio fisico, …). Programmi di "screening" organizzato, per i tumori mammari, colo-rettali e della cervice uterina dovrebbero essere estesi e offerti a tutta la popolazione potenzialmente interessata. Nelle regioni ove la mortalità per cancro è più elevata, sono necessari sia un accesso rapido alla diagnosi ed all'assistenza clinica multidisciplinare, utilizzando l'intera gamma di trattamenti idonei, sia la riabilitazione dei pazienti neoplastici e appropriate cure palliative.

Zusammenfassung und Schlussfolgerungen

Für beide Geschlechter besteht im Veneto und in der Region Sondrio ein erhöhtes Krebsrisiko. Für Männer besteht eine Risikoerhöhung auch in Friaul Julisch Venetien und in Varese. In Slowenien sind die Mortalitätsraten höher als man auf Grund der Inzidenzraten erwarten würde. Letzteres kann auch für die männliche Bevölkerung im Trentino beobachtet werden. Die Krebshäufigkeit könnte reduziert werden, wenn in der Bevölkerung entsprechende Aktionen bezüglich Gesundheitsbewusstsein und Lebensstiländerungen etabliert werden könnten. Die Aktivitäten auf den Gebieten der Gesundheitsförderung und der Prävention (z.B. Nichtraucherprogramme, gesunde Ernährung, Reduktion von Rauch, Steigerung körperlicher Aktivität) sollten in nationale und regionale Krebsstrategien eingebunden werden und organisierte bevölkerungsbezogene Screening-Programme für Zervix-, Mamma- und kolorektales Karzinom sollten angeboten werden. In den Regionen, mit hoher Krebsmortalität ist ein schneller Zugang zu diagnostischen und multidisziplinären, klinischen Einrichtungen notwendig, wobei das gesamte Spektrum der in Frage kommenden Behandlung, genauso wie die Rehabilitation oder Palliativeinrichtungen, angeboten werden sollten.

Povzetek in poziv k ukrepanju

Pri obeh spolih opažamo večjo ogroženost za rakom v Benečiji in pokrajini Sondrio, pri moških pa tudi v pokrajinah Furlanija-Julijska krajina in Varese. V Sloveniji je umrljivost zaradi raka tako pri moških kot pri ženskah večja, kot bi pričakovali glede na tamkajšnjo stopnjo zbolevanja. Enak pojav smo opazili tudi v pokrajini Trentino pri moških.

Breme raka bi lahko zmanjšali, če bi ljudje izbirali ustrezen, zdrav življenjski slog (9). Dejavnosti, ki krepijo zdravje in preprečujejo bolezen (življenje brez kajenja, uživanje zdrave hrane in čimmanj alkohola ter redna telesna vadba), bi morale biti del vsakega državnega ali lokalnega programa za obvladovanje raka; ciljnemu prebivalstvu bi morali zagotoviti možnost udeležbe v presejalnih programih za odkrivanje raka materničnega vratu, dojk ter debelega črevesa in danke. Prebivalstvu v pokrajinah, kjer je umrljivost zaradi raka zelo visoka, je treba omogočiti čim hitrejši dostop do diagnostike in multidisciplinarno klinično obravnavo, ki zajema ustrezno zdravljenje, rehabilitacijo in paliativno oskrbo bolnikov z rakom.

5.1.2 Introduction

The term 'cancer' covers a complex group of diseases, which can affect virtually any organ. Despite the fact that each cancer type is practically a unique disease with its own risk factors, treatment and prognosis, the group of all cancer sites together is important, as only this number can give us a full insight into the cancer burden in certain populations and allow us to suggest adequate public health interventions. However, in comparative international studies, cases of non-melanoma skin cancer (NMSC) are typically excluded from the analyses. NMSC is a very frequent but practically fully curable disease, yet its reporting is predictably incomplete and the proportion of unregistered cases varies greatly between cancer registries [1]. In the present analysis all cases of prostate cancer were excluded from the all sites analysis as well, as the PSA screening practice varies greatly among regions included in the Alpine region.

5.1.3 Epidemiology

It was estimated that there were 10.9 million new cancer cases and 24.6 million persons alive with cancer (within three years of diagnosis) in 2002 worldwide. About one-quarter of these cancers occur in Europe (approx. one-eighth of the world population lives in Europe) – in 2004 there were 2.9 million new cancer cases, approximately 54% of those occurring in men and 46% in women [2]. Even within Europe, incidence, mortality and survival rates vary considerably [3]. In the Alpine region, according to the last release of the publication Cancer Incidence in Five Continents, the crude incidence rates per 100,000 inhabitants are highest in Italy (about 700 in males and about 550 in females) and lowest in Slovenia (420 and 370 in males and females, respectively). The reported rates for Austria and Switzerland are very similar, being slightly below 500 in males and about 400 in females.

There were about 6.7 million cancer deaths in 2002 worldwide. Of these, 1.7 million cancer deaths occur in Europe; 56% in men, 44% in women [2]. When exploring the variability in rates among Alpine countries in the WHO mortality database, the highest cancer mortality was registered in Italy (325/100,000 in males and 225/100,000 in females), in Slovenia the rate in females was the same as in Italy, but in males it was somewhat lower (290/100,000). In Austria and Switzerland, the male rates were comparable (about 245/100,000), but lower than in Italy or Slovenia. Female mortality rate in Austria was 215/100,000 and in Switzerland only 185/100,000.

The 5-year relative survival of European adult patients diagnosed between 1995–1999 was 52%, being much better in female patients (58%) than in male (46%) patients. There is a remarkable difference in overall cancer survival between countries participating in our study: the 5-year relative survival of Slovenian patients was only 42%, of Italian it was 52%, of patients from Switzerland 55% and of Austrian patients 56% [4]. Population-based survival of cancer patients, as shown by cancer registries, is a complex indicator that reflects patients' characteristics as well as the organization, accessibility, quality and efficiency of the healthcare system.

5.1.4 Data quality

The proportion of DCO cases in our data set is small: the area average proportion of DCO is 2.0% in females and 1.5% in males (when prostate cancer cases are excluded from all sites but the NMSC dataset, the proportion of DCO cases in males rises by 0.1%). The highest proportion of DCO cases is noticed in Austrian registries, being 3.3% in females and 2.5% in males (3% without prostate cases). On average 93% of cases were microscopically verified in females and males. There is some variation between states in this indicator: the lowest proportion of microscopically verified cases was noticed in Friuli Venezia Giulia Province in females (86.1%) and in Sondrio Province in males (87.6%). The variation in the mortality/incidence ratio is reasonable. This indicator ranges from 0.44 to 0.53 in females and from 0.53 to 0.66 in males (prostate cancer cases not included). The highest values in both sexes are seen in Slovenia and the Trentino region, as was expected considering their highest mortality rates (see above). None of the data quality indicators exceeds the acceptable level, so the data applied seem to be adequate for proper cancer burden estimation.

5.1.5 Risk factors, early detection and screening

A set of lifestyle and environmental factors involved in the causation of cancer is already well defined – according to Doll's and Peto's estimates, which were published in 1981 [5] and reviewed in 1996 [6], the most important preventable risk factors for cancer death in the western population are tobacco and diet, each of which accounts for about one-third of all cancer deaths. The next important group of risk factors is infection, hormones, background ionizing radiation, occupation and alcohol, each of those accounting for 3%-10% of cancer deaths. Of relatively less importance are ultraviolet radiation, industrial products, water and air pollution and food contamination and additives. Danaei et al [7] estimated that about 40% of all cancer deaths are associated with nine leading modifiable risk factors in developed countries.

Treatment success is increased and mortality is lower if the cancer can be diagnosed at an early stage or even at a premalignant stage. Awareness of different visual body signs and symptoms that could easily be observed by anyone (patients or their general practitioners') is of crucial importance for early diagnosis.

Tests that are able to detect cancer before the disease is clinically recognized are screening tests. It is evidence-based that population-based screening effectively reduces cancer mortality in three cancer sites: it is nowadays recommended that screening tests be administered as a public health intervention for detecting cervical cancer (pap test of cervical smear in women over the age of 25 years), for detecting breast cancer (mammography for women over 50 years of age) and for detecting colorectal cancer (fecal occult blood test for men and women over the age of 50 years) [8-10].

5.1.6 Geographical variation

Females. The geographical variation in overall cancer risk in females in the Alpine region is small. The smoothed female cancer incidence map shows the highest cancer risk in the Veneto region, following by the Sondrio region and central parts of Carinthia and Tyrol regions.

The smoothed female cancer mortality map points out the statistically significant excess risk in Slovenia. The smallest mortality risks are in cantons in the western part of the Alpine region: St. Gallen – Appenzell, Graubünden - Glarus and Ticino.

Males. The smoothed male cancer incidence maps for all sites but NMSC and for all sites but NMSC and prostate are similar with the exception of higher incidence in some Austrian regions (i.e. Vorarlberg, Tyrol) on the map where prostate cancer cases are included. This difference can be explained by more intensive PSA screening in that state [11]. The regions with overall male cancer excess risk are similar to the female regions, but the extremes are even more evident. The highest risk areas are in Veneto and Friuli Venezia Giulia regions, following by the Varese and Sondrio regions.

The smoothed male cancer mortality maps for all sites but NMSC and all sites but NMSC and prostate are almost identical. There is a clear north to south gradient with excess risk in southern parts of the Alpine region. A special problem is seen in those regions, where the cancer incidence rate is low but the mortality rate is high, like in Slovenia and Trentino. These data probably reflect poor treatment results.

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Tab. 7: All except NMSC – Numbers and Rates - Females

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	6,910	477.6	242.0 (235.5, 248.5)	1.05 (1.03, 1.08)	3,028	209.3	83.0 (79.5, 86.5)	0.95 (0.92, 0.99)
Salzburg	5,375	400.4	234.9 (228.0, 241.9)	0.98 (0.96, 1.01)	2,403	179.0	84.0 (80.2, 87.9)	0.95 (0.91, 0.99)
Tyrol	7,253	414.0	241.8 (235.6, 248.0)	1.02 (1, 1.05)	3,294	188.0	85.1 (81.8, 88.4)	1 (0.96, 1.03)
Vorarlberg	3,214	356.7	223.3 (214.9, 231.7)	0.93 (0.89, 0.96)	1,581	175.5	85.7 (80.9, 90.4)	1 (0.95, 1.05)
Friuli Venezia Giulia	1,174	602.7	250.6 (231.7, 269.5)	1.01 (0.96, 1.07)	617	316.7	90.3 (80.4, 100.2)	0.96 (0.88, 1.03)
Varese	1,425	489.2	244.8 (230.2, 259.4)	1.03 (0.98, 1.09)	665	228.3	86.1 (78.4, 93.7)	0.97 (0.9, 1.05)
Sondrio	2,348	516.1	255.9 (243.8, 267.9)	1.07 (1.03, 1.11)	1,107	243.3	89.5 (82.9, 96.1)	1.01 (0.95, 1.07)
South Tyrol	5,156	437.6	235.9 (228.6, 243.2)	1.02 (0.99, 1.05)	2,424	205.7	84.4 (80.5, 88.4)	0.99 (0.95, 1.03)
Trentino	5,854	473.4	234.0 (227.0, 241.0)	0.98 (0.96, 1.01)	3,043	246.1	89.0 (85.1, 92.9)	1.01 (0.97, 1.05)
Veneto	3,732	618.8	278.2 (267.3, 289.2)	1.15 (1.11, 1.18)	1,724	285.9	93.2 (87.0, 99.3)	1 (0.96, 1.05)
Slovenia	16,161	419.0	233.3 (229.3, 237.3)	0.98 (0.97, 1)	8,378	217.2	91.4 (89.2, 93.6)	1.14 (1.12, 1.17)
Graubünden/ Glarus	2,358	413.6	226.4 (216.0, 236.7)	0.95 (0.92, 0.99)	1,049	184.0	81.4 (75.6, 87.2)	0.86 (0.81, 0.91)
St.Gallen/ Appenzell	4,902	372.9	217.4 (210.6, 224.2)	0.9 (0.88, 0.93)	2,159	164.2	77.0 (73.2, 80.8)	0.81 (0.78, 0.85)
Ticino	4,119	498.0	246.0 (237.3, 254.7)	1.02 (0.99, 1.05)	1,807	218.5	81.9 (77.3, 86.4)	0.89 (0.84, 0.93)
Total	**69,981**	**438.2**	**237.1 (235.1, 239.0)**	**1 (0.99, 1.01)**	**33,279**	**208.4**	**84.9 (83.9, 86.0)**	**1 (0.99, 1.01)**

Tab. 8: All except NMSC – Numbers and Rates - Males

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	7,955	588.2	340.4 (332.5, 348.3)	1.04 (1.02, 1.07)	3,568	263.8	144.5 (139.5, 149.6)	0.93 (0.9, 0.96)
Salzburg	6,009	477.6	325.3 (316.8, 333.8)	0.96 (0.94, 0.98)	2,531	201.2	126.1 (121.1, 131.2)	0.82 (0.79, 0.85)
Tyrol	8,430	505.1	343.9 (336.4, 351.5)	1.01 (0.99, 1.03)	3,444	206.4	129.5 (125.0, 134.0)	0.84 (0.82, 0.87)
Vorarlberg	4,658	530.4	382.6 (371.3, 393.8)	1.13 (1.1, 1.17)	1,770	201.6	138.7 (132.1, 145.4)	0.91 (0.86, 0.95)
Friuli Venezia Giulia	1,625	868.8	401.1 (379.9, 422.4)	1.21 (1.15, 1.27)	841	449.6	188.5 (174.4, 202.6)	1.18 (1.1, 1.27)
Varese	1,862	681.9	387.9 (369.4, 406.3)	1.17 (1.12, 1.22)	950	347.9	183.9 (171.9, 195.9)	1.19 (1.11, 1.26)
Sondrio	3,075	706.0	390.7 (376.1, 405.2)	1.17 (1.13, 1.22)	1,638	376.1	193.8 (184.0, 203.6)	1.26 (1.2, 1.32)
South Tyrol	6,385	556.9	346.3 (337.4, 355.1)	1.05 (1.02, 1.07)	2,932	255.7	148.0 (142.5, 153.6)	0.96 (0.92, 0.99)
Trentino	6,468	549.1	302.3 (294.4, 310.2)	0.91 (0.89, 0.93)	3,933	333.9	167.2 (161.7, 172.8)	1.08 (1.04, 1.11)
Veneto	4,500	807.7	403.5 (390.8, 416.2)	1.22 (1.19, 1.26)	2,233	400.8	183.9 (175.6, 192.1)	1.17 (1.13, 1.22)
Slovenia	16,970	460.9	311.9 (307.1, 316.8)	0.93 (0.92, 0.95)	10,210	277.3	198.0 (194.1, 202.0)	1.21 (1.19, 1.24)
Graubünden/ Glarus	2,848	512.1	311.0 (298.8, 323.3)	0.93 (0.89, 0.96)	1,381	248.3	135.3 (127.7, 142.9)	0.86 (0.81, 0.9)
St.Gallen/ Appenzell	6,155	477.1	311.3 (303.1, 319.5)	0.93 (0.91, 0.95)	2,748	213.0	127.9 (122.8, 133.0)	0.8 (0.77, 0.83)
Ticino	4,467	592.3	324.1 (313.9, 334.2)	0.95 (0.92, 0.98)	2,126	281.9	137.0 (130.8, 143.2)	0.87 (0.84, 0.91)
Total	**81,407**	**535.0**	**335.1 (332.7, 337.5)**	**1 (0.99, 1.01)**	**40,305**	**264.9**	**153.6 (152.1, 155.2)**	**1 (0.99, 1.01)**

Tab. 9: All except NMSC – Data quality

	FEMALES			MALES		
Country description	% DCO	% HV	RMI	% DCO	% HV	RMI
Carinthia	6.2%	95.2%	0.44	4.9%	94.9%	0.45
Salzburg	2.1%	92.3%	0.45	1.5%	93.2%	0.42
Tyrol	1.2%	94.3%	0.45	0.7%	95.8%	0.41
Vorarlberg	3.9%	97.2%	0.49	2.6%	97.8%	0.38
Friuli Venezia Giulia	0.6%	86.1%	0.53	0.3%	89.0%	0.52
Varese	0.1%	87.9%	0.47	0.2%	87.1%	0.51
Sondrio	0.7%	87.7%	0.47	0.5%	86.5%	0.53
South Tyrol	1.5%	91.4%	0.47	1.4%	91.7%	0.46
Trentino	1.8%	88.0%	0.52	1.0%	87.1%	0.61
Veneto	2.2%	88.2%	0.46	1.2%	88.8%	0.50
Slovenia	1.4%	95.5%	0.52	1.1%	94.9%	0.60
Graubünden/Glarus	0.5%	92.8%	0.44	0.3%	93.2%	0.48
St.Gallen/Appenzell	0.4%	94.7%	0.44	0.2%	95.3%	0.45
Ticino	2.7%	95.0%	0.44	2.0%	92.0%	0.48
Total	**2.0%**	**93.3%**	**0.48**	**1.5%**	**93.2%**	**0.50**

Fig. 1: All except NMSC – Incidence –Smoothed Map – Females

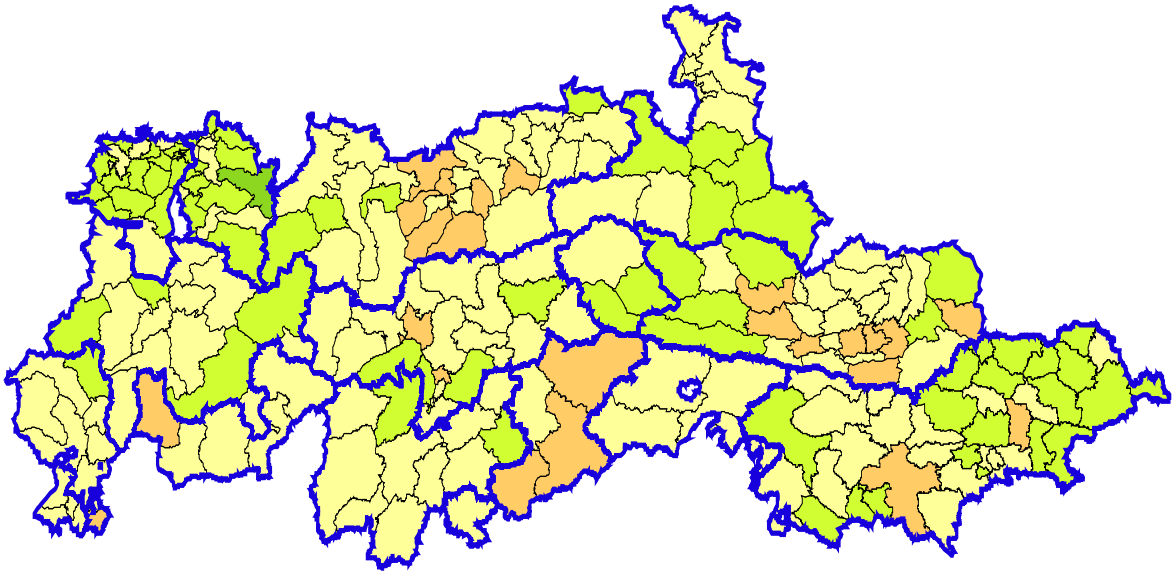


Fig. 2: All except NMSC – Mortality – Smoothed Map – Females

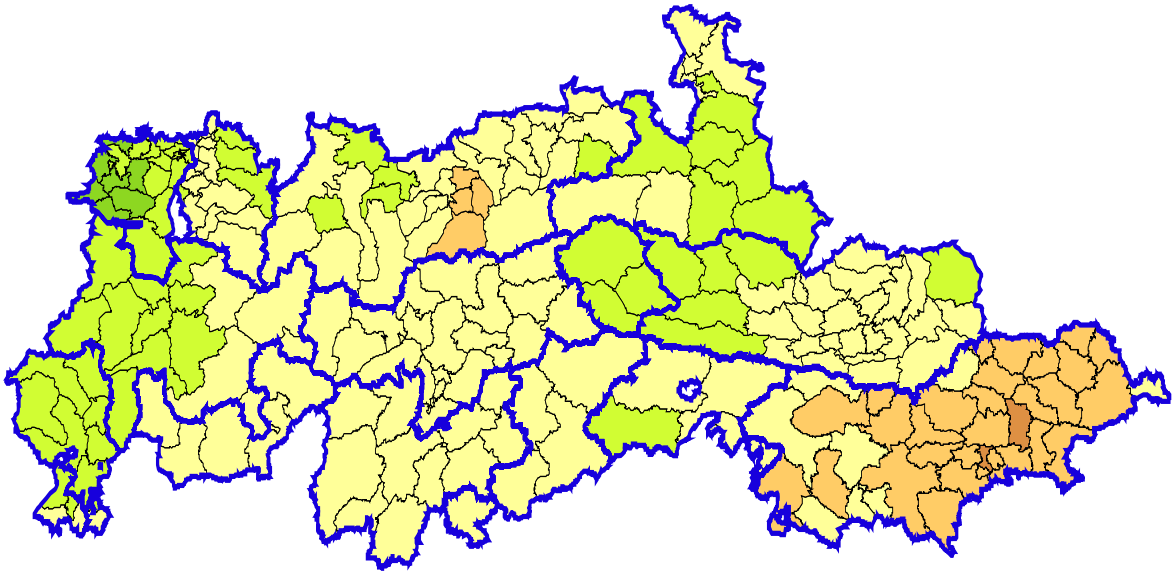


Fig. 3: All except NMSC – Incidence –Smoothed Map - Males

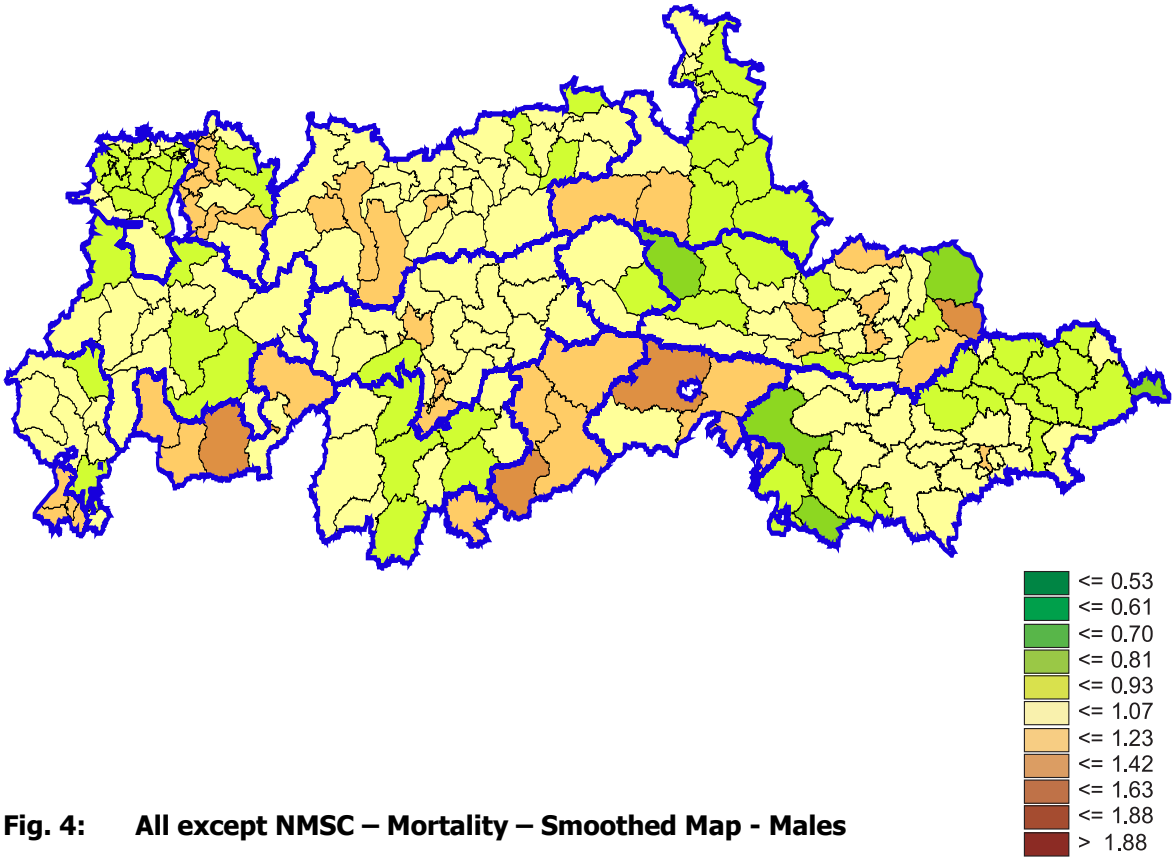
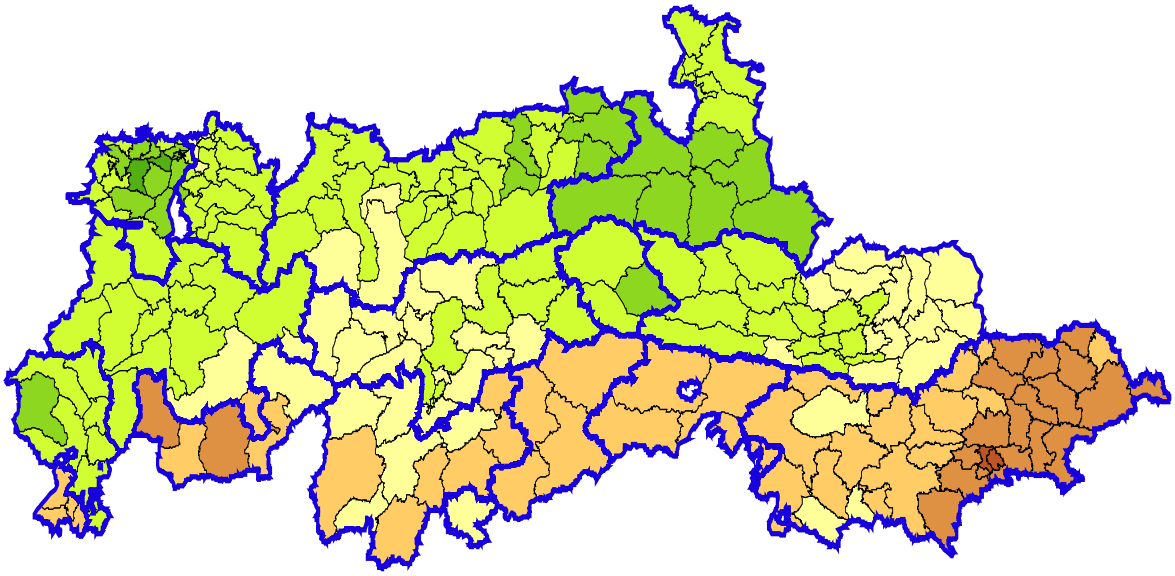


Fig. 4: All except NMSC – Mortality – Smoothed Map - Males



Tab. 10: All except NMSC and prostate – Numbers and Rates - Males

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	5,644	417.3	246.1 (239.3, 253.0)	0.99 (0.96, 1.01)	3,100	229.2	128.6 (123.8, 133.5)	0.91 (0.87, 0.94)
Salzburg	4,177	332.0	227.7 (220.5, 234.9)	0.88 (0.86, 0.91)	2,207	175.4	111.6 (106.8, 116.4)	0.8 (0.77, 0.84)
Tyrol	5,807	348.0	236.6 (230.3, 242.9)	0.92 (0.9, 0.95)	3,091	185.2	117.5 (113.3, 121.8)	0.85 (0.82, 0.88)
Vorarlberg	2,776	316.1	229.7 (220.9, 238.5)	0.89 (0.86, 0.93)	1,519	173.0	120.2 (114.0, 126.3)	0.87 (0.82, 0.91)
Friuli Venezia Giulia	1,217	650.7	308.0 (289.0, 327.0)	1.21 (1.14, 1.28)	770	411.7	175.9 (162.1, 189.6)	1.23 (1.14, 1.32)
Varese	1,497	548.2	318.1 (301.2, 335.1)	1.25 (1.19, 1.32)	889	325.6	174.0 (162.3, 185.8)	1.25 (1.17, 1.33)
Sondrio	2,391	549.0	310.2 (297.1, 323.4)	1.22 (1.17, 1.27)	1,520	349.0	181.9 (172.3, 191.4)	1.31 (1.25, 1.38)
South Tyrol	4,782	417.1	263.5 (255.7, 271.3)	1.04 (1.01, 1.07)	2,618	228.4	134.3 (129.0, 139.7)	0.96 (0.93, 1)
Trentino	5,377	456.4	255.6 (248.2, 263.0)	1.01 (0.98, 1.04)	3,575	303.5	154.5 (149.1, 159.9)	1.11 (1.07, 1.14)
Veneto	3,663	657.4	335.5 (323.7, 347.2)	1.33 (1.29, 1.38)	2,100	376.9	174.4 (166.3, 182.4)	1.25 (1.19, 1.3)
Slovenia	14,104	383.1	261.4 (257.0, 265.8)	1.02 (1.01, 1.04)	9,170	249.1	178.0 (174.2, 181.7)	1.21 (1.18, 1.23)
Graubünden/ Glarus	2,065	371.3	231.9 (221.2, 242.7)	0.89 (0.85, 0.93)	1,175	211.3	119.7 (112.4, 127.0)	0.83 (0.78, 0.87)
St.Gallen/ Appenzell	4,276	331.4	221.0 (214.0, 228.0)	0.86 (0.83, 0.88)	2,329	180.5	112.7 (107.9, 117.5)	0.77 (0.73, 0.8)
Ticino	3,520	466.7	260.4 (251.1, 269.6)	1 (0.97, 1.04)	1,864	247.1	123.6 (117.7, 129.6)	0.87 (0.83, 0.91)
Total	**61,296**	**402.8**	**255.8 (253.7, 258.0)**	**1 (0.99, 1.01)**	**35,927**	**236.1**	**138.9 (137.4, 140.4)**	**1 (0.99, 1.01)**

Tab. 11: All except NMSC and prostate – Data quality

	FEMALES			MALES		
Country description	% DCO	% HV	RMI	% DCO	% HV	RMI
Carinthia	6.2%	95.2%	0.44	6.0%	93.4%	0.55
Salzburg	2.1%	92.3%	0.45	1.7%	92.1%	0.53
Tyrol	1.2%	94.3%	0.45	0.8%	94.4%	0.53
Vorarlberg	3.9%	97.2%	0.49	3.6%	96.5%	0.55
Friuli Venezia Giulia	0.6%	86.1%	0.53	0.3%	86.0%	0.63
Varese	0.1%	87.9%	0.47	0.3%	85.1%	0.59
Sondrio	0.7%	87.7%	0.47	0.5%	84.0%	0.64
South Tyrol	1.5%	91.4%	0.47	1.5%	90.7%	0.55
Trentino	1.8%	88.0%	0.52	1.1%	85.2%	0.66
Veneto	2.2%	88.2%	0.46	1.3%	86.8%	0.57
Slovenia	1.4%	95.5%	0.52	1.1%	94.7%	0.65
Graubünden/Glarus	0.5%	92.8%	0.44	0.2%	92.6%	0.57
St.Gallen/Appenzell	0.4%	94.7%	0.44	0.2%	94.6%	0.54
Ticino	2.7%	95.0%	0.44	2.1%	91.8%	0.53
Total	**2.0%**	**93.3%**	**0.48**	**1.6%**	**91.9%**	**0.59**

Fig. 5: All except NMSC and Prostate – Incidence –Smoothed Map - Males

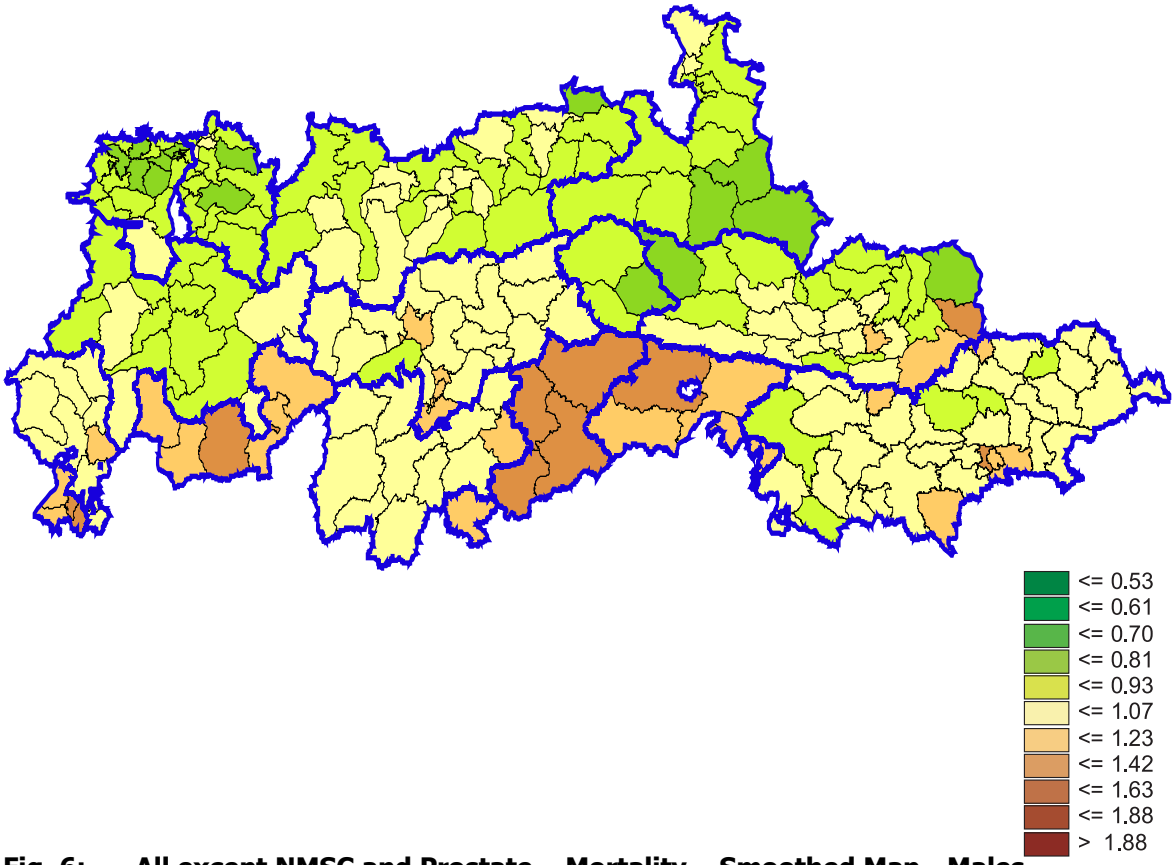
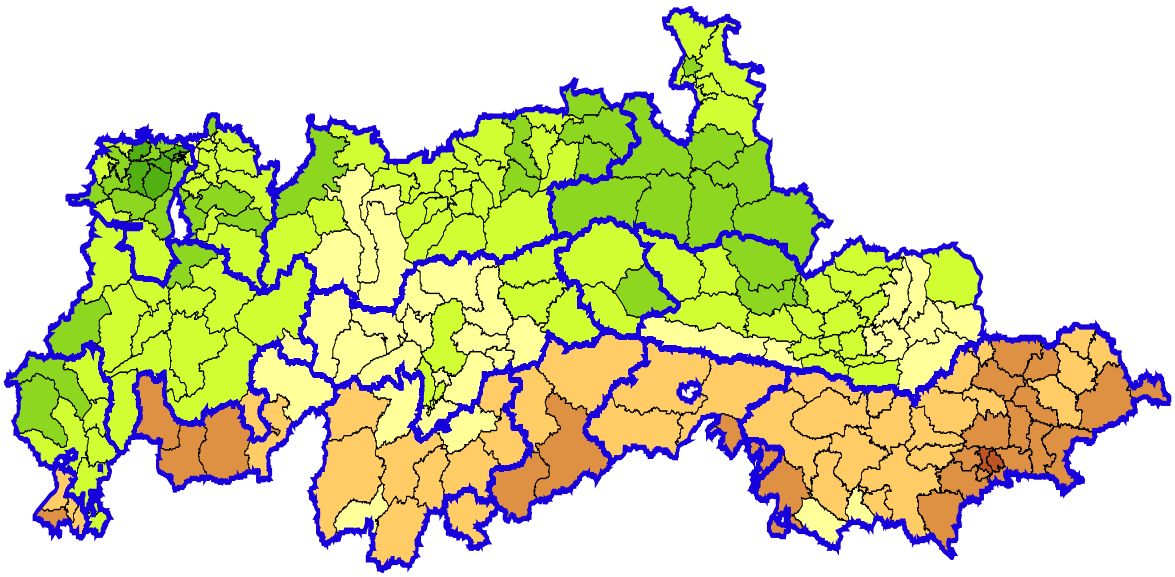


Fig. 6: All except NMSC and Prostate – Mortality – Smoothed Map - Males



5.2 Head & Neck and Oesophagus and Larynx

Silvano Piffer

Testa e Collo, Esofago e Laringe
Kopf & Hals und Speiseröhre und Kehlkopf
Glava in vrat, požiralnik in grlo

5.2.1 Summary and Call for Action

Summary and Call for Action

For males, the maps of Alpine regions display a noticeable North-South gradient in incidence and mortality: Veneto and Friuli Venezia Giulia appear to be the highest risk areas.

Primary prevention is the major tool for controlling these kinds of tumor and measures are needed to fight against smoke, active and passive, and programs for dietary education, geared towards the consistent reduction of alcohol abuse, especially in Italian regions.

From a clinical or theoretical point of view, recommending a yearly otorhinolaryngological examination for subjects with higher risk (smokers and hard drinkers) should be reliable and most likely also helpful. Really, all attempts to plan screening programs based on this approach have nearly always failed due to poor compliance by the subjects themselves. On the contrary, a specialist visit is clearly recommended when critical symptomatology (like dysphagia or dysphonia) has manifested and continued over two weeks.

Sintesi e proposte operative

Le mappe delle regioni alpine mostrano un marcato incremento di rischio secondo un gradiente Nord-Sud nei maschi, tanto per l'incidenza che per la mortalità; Veneto e Friuli Venezia Giulia appaiono come le aree di maggior rischio.

Lo strumento principale per contrastare questi tipi di tumori è rappresentato dalla prevenzione primaria che deve comprendere misure più efficaci per la lotta al fumo, attivo e passivo, e programmi per l'educazione alimentare orientati ad una consistente riduzione dell'abuso di alcol. Tali politiche sono urgenti soprattutto nelle regioni italiane.

In teoria, una misura verosimilmente utile potrebbe essere quella di sottoporre ad esame otorinolaringoiatrico periodico i soggetti ad alto rischio (fumatori e forti bevitori). In realtà, ogni tentativo di avviare programmi di "screening" basati su questo approccio è quasi sempre fallito, per la scarsa adesione da parte dei soggetti stessi. D'altro canto, in presenza di una sintomatologia critica (disfagia o disfonia) che si manifesti per almeno due settimane, deve essere consigliata una visita specialistica.

Zusammenfassung und Schlussfolgerungen

Die Alpenregionen zeigen für Männer einen bemerkenswerten Nord-Süd-Gradient für Inzidenz und Mortalität von HNO-Tumoren. Veneto und Friaul Julisch Venetien sind die Regionen mit dem höchsten Risiko. Die besten Maßnahmen zur Reduktion der HNO-Tumore sind primäre Präventionsmaßnahmen. Deshalb sollten neue Maßnahmen gegen das aktive und passive Rauchen, sowie gegen Alkoholmissbrauch gesetzt werden. Für Patienten mit hohem Risiko empfehlen wir vom klinischen Standpunkt jährlich eine HNO-Untersuchung durchzuführen. In der Praxis allerdings haben alle Anstrengungen, Screeningprogramme auf dieser Basis zu planen, praktisch immer aufgrund der mangelnden Compliance der Patienten, versagt. Andererseits jedoch wird das Aufsuchen eines Facharztes dringendst empfohlen, wenn eine kritische Symptome wie Schluckstörungen oder Heiserkeit über mehr als 2 Wochen manifest sind.

Povzetek in poziv k ukrepanju

Iz zemljevidov alpskih regij je razvidno, da se pri moških tako ogroženost kot umrljivost za temi raki zmanjšujeta od severa proti jugu, tako da je tveganje največje v Benečiji in Furlaniji-Julijski krajini.
Primarna preventiva, ki zajema ukrepe proti aktivnemu in pasivnemu kajenju in izobraževalne programe o zdravi prehrani z doslednim omejevanjem uživanja alkohola, zlasti v italijanskih deželah, je temeljno sredstvo za obvladovanje tumorjev glave in vratu ter grla in požiralnika. Priporočilo ogroženim osebam (kadilci in prekomerni uživalci alkohola), naj se enkrat na leto udeležijo preiskave pri otorinolaringologu, je tako s kliničnega kot teoretičnega vidika zanesljiv in koristen ukrep. Doslej so vsi poskusi načrtovanja presejalnih programov zaradi slabega odziva ciljne populacije padli v vodo. Vsekakor pa se posamezniku s kritično simptomatiko (disfagia, disfonija), ki traja več kot štirinajst dni, priporoča takojšnji pregled pri specialistu.

5.2.2 Introduction

This paragraph analyzes a group of smaller cancer sites, referred to by ICD 9 codes 140-150, 161 (ICD 10: C00 - C15, C32). This group includes sites for which topography is sometimes difficult to distinguish. However, the prevalent histomorphology is the squamous cell carcinoma. Moreover, the etiology of these malignant neoplasms, particularly in Western countries, is common. A great difference in incidence is evident between males and females.

European countries show a clear variability in male incidence, ranging from higher values observed in Hungary (60.4) and France (53.1), to lower values in Nordic countries - Norway (14.8), Finland (12.7), and Sweden (12.5) – where these tumors are considerably less frequent. The incidence in Northern America (24.1) is in line with average European values. Mortality rates in male populations are lower; generally between 10 and 20/100,000. In Eastern Europe population - Hungary (39.3) and Slovakia (31.2) – we observe higher rates, while Northern American countries (9.6) present a more favorable situation [1]

IARC estimates that in the year 2006 there were 155,000 new head/neck cancer cases in men in Europe, while the number of deaths from head/neck cancer was estimated at around 82,000; in women the corresponding values are 38,000 and 20,000 respectively. Head & neck cancers are responsible for 9.1% of all new cancer cases among men and for 6.1% among women in Europe and for 8.6% of all cancer death in men and for 2.6% in women [2].

5.2.3 Epidemiology

In more developed countries, the standardized incidence rates are approximately 27.0/100,000 (males) and 5.4/100,000 (females), which are fairly close to the values observed in our area (27.9/100,000 and 5.4/100,000, respectively).

In the whole area, during the period considered, we observed 6,469 new cases in males (1,294 per year) as compared to only 1,569 new cases in females (314 per year), with a 4:1 ratio of males to females. On the whole, these tumors represent 2.2% of all tumors (except NMSC) in the female population and 7.7% of all tumors (except NMSC) in the male population. Concerning females, the frequency of incident cases is low and substantially homogeneous in the Alpine area: the weight of this group on the total number of new cases ranges from 1.8% (Tyrol) to 2.9% (Veneto and Friuli Venezia Giulia). On the contrary, males display a wider range in percentage weights distribution (5.8%-10.9%) of these groups for all tumors: Austrian regions are all grouped around 6%-6.5%, while Italian areas range from 7.3% to 10.9%.

This group of tumors accounts for 8.5% of all cancer deaths except NMSC in males (from 6.9 for Graubünden to 14.9 for Friuli Venezia Giulia) and for 2.3% of all cancer death in females (from 1.7 for Varese to 5.1% for Friuli Venezia Giulia).

5.2.4 Data quality

Data quality seems sufficient in the whole area: DCO value is 2.23% for females (0.0-6.0), with Trentino showing higher values, and 0.87% for males (0.0-3.5), with Carinthia showing higher values. The percentage of incident cases with microscopic verification is high for both sexes: 98.3% for males

(95.4-99.7) and 98.5% for females (88.7-100.0). Austrian regions and Slovenia show higher values of microscopic verification. M/I ratio is in line with our knowledge of these malignant tumors, presenting a value around 0.50 (0.54 in males and 0.49 in females). The highest values are observed for the smallest sub-regional areas of the Italian part.

5.2.5 Risk factors, early detection, screening

Apart from selected sites, smoking and alcohol abuse (particularly wine) are the major risk factors [3]. Combined exposure to alcohol and tobacco causes a multiplicative effect on cancer risk for this group of tumors [4-6]. IARC estimated that elimination of smoke and reduction of alcohol consumption could reduce, in Europe, the incidence of these tumors by 60-80% [7]. Nutritional factors are also important considering that in developed countries, selected aspects of diet (low intake of fruit and vegetables in particular) may account for 20% to 25% of tumors of the upper respiratory and digestive tract, as reported by case-control and cohort studies [8-11]. Up today, screening programs for these tumors have not proved to be effective, however prevention could occur – for oral sites - through a dental or otorhinolaryngological examination, which is clinically advisable even if not yet recommendable as a public health measure [12,13].

Primary prevention addressing tobacco, alcohol and dietary habits represents the major tool for controlling risk factors in the general population [14]. Specific no smoking laws, in combination with a continuous health promotion campaign targeting the general population can contribute to lower smoking prevalence and also the risk [15,16].

5.2.6 Geographical variation

Females: The Smoothed Map reveals substantial homogeneity of the relative risk in the whole Alpine area, except for the district around the city of Bolzano, some areas of the Trentino region and Sondrio and, above all, the mountainous areas of Veneto region. Other scattered small areas with a slight excess risk are evident in Graubünden, Friuli Venezia Giulia and Slovenia.

With regard to mortality, the smoothed map shows two adjacent areas with risk excess, mainly in the mountainous part of Veneto and Friuli Venezia Giulia regions; a small area with a slight risk excess is also evident in eastern Slovenia.

Males: As opposed to females, the smoothing procedure shows a noticeable increase in risk from North to South. Veneto and Friuli Venezia Giulia region appear to be the areas with the greatest incidence, but Trentino, South Tyrol and Sondrio are also characterized by a higher risk. On the contrary, Swiss and Austrian regions show lower risk levels.

Standardized mortality rates are noticeably higher (from 9.88 to 30.9/100,000) and the SMR distribution shows a clear pattern (risk increase) from North to South. This pattern is illustrated by the smoothed map, where the Friuli Venezia Giulia region shows the highest mortality rates. Other Italian regions show a higher mortality rate, with the exception of South Tyrol which presents a rate closer to that of Austrian regions than that of Italian regions. Also, Slovenia shows an excess of mortality. German-speaking people present the lowest mortality rate. The figures for Italian regions are coherent with previous reports by the Italian Association of Cancer Registries [17].

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Tab. 12: Head & Neck and Oesophagus and Larynx – Numbers and Rates - Females

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	137	9.5	5.0 (4.1, 6.0)	0.93 (0.78, 1.11)	60	4.1	1.9 (1.4, 2.5)	0.83 (0.63, 1.07)
Salzburg	102	7.6	4.5 (3.5, 5.4)	0.83 (0.68, 1.01)	43	3.2	1.8 (1.2, 2.4)	0.73 (0.53, 0.99)
Tyrol	132	7.5	4.9 (4.0, 5.8)	0.83 (0.69, 0.99)	67	3.8	2.1 (1.6, 2.7)	0.87 (0.68, 1.11)
Vorarlberg	72	8.0	5.1 (3.9, 6.4)	0.93 (0.72, 1.17)	42	4.7	2.5 (1.7, 3.3)	1.14 (0.82, 1.53)
Friuli Venezia Giulia	35	18.0	6.7 (3.9, 9.5)	1.35 (0.94, 1.88)	32	16.4	5.7 (3.2, 8.2)	2.26 (1.55, 3.19)
Varese	27	9.3	4.8 (2.6, 7.1)	0.87 (0.57, 1.26)	13	54.5	1.7 (0.6, 2.7)	0.82 (0.44, 1.4)
Sondrio	64	14.1	6.5 (4.7, 8.3)	1.3 (1, 1.66)	24	5.3	2.5 (1.4, 3.7)	0.96 (0.61, 1.42)
South Tyrol	130	11.0	6.5 (5.2, 7.7)	1.15 (0.96, 1.36)	58	4.9	2.5 (1.8, 3.2)	1.03 (0.78, 1.33)
Trentino	133	10.8	5.0 (4.0, 6.0)	1 (0.83, 1.18)	64	5.2	2.0 (1.4, 2.6)	0.93 (0.72, 1.19)
Veneto	111	18.4	9.0 (6.9, 11.2)	1.52 (1.25, 1.83)	70	11.6	4.0 (2.5, 5.4)	1.81 (1.41, 2.29)
Slovenia	361	9.4	5.2 (4.6, 5.8)	0.98 (0.88, 1.09)	169	4.4	2.0 (1.7, 2.3)	0.98 (0.83, 1.14)
Graubünden/Glarus	55	9.6	4.8 (3.3, 6.2)	0.99 (0.75, 1.29)	29	5.1	2.4 (1.3, 3.4)	1.03 (0.69, 1.48)
St.Gallen/Appenzell	124	9.4	5.6 (4.6, 6.7)	1.02 (0.85, 1.21)	50	3.8	1.8 (1.2, 2.4)	0.82 (0.61, 1.08)
Ticino	86	10.4	5.5 (4.2, 6.8)	0.94 (0.75, 1.17)	50	6.0	2.8 (1.8, 3.7)	1.07 (0.79, 1.41)
Total	**1,569**	**9.8**	**5.4 (5.1, 5.7)**	**1 (0.95, 1.05)**	**771**	**4.8**	**2.2 (2.0, 2.4)**	**1 (0.93, 1.07)**

Tab. 13: Head & Neck and Oesophagus and Larynx – Numbers and Rates - Males

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	517	38.2	25.3 (23.1, 27.5)	0.87 (0.8, 0.95)	275	20.3	13.1 (11.5, 14.7)	0.85 (0.75, 0.96)
Salzburg	396	31.5	22.2 (19.9, 24.4)	0.79 (0.71, 0.87)	183	14.5	10.0 (8.5, 11.5)	0.69 (0.59, 0.79)
Tyrol	494	29.6	21.0 (19.1, 22.9)	0.74 (0.68, 0.81)	256	15.3	10.4 (9.1, 11.7)	0.73 (0.64, 0.82)
Vorarlberg	296	33.7	24.9 (22.0, 27.8)	0.89 (0.79, 0.99)	127	14.5	10.5 (8.7, 12.4)	0.73 (0.61, 0.87)
Friuli Venezia Giulia	178	95.2	48.9 (41.4, 56.3)	1.72 (1.48, 1.99)	126	67.4	30.9 (25.3, 36.5)	2.16 (1.8, 2.58)
Varese	137	50.2	30.3 (25.1, 35.5)	1.09 (0.91, 1.29)	75	27.5	16.2 (12.4, 19.9)	1.1 (0.87, 1.38)
Sondrio	250	57.4	32.9 (28.7, 37.0)	1.22 (1.07, 1.38)	140	32.1	17.3 (14.3, 20.2)	1.26 (1.06, 1.49)
South Tyrol	581	50.7	33.5 (30.7, 36.3)	1.22 (1.12, 1.32)	282	24.6	15.5 (13.6, 17.4)	1.09 (0.97, 1.22)
Trentino	649	55.1	32.1 (29.5, 34.6)	1.18 (1.09, 1.28)	420	35.7	19.5 (17.6, 21.5)	1.39 (1.26, 1.53)
Veneto	483	86.7	47.3 (42.9, 51.7)	1.71 (1.56, 1.87)	234	42.0	21.2 (18.4, 24.1)	1.49 (1.3, 1.69)
Slovenia	1,565	42.5	29.0 (27.6, 30.5)	1.03 (0.98, 1.09)	865	23.5	17.0 (15.9, 18.2)	1.12 (1.05, 1.2)
Graubünden/Glarus	187	33.6	22.3 (19.0, 25.6)	0.78 (0.67, 0.9)	95	17.1	09.9 (7.8, 12.0)	0.71 (0.58, 0.87)
St.Gallen/Appenzell	419	32.5	22.3 (20.1, 24.5)	0.81 (0.73, 0.89)	193	15.0	10.1 (8.7, 11.6)	0.67 (0.58, 0.78)
Ticino	317	42.0	23.7 (21.0, 26.4)	0.87 (0.78, 0.97)	175	23.2	12.2 (10.3, 14.0)	0.86 (0.74, 1)
Total	**6,469**	**42.5**	**28.0 (27.3, 28.7)**	**1 (0.98, 1.02)**	**3,446**	**22.7**	**14.2 (13.7, 14.7)**	**1 (0.97, 1.03)**

Tab. 14: Head & Neck and Oesophagus and Larynx – Data quality

	FEMALES			MALES		
Country description	% DCO	% HV	RMI	% DCO	% HV	RMI
Carinthia	4.4%	96.9%	0.44	3.5%	98.4%	0.53
Salzburg	1.0%	98.0%	0.42	1.0%	97.2%	0.46
Tyrol	0.0%	98.5%	0.51	0.6%	99.2%	0.52
Vorarlberg	5.6%	98.6%	0.58	2.4%	99.7%	0.43
Friuli Venezia Giulia	0.0%	97.1%	0.91	0.0%	97.8%	0.71
Varese	0.0%	92.6%	0.48	0.0%	95.6%	0.55
Sondrio	0.0%	93.8%	0.38	0.4%	96.0%	0.56
South Tyrol	2.3%	100.0%	0.45	0.7%	98.6%	0.49
Trentino	6.0%	94.4%	0.48	0.5%	95.8%	0.65
Veneto	1.8%	96.3%	0.63	0.6%	98.5%	0.48
Slovenia	2.2%	101.4%	0.47	0.6%	99.2%	0.55
Graubünden/Glarus	0.0%	96.4%	0.53	0.5%	98.4%	0.51
St.Gallen/Appenzell	1.6%	98.4%	0.40	0.2%	98.8%	0.46
Ticino	1.2%	100.0%	0.58	0.6%	98.7%	0.55
Total	**2.2%**	**98.6%**	**0.49**	**0.9%**	**98.4%**	**0.53**

Fig. 7: Head & Neck and Oesophagus and Larynx – Incidence – Smoothed Map - Females

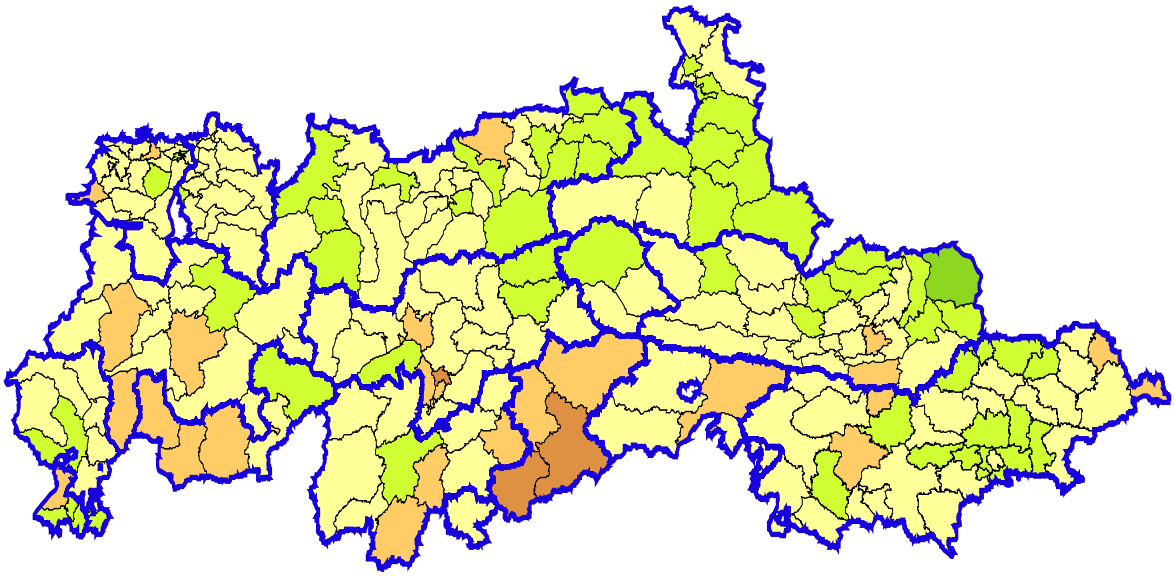


Fig. 8: Head & Neck and Oesophagus and Larynx – Mortality – Smoothed Map - Females

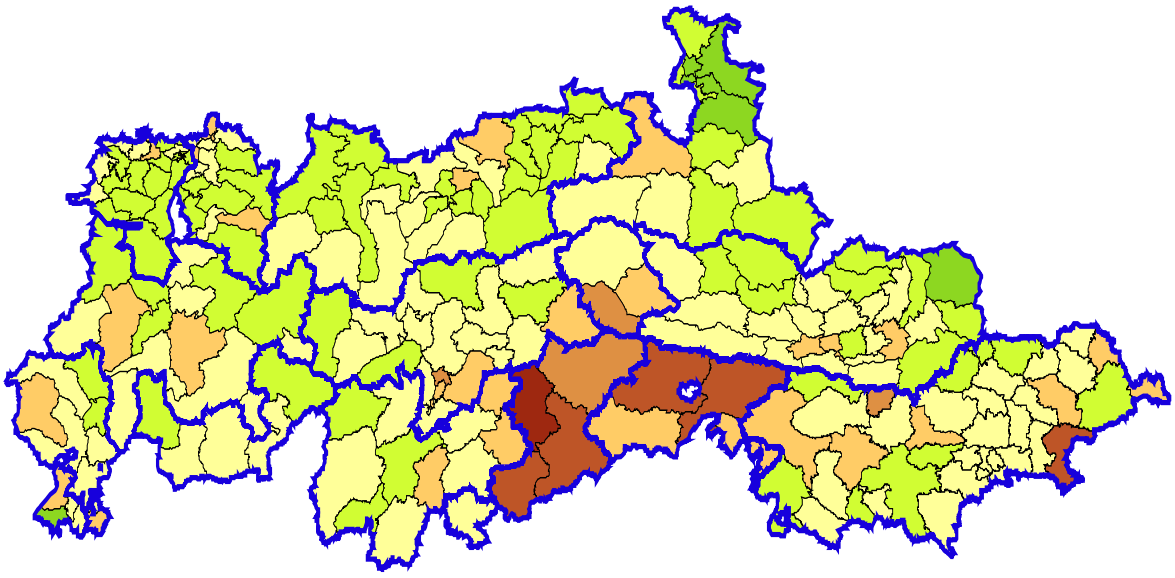


Fig. 9: Head & Neck and Oesophagus and Larynx – Incidence – Smoothed Map - Males

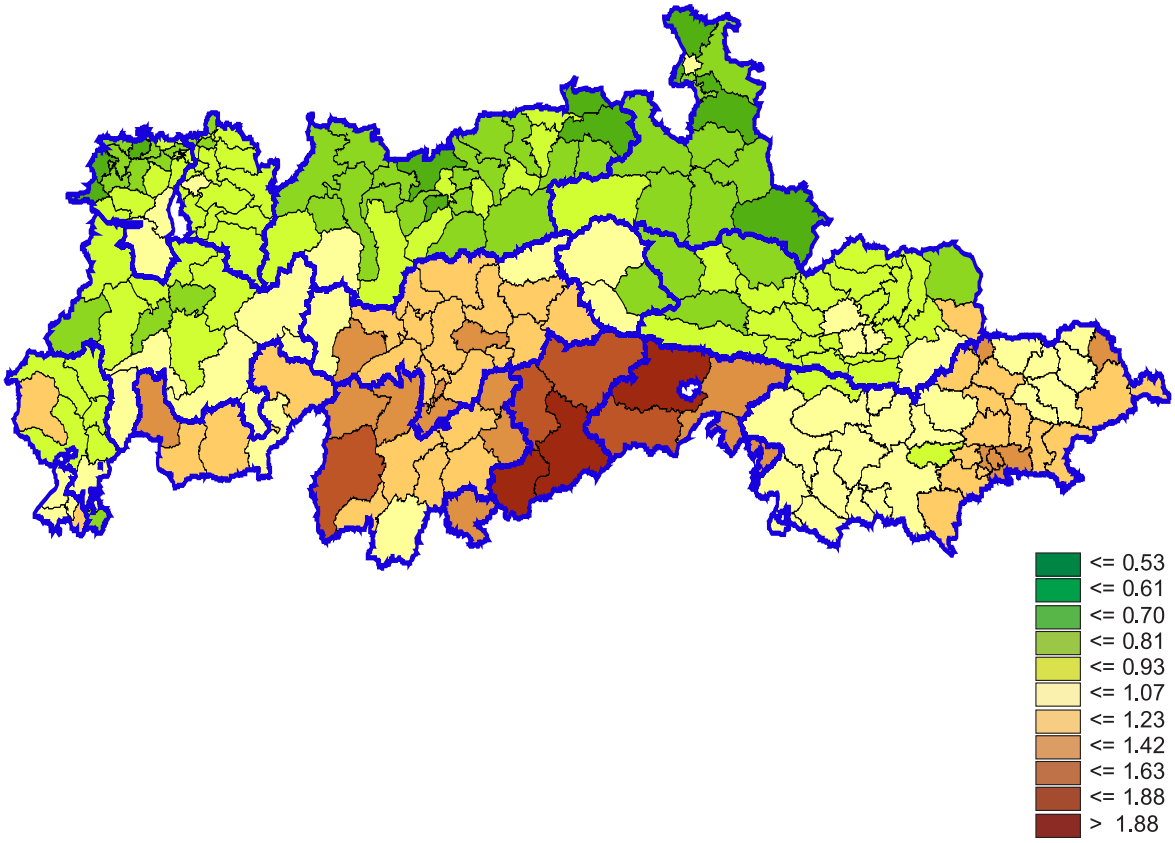
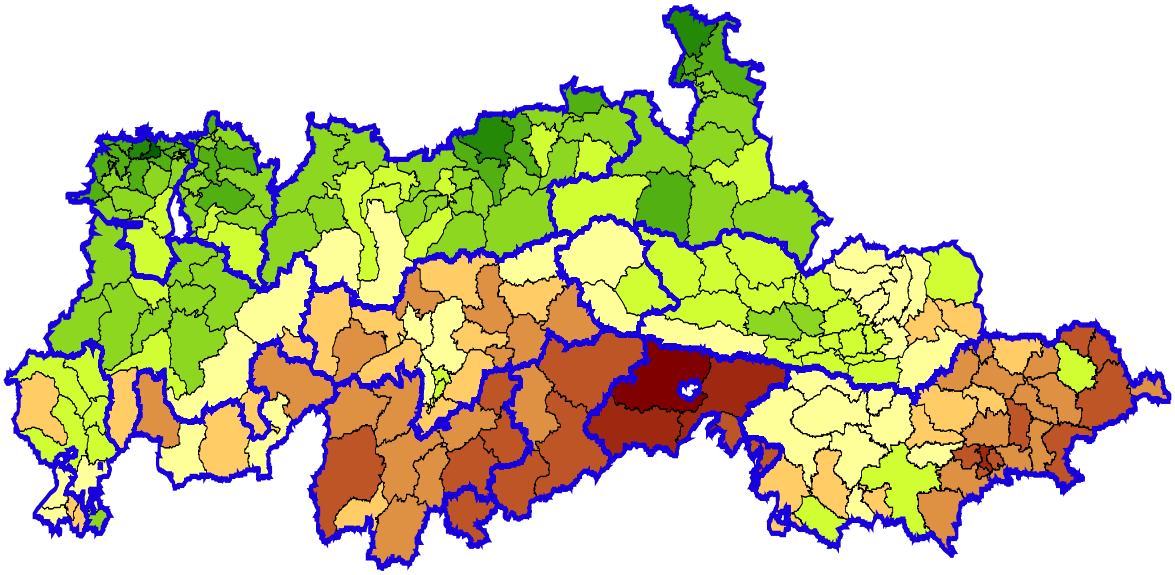


Fig. 10: Head & Neck and Oesophagus and Larynx – Mortality – Smoothed Map - Males



5.3 *Stomach* Paola Zambon

Stomaco
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5.3.1 Summary and Call for Action

Summary and Call for Action

This study has highlighted the existence of high-risk regions (Slovenia, South Tyrol, Varese and Sondrio), within a wider, geographically homogenous (Alpine) region; these are regions where risk is almost twice that to be found in the western parts of the region studied. In these regions, risk is much higher than the average European values.

Two aspects of the epidemiology of stomach cancer that should be highlighted are: despite the decrease in the incidence rate, there has been a notable increase in the absolute number of cases because of the aging population; and survival rates are still very low. Thus, it is important not only to continue to study the aetiology and pathogenesis of this tumor, but also to develop and implement prevention and treatment strategies.

Some studies have indicated that eradication of Helicobacter pylori has led to regression of preneoplasia, but there is not enough evidence as to the real benefits and, as yet, there is no agreement about who should be treated and when [9]. VCRF/AICR (World Cancer Research Fund/American Institute for Cancer Research, 1997 [10]) has recommended that the best means of prevention is consumption of diets high in vegetables and fruits and low in salt as well as industrial and domestic uses of refrigeration for perishable foods. Weight control leading to reducing acid reflux and consequent mucosal damage and pathological changes would reduce the risk of cancer of the gastric cardia and gastroesophageal junction. These recommendations are still appropriate.

Secondary control is based on the concept of early gastric cancer.

Since most cases of cancer are associated with histologically recognizable premalignant lesions, endoscopy follow-up might be important for detection of earlier stages of disease that are eminently treatable. However, only a small proportion of patients with these lesions will progress to gastric cancer and currently guidelines for surveillance of these patients are lacking.

Sintesi e proposte operative

Questo studio ha evidenziato l'esistenza di zone, all'interno di una più ampia e geograficamente omogenea regione alpina (Slovenia, Alto Adige, Varesino e Sondrio), nelle quali il rischio è doppio, rispetto a quello riscontrato nelle aree Alpine occidentali, e molto più elevato rispetto ai valori medi europei.

Due aspetti dell'epidemiologia del cancro dello stomaco vanno sottolineati. Innanzitutto, nonostante la diminuzione dei tassi d'incidenza, il numero assoluto di casi è sensibilmente aumentato a causa dell'invecchiamento della popolazione; in secondo luogo, la sopravvivenza rimane molto bassa. Di conseguenza, è importante non solo proseguire lo studio dell'eziologia e patogenesi di questo tumore, ma anche sviluppare ed implementare strategie di prevenzione e trattamento.
Alcuni studi hanno indicato come l'eliminazione dell'Helicobacter pylori comporti la regressione della pre-neoplasia; tuttavia non vi è sufficiente evidenza dei reali benefici e, inoltre, non vi è accordo su chi andrebbe trattato e quando. Il World Cancer Research Fund/American Institute for Cancer Research ha raccomandato recentemente, come migliori mezzi di prevenzione, il consumo di diete ricche di vegetali e frutta e povere di sale, nonché l'utilizzo della refrigerazione, sia domestica che industriale, per i cibi deperibili. Viene suggerito anche il controllo del peso che, comportando una riduzione del reflusso acido e dei conseguenti danni alla mucosa ed alterazioni patologiche, ridurrebbe il rischio di cancro al cardias gastrico ed alla giunzione gastro-esofagea.
La prevenzione secondaria è basata sul concetto di tumore gastrico precoce.
Poiché la maggior parte dei cancri è associata a lesioni pre-maligne individuabili istologicamente, il "follow-up" endoscopico è in grado di rilevare gli stadi iniziali della malattia, che sono generalmente trattabili. Tuttavia, solo una bassa proporzione di pazienti con tali lesioni svilupperanno un cancro gastrico e, al presente, non esistono linee guida condivise per la sorveglianza di questi soggetti.

Zusammenfassung und Schlussfolgerungen

Diese Untersuchung beleuchtet die Gebiete mit hohem Risiko (Slowenien, Südtirol, Varese) in einer geographisch homogenen (alpinen) Region. Das Risiko zwischen den einzelnen Regionen kann bis zum Faktor 2 schwanken. In diesen Regionen ist das Risiko wesentlich höher als im europäischen Durchschnitt. Zwei epidemiologische Aspekte des Magenkrebses sollten besonders beleuchtet werden: Trotz eines Abfalls in der Inzidenz gibt es einen bemerkenswerten Zuwachs in der absoluten Zahl der Fälle aufgrund des Alters der Bevölkerung und aufgrund der Tatsache, dass die Überlebensraten noch immer sehr niedrig sind. Daher ist es wichtig, nicht nur Ätiologie und Pathogenese dieses Tumors zu untersuchen, sondern es müssen auch Behandlungstrategien entwickelt und implementiert werden. In einigen Studien gab es Hinweise, dass die Eradikation von Helicobacter pylori zu einer Reduktion der Präneoplasierate geführt hat. Dennoch gibt es bezüglich der Behandlungsindikation noch keine klare Evidenz. Vom World Cancer Research wurde als bestes Mittel der Prävention eine Ernährung mit einem hohen Anteil an Gemüse und Obst und einem niedrigen Salzanteil empfohlen. Wichtig ist auch der industrielle und häusliche Gebrauch von Kühlgeräten für verderbliche Nahrungsmittel. Gewichtsreduktion kann das Risiko, am gastroösophagialen Übergangskarzinom zu erkranken, durch Reduktion des sauren Reflux, veringern. Diese Empfehlungen sind nach wie vor gültig.

Povzetek in poziv k ukrepanju

V študiji so posebej izpostavljena visoko ogrožena območja (Slovenija, Južna Tirolska, Varese in Sondrio), kjer je tveganje želodčnega raka dvakrat višje kot v zahodnih predelih geografsko homogene alpske regije. V vseh teh območjih je tveganje tudi višje od povprečnih evropskih vrednosti.

V epidemiologiji želodčnega raka sta posebej pomembni dve dejstvi: da se je kljub nižji incidenčni stopnji absolutno število novih primerov želodčnega raka zaradi staranja prebivalstva občutno povečalo in da je preživetja bolnikov še vedno zelo nizko. Zato je nujno nadaljevati z raziskovanjem etiologije in patogeneze tega raka, kot tudi z razvojem in izvajanjem metod za njegovo preprečevanje in zdravljenje. Nekatere študije so pokazale, da izkoreninjanje bakterije Helicobacter pylori vodi v regresijo premalignih tvorb, vendar je dokazov za potrditev takšnih prednosti še premalo, pa tudi soglasja o tem, koga je treba zdraviti in kdaj, še ni (9). Svetovni sklad za raziskovanje raka pri Ameriškem inštitutu za raziskovanje raka (VCRF/AICR - World Cancer Research Fund/American Institute for Cancer Research, 1997 b. 10) ugotavlja, da je najuspešnejše orožje proti raku uživanje dietne prehrane z veliko zelenjave in sadja, čim manj soli kot tudi hrane, ki je zaradi hitre pokvarljivosti industrijsko hlajena ali hranjena v domačem hladilniku. Z nadzorom nad telesno težo, omejevanjem gastroezofagealnega refluksa in posledičnih okvar sluznice ter patoloških sprememb se manjša ogroženost za nastanek raka želodčne kardije in gastroezofagealnega prehoda. Vsa našteta priporočila so še vedno v veljavi.
Sekundarna preventiva temelji na prepoznavanju zgodnjih stadijev želodčnega raka.
V večini primerov se želodčni rak razvije iz histološko prepoznavnih predrakavih lezij, zato bi bilo zelo koristno spremljanje posameznikov z rednimi endoskopskimi pregledi, saj je bolezen, odkrito v zgodnjem stadiju, še mogoče zdraviti. Po drugi strani pa le manjši delež bolnikov s takšnimi lezijami zboli za želodčnim rakom, poleg tega pa so tudi navodila za nadziranje teh bolnikov pomanjkljiva.

5.3.2 Introduction

The epidemiology of stomach cancer has two main features: wide geographic distribution and a steadily declining trend.
Despite a steadily decreasing worldwide trend over several decades, stomach cancer is now the fourth most common cancer diagnosed, and the second most frequent cause of cancer death [1]. Its geographical distribution is characterized by wide international variations: incidence rates in Japan and China (62.1/100,000 – 41.4/100,000) are 10/20 times higher than in low-risk areas (North and East Africa, North America). In Europe, the average age-standardized incidence rates (world population) are 14.6/100,000 for men and 6.9/100,000 for women, but values range from 7.0/100,000 in France (Herault) to 35.7/100,000 in Belarus for males and from 2.5/100,000 in France (Tarn) to 17.1/100,000 in Portugal (Porto) for females [2].

5.3.3 Epidemiology

During the period 2001-2005, we observed 4,002 new cases in males and 3,017 in females in the Alpine regions; corresponding numbers for mortality were, respectively, 2,767 and 2,128. Overall, stomach cancer accounts for 4.6% of incidence cases and 6.6% of stomach cancer mortality, with an annual incidence rate of 15.4/100,000 in men and 7.8/100,000 in women; mortality rates were 10.3 and 4.6/100,000, respectively. The male: female sex ratio is 2, and is constant in all registries.
Average age of diagnosis is high: 70 years for men and 73 for women. Slightly more than half the male cases (54%) and two-thirds of cases among females (68%) appear after age 70: only 10% of cases appear before age 50 in both sexes.

5.3.4 Data quality aspects

The quality of data was good considering the high proportion of cases microscopically verified (average value 97%) in the whole area and the low proportion of cases (2.5%) identified by death certificates only (DCO). Only Carinthia, Salzburg and Vorarlberg showed a higher DCO percentage: 6% to 8%. Mortality/incidence ratio was 0.7 in both males and females with no differences between registries; this value is consistent with data reported in Cancer Incidence in Five Continents Vol. 9.

5.3.5 Risk factors

There is clearly a strong environmental component behind these risk differences. Studies of migrant populations have shown that environment has more influence than do genetic factors in the occurrence of stomach cancer. The importance and role of dietary habits has been well established: a diet poor in fresh fruit and vegetables, high level of salt consumption and poor food preservation increase the risk of gastric cancer; both tobacco smoking and obesity have also been accepted as risk factors [3-5]. In 1994 the International Agency for Research on Cancer (IARC) classified Helicobacter pylori as a Class 1 (definite) human carcinogen. Further studies have suggested that this action is probably indirect: H. pylori may only offer an environment conducive to carcinogenesis when certain other lifestyle and environmental factors are involved [6].

5.3.6 Early detection, screening

Despite the fact that the rate of survival for stomach cancers has improved, it is still among the cancer sites with poor survival rates in most regions of the world. Of the cases diagnosed in Europe over the period 1995 – 99, there was an age- and area-adjusted 1-year relative survival of 46% (55% in Italy – 40% in Slovenia) but only a 25% relative survival rate at 5 years (32% in Italy – 21 % in Slovenia) [7]. This poor survival rate is due to the fact that cancer diagnosis is often made only at an advanced stage because the early stages are usually asymptomatic and there are few curative treatments available at this late stage.

Efficient monitoring of pre-cancerous conditions might contribute to the early detection of cancer and to increased survival [8].

The cost of population-based surveillance programs is high and not feasible in countries where gastric cancer incidence is not very high and/or declining.

Furthermore, there are no shared guidelines.

5.3.7 Geographical variations

There are marked geographical differences in incidence for both sexes: in Sondrio, Varese, South Tyrol and Slovenia males show a significant excess of incidence (SIR = 1.47 – 1.21), with incidence rates that vary from 18.7/100,000 to 23.7/100,000; while in the regions in the western part of the area studied (Vorarlberg, St. Gallen, Graubünden, Ticino) and in the Salzburg area incidence is significantly lower (SIR from 0.48 to 0.85), with IRs varying from 7.4/100,000 to 13.1/100,000). In these same regions, excepting Salzburg women show a lower incidence (SIR from 0.42 to 0.78 with IRs from 3.2 to 7.4/100,000). Just as for men, the highest rates of incidence for women are to be

found in South Tyrol, Varese, Friuli and Veneto. Standardized Mortality Ratio and mortality rates accurately reflect those of incidence.

Because five registries (Carinthia, Tyrol, Vorarlberg, South Tyrol, Trentino) had taken part in Cancer Mapping in the Alpine region 1996-2000, we were able to compare the values of the incidences rates for that period with those obtained in 2001-2005. In Carinthia, incidence rates had decreased by 27% for men (19.7 to 14.40/100,000) and by 18% for females (10.8 to 8.08/100,000); the decrease was 13% for men (17.6 to 15.34/100,000) and 26% for females (10.5 to 7.81/100,000) in Tyrol and 10% for men (18.3 to 16.53/100,000) and 14% for females (9.2 t0 7.89/100,000) in Trentino.
The rates had remained the same in Vorarlberg (a low-risk area) for men and in South Tyrol (a high-risk area) for women: however, the rate for men decreased by 10%.
Analysis by geographical unit has also revealed three areas of low, intermediate and high risk: risk distribution is homogeneous in each area.

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Tab. 15: Stomach – Numbers and Rates - Females

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	310	21.4	8.1 (7.0, 9.2)	1.08 (0.96, 1.2)	198	13.7	4.5 (3.7, 5.2)	0.97 (0.84, 1.11)
Salzburg	222	16.5	7.4 (6.3, 8.5)	0.97 (0.85, 1.11)	162	12.1	4.8 (4.0, 5.7)	1.01 (0.86, 1.18)
Tyrol	306	17.5	7.8 (6.8, 8.8)	1.02 (0.91, 1.15)	226	12.9	5.1 (4.3, 5.9)	1.07 (0.94, 1.22)
Vorarlberg	107	11.9	5.8 (4.5, 7.0)	0.75 (0.61, 0.9)	93	10.3	4.4 (3.4, 5.4)	0.93 (0.75, 1.15)
Friuli Venezia Giulia	86	44.1	12.7 (9.1, 16.3)	1.51 (1.2, 1.86)	51	26.2	5.0 (3.2, 6.8)	1.15 (0.86, 1.52)
Varese	80	27.5	11.1 (8.2, 14.0)	1.31 (1.04, 1.63)	59	20.3	7.7 (5.1, 10.0)	1.32 (1.01, 1.7)
Sondrio	111	24.4	10.1 (7.9, 12.3)	1.13 (0.93, 1.36)	72	15.8	5.4 (3.9, 6.9)	1 (0.78, 1.26)
South Tyrol	332	28.2	11.4 (10.0, 12.8)	1.51 (1.36, 1.69)	210	17.8	6.5 (5.5, 7.5)	1.34 (1.16, 1.53)
Trentino	278	22.5	7.9 (6.8, 9.0)	1.03 (0.91, 1.16)	185	15.0	4.1 (3.4, 4.8)	0.93 (0.8, 1.08)
Veneto	180	29.8	8.7 (7.1, 10.3)	1.18 (1.01, 1.37)	124	20.6	5.1 (3.6, 6.6)	1.08 (0.9, 1.29)
Slovenia	699	18.1	8.2 (7.5, 8.8)	1.04 (0.96, 1.12)	532	13.8	5.3 (4.8, 5.8)	1.19 (1.09, 1.29)
Graubünden/Glarus	62	10.9	4.4 (3.1, 5.8)	0.57 (0.44, 0.73)	42	7.4	2.3 (1.5, 3.2)	0.53 (0.38, 0.71)
St,Gallen/Appenzell	102	7.8	3.2 (2.5, 4.0)	0.43 (0.35, 0.52)	76	5.8	2.1 (1.5, 2.6)	0.44 (0.35, 0.55)
Ticino	142	17.2	6.2 (5.0, 7.4)	0.78 (0.66, 0.92)	98	11.8	3.6 (2.7, 4.5)	0.73 (0.59, 0.89)
Total	**3,017**	**18.9**	**7.8 (7.4, 8.1)**	**1 (0.96, 1.04)**	**2,128**	**13.3**	**4.6 (4.4, 4.9)**	**1 (0.96, 1.04)**

Tab. 16: Stomach – Numbers and Rates - Males

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	392	29.0	14.4 (12.9, 15.9)	1.03 (0.93, 1.14)	254	18.8	9.3 (8.1, 10.5)	0.95 (0.83, 1.07)
Salzburg	259	20.6	13.1 (11.5, 14.8)	0.85 (0.75, 0.96)	182	14.5	8.8 (7.5, 10.1)	0.86 (0.74, 0.99)
Tyrol	410	24.6	15.3 (13.8, 16.9)	1.01 (0.91, 1.11)	271	16.2	9.8 (8.6, 11.0)	0.96 (0.85, 1.09)
Vorarlberg	155	17.7	12.0 (10.1, 14.0)	0.78 (0.67, 0.92)	102	11.6	7.8 (6.2, 9.3)	0.77 (0.62, 0.93)
Friuli Venezia Giulia	79	42.2	17.0 (13.0, 21.0)	1.15 (0.91, 1.43)	55	29.4	11.0 (7.9, 14.2)	1.1 (0.83, 1.43)
Varese	109	39.9	21.5 (17.3, 25.6)	1.39 (1.14, 1.67)	76	27.8	14.5 (11.2, 17.9)	1.38 (1.09, 1.73)
Sondrio	190	43.6	23.7 (20.2, 27.2)	1.47 (1.27, 1.69)	118	27.1	14.5 (11.8, 17.2)	1.31 (1.09, 1.57)
South Tyrol	366	31.9	18.7 (16.7, 20.7)	1.22 (1.09, 1.35)	247	21.5	12.4 (10.8, 13.9)	1.17 (1.03, 1.32)
Trentino	378	32.1	16.5 (14.8, 18.3)	1.06 (0.95, 1.17)	266	22.6	10.8 (9.4, 12.2)	1.04 (0.92, 1.18)
Veneto	177	31.8	14.7 (12.4, 17.0)	0.95 (0.82, 1.11)	117	21.0	8.8 (7.1, 10.5)	0.88 (0.73, 1.06)
Slovenia	1,047	28.4	18.8 (17.6, 19.9)	1.21 (1.14, 1.28)	790	21.5	15.2 (14.1, 16.3)	1.39 (1.3, 1.49)
Graubünden/Glarus	107	19.2	10.5 (8.4, 12.6)	0.69 (0.56, 0.83)	74	13.3	7.4 (5.6, 9.2)	0.65 (0.51, 0.82)
St.Gallen/Appenzell	160	12.4	7.4 (6.2, 8.6)	0.48 (0.41, 0.56)	120	9.3	5.5 (4.4, 6.5)	0.5 (0.41, 0.59)
Ticino	173	22.9	12.0 (10.1, 13.8)	0.73 (0.63, 0.85)	95	12.6	6.2 (4.9, 7.5)	0.56 (0.45, 0.68)
Total	**4,002**	**26.3**	**15.5 (15.0, 15.9)**	**1 (0.97, 1.03)**	**2,767**	**18.2**	**10.3 (9.9, 10.7)**	**1 (0.96, 1.04)**

Tab. 17: Stomach – Data quality

	FEMALES			MALES		
Country description	% DCO	% HV	RMI	% DCO	% HV	RMI
Carinthia	8.1%	95.1%	0.64	8.4%	98.3%	0.65
Salzburg	5.9%	90.4%	0.73	2.7%	96.4%	0.70
Tyrol	1.0%	97.4%	0.74	0.2%	98.8%	0.66
Vorarlberg	6.5%	98.1%	0.87	2.6%	98.7%	0.66
Friuli Venezia Giulia	1.2%	97.6%	0.59	0.0%	97.5%	0.70
Varese	0.0%	93.8%	0.74	0.0%	95.4%	0.70
Sondrio	1.8%	92.7%	0.65	0.0%	95.8%	0.62
South Tyrol	2.4%	96.6%	0.63	1.1%	98.6%	0.67
Trentino	2.5%	91.1%	0.67	1.3%	96.2%	0.70
Veneto	3.9%	93.6%	0.69	1.1%	96.6%	0.66
Slovenia	2.9%	98.8%	0.76	2.0%	100.0%	0.75
Graubünden/Glarus	0.0%	88.7%	0.68	0.0%	97.2%	0.69
St.Gallen/Appenzell	0.0%	86.3%	0.75	0.6%	96.9%	0.75
Ticino	4.9%	98.5%	0.69	1.2%	98.2%	0.55
Total	**3.3%**	**95.6%**	**0.71**	**2.0%**	**98.3%**	**0.69**

Fig. 11: Stomach – Incidence – Smoothed Map - Females

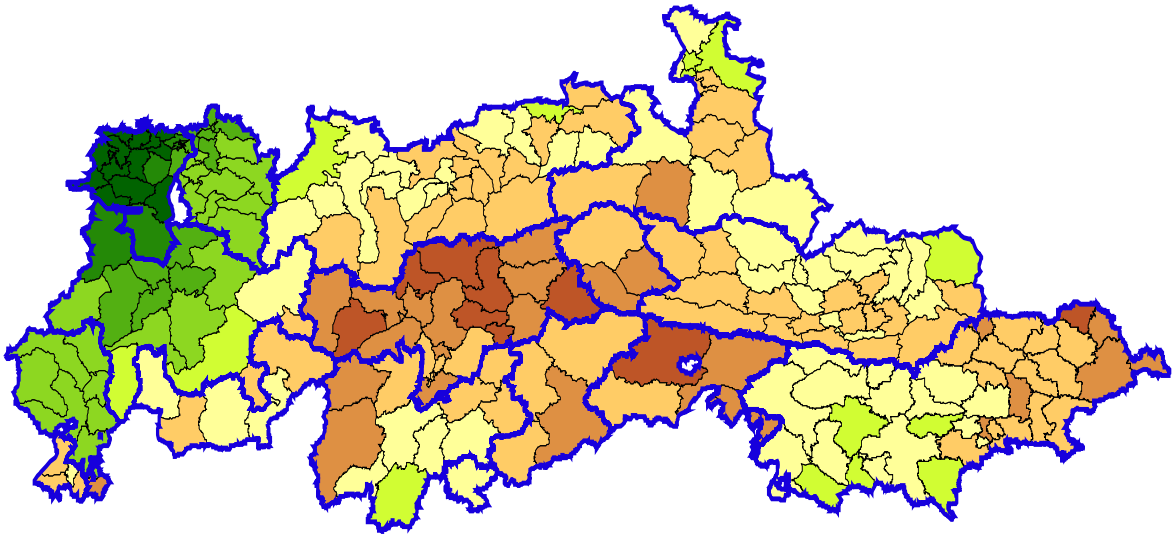


Fig. 12: Stomach – Mortality – Smoothed Map - Females

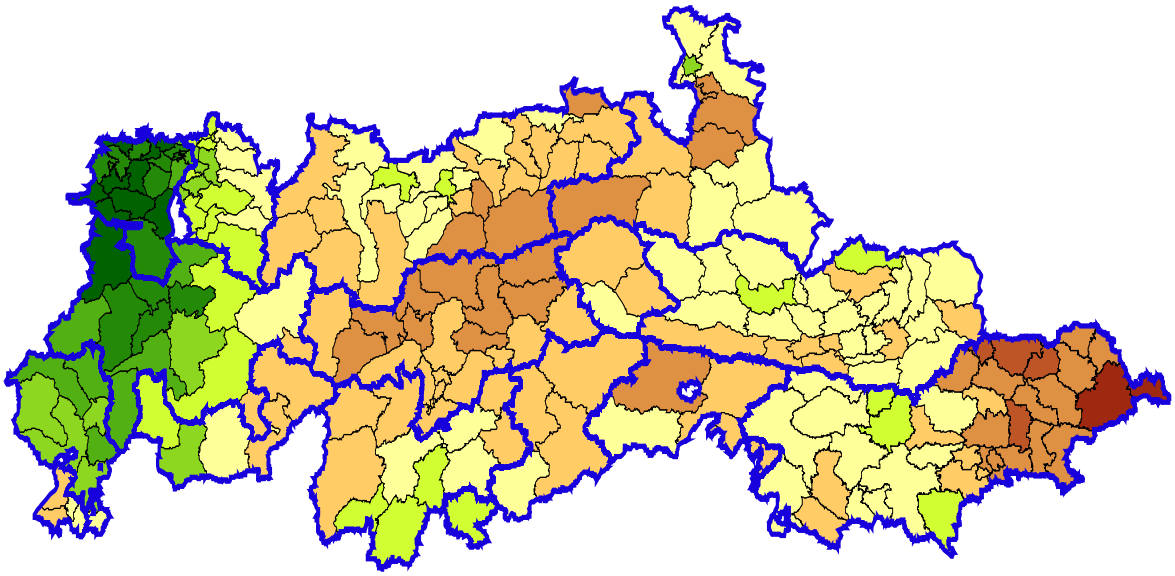


Fig. 13: Stomach – Incidence – Smoothed Map - Males

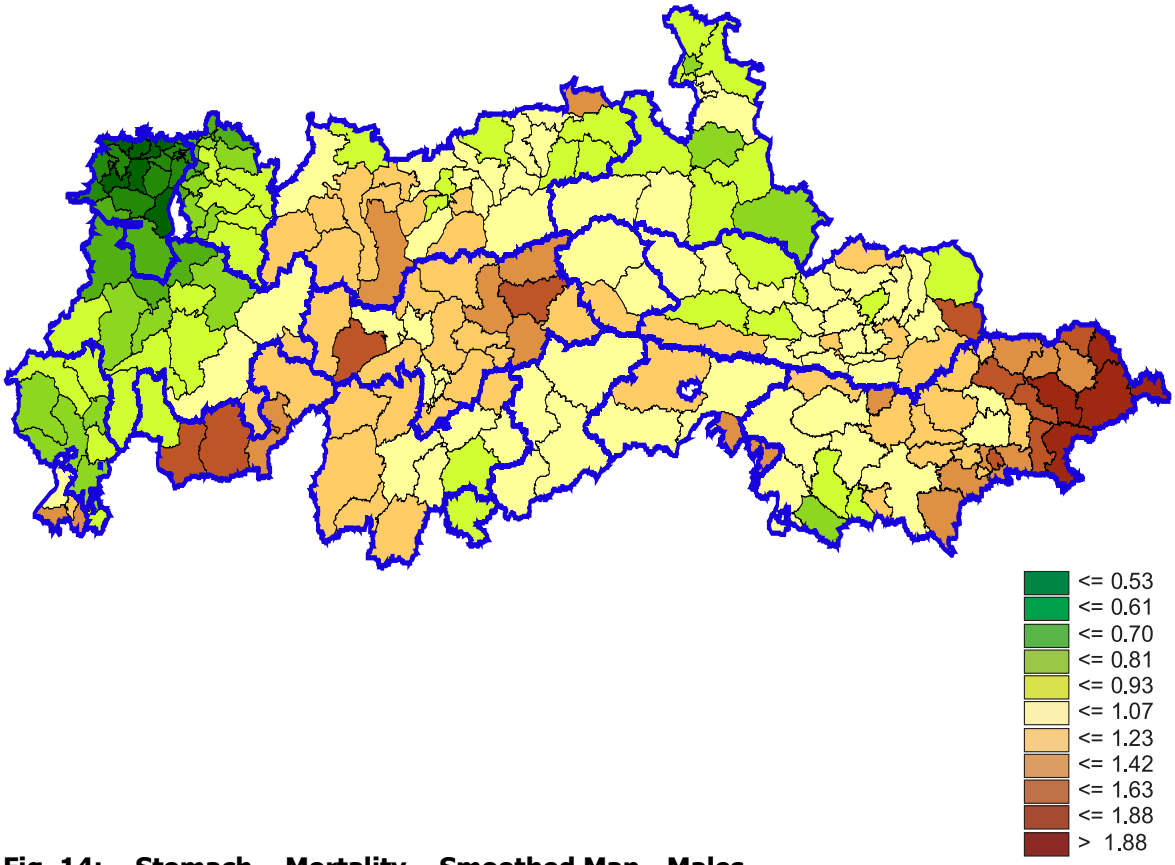
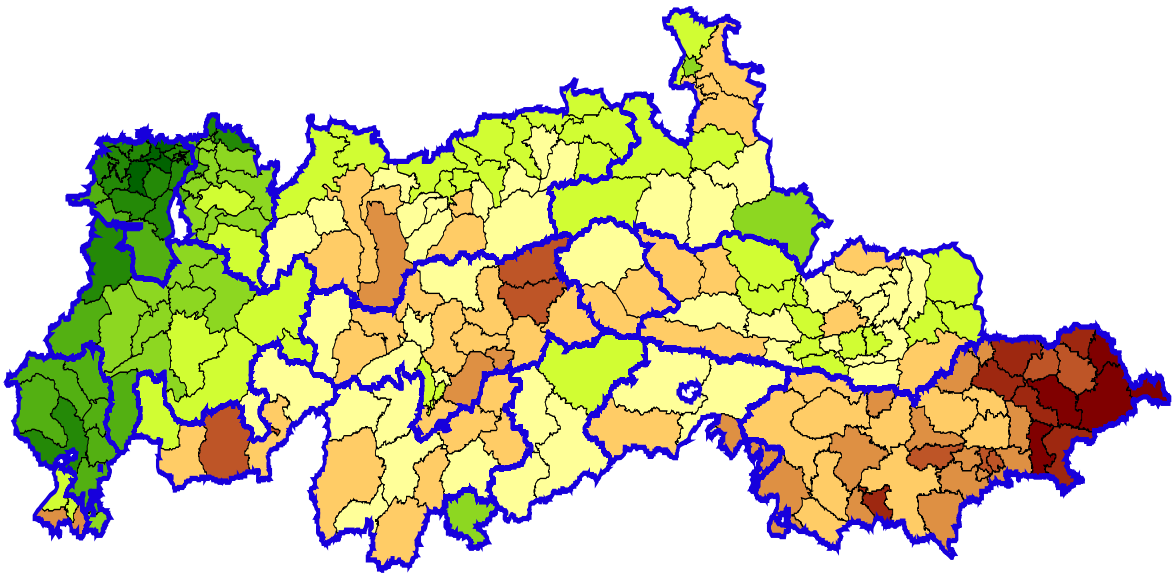


Fig. 14: Stomach – Mortality – Smoothed Map - Males



5.4 Colon and Rectum Harald Frick

Colon e Retto
Colon und Rektum
Debelo črevo in danka

5.4.1 Summary and Call for Action

Summary and Call for Action

SMR/SIR is below 1.3 in almost areas. In Slovenia the rates are slightly higher, but - as compared to other cancer sites - the excess risk is rather small. Higher mortality might not only refer to differences in screening programs, but also to the fact that symptomatic patients are seen in later stages.

Primary prevention may include healthy lifestyles and nutritional education to avoid obesity and metabolic syndroms. Secondary prevention includes yearly haemoccult testing (as it is recommended by the European Council) starting by the age of 50 and sigmoidoscopy every five years. Alternatively, colonoscopy every 10 years, starting at the age of 55 might improve patient outcome.

Surgery procedures following good practice guidelines (i.e. total mesorectal excision) may also reduce the risk of relapse and mortality.

Sintesi e proposte operative

Il valore dei SIR e SMR, al di sotto di 1,3 in quasi tutte le aree, indica una scarsa eterogeneità geografica. I tassi sono leggermente maggiori in Slovenia, ma – in confronto alle altre sedi tumorali – l'eccesso di rischio è piuttosto piccolo. La mortalità più alta può essere ricondotta non solo a differenze nei programmi di screening, ma anche al fatto che il paziente sintomatico viene diagnosticato in stadio più avanzato.

La prevenzione primaria di questo tumore è possibile attraverso l'adozione di stili di vita salutari e l'educazione alimentare, tesa ad evitare l'obesità e le sindromi metaboliche. La prevenzione secondaria comprende, a partire dai 50 anni, il test annuale del sangue occulto (secondo le raccomandazioni del Consiglio Europeo) e la sigmoidoscopia ogni 5 anni. In alternativa, una colonscopia ogni 10 anni a partire dall'età di 55 anni può migliorare l'esito per il paziente.

Procedure chirurgiche aderenti a linee guida accurate (es. escissione meso-rettale totale) possono ridurre il rischio di recidive e la mortalità.

Zusammenfassung und Schlussfolgerungen

SMR/SIR sind in fast allen Regionen unter 1.3. In Slowenien sind die Raten geringgradig höher, aber verglichen mit anderen Krebslokalisationen ist die Risikoerhöhung sehr gering. Die höhere Mortalität kann unter Umständen nicht nur auf den Unterschied in den Screeningprogrammen zurückgeführt werden, sondern auch auf die Tatsache, dass symptomatische Patienten in späteren Stadien

diagnostiziert werden. Primärprävention kann Lebensstilveränderungen und Ernährungsberatung zur Vermeidung von Fettleibigkeit und metabolischen Syndromen beinhalten. Sekundärprävention schließt den jährlichen Hämokkult-Test (wie es von der EU empfohlen wird) beginnend mit dem 50. Lebensjahr und eine Sigmoidoskopie alle 5 Jahre ein. Alternativ kann auch die Koloskopie, beginnend mit dem 55. Lebensjahr, alle 10 Jahre durchgeführt, das Outcome verbessern. Auch die operative Behandlung, wenn sie exakten Guidelines folgt, kann das Risiko von Rezidiva und Mortalität senken.

Povzetek in poziv k ukrepanju

Standardizirana količnika umrljivosti in incidence sta na vseh območjih nižja od 1,3. V Sloveniji sta oba količnika nekoliko višja od povprečja, toda v primerjavi z drugimi raki je presežek precej nizek. Višje umrljivosti ne pripisujemo samo razlikam v presejalnih programih, temveč tudi temu, da so simptomatični bolniki odkriti, ko je njihova bolezen že v razsejani obliki.

V primarni preventivi se priporoča zdrav način življenja, osveščenost o zdravi prehrani z namenom preprečevanja debelosti kot tudi ostalih presnovnih bolezni. Sekundarna preventiva pa vključuje vsakoletno testiranje na prikrito krvavitev (kot ga priporoča Svet Evrope), ki naj se začne pri 50. letu, in sigmoidoskopijo vsako peto leto. Druga možnost, ki tudi lahko prispeva k boljšemu izidu bolezni, je kolonoskopija, opravljena vsako deseto leto.

Tudi natančno in po smernicah izvedeno operativno zdravljenje (totalna mezorektalna ekscizija) lahko zelo zniža tveganje ponovitve bolezni ali smrti.

5.4.2 Introduction

Cancer of the large bowel (colorectal cancer) is a common form of malignancy in the developed countries with an overall male predominance, which is even more accentuated for rectal cancer. Anatomically the large bowel is about 5 feet long. More than 20% of cancers occur on the left side (sigmoid) and about 13% – 20% in the right-sided coecum. About one-fourth to one-third is located in the rectum. High regional incidence is associated with a higher proportion of sigmoid cancers.

5.4.3 Epidemiology

Colorectal cancer is a malignant disease of the elderly. Only about 5% occur below the age of 40. Starting at the age of 45 the incidence doubles every 10 years. In the study area age-standardized colorectal cancer incidence is about 24 cases per 100,000 females and 40 cancers per 100,000 males. Lower rates were observed in Carinthia and the Swiss regions Graubünden/Glarus, Ticino and St. Gallen/Appenzell (21 to 24 cases per 100,000 females and 36 to 38 cases per 100,000 males). In Friuli/Venezia, Sondrio and South Tyrol we observe about 27 cases per 100,000 females, and about 44 to 45 cases per 100,000 males. Crude rates range from 48.8 (Salzburg) to 78 (Friuli/Venezia) per 100,000 females and from 53 (Vorarlberg) to 98 (Friuli/Venezia) cases per 100,000 males. The mortality rate is approx. 9 cases per 100,000 females and 17 cases per 100,000 males.

Internationally, colorectal cancer accounts for more than 10% of all new cancer cases each year. In Europe the incidence of colorectal cancer is increasing. Southern and eastern Europe shows an even more striking increase in colorectal cancer prevalence. Worldwide colorectal cancer incidence is much lower in South Africa, Asia and South America than in Western Europe and the United States.

5.4.4 Data quality aspects

SIR ranged from 0.88 to 1.1 (men; mean 1.0 (0.98 – 1.02 95% IC)) and 0.89 to 1.07 (women). The SMR (overall 0.97 – 1.03 95% IC) from 0.65 up to 1.41 (men) and 0.67 to 1.31 (women), respectively. Mortality to incidence ratio ranged from 0.31 to o.52 (men) and 0.35 to 0.6 (women). Altogether, the ranges are rather high. DCO only rates range from 0% (St. Gallen/Appenzell and Varese) to 5% in Carinthia (overall rate is 1.7%).

5.4.5 Risk factors, early detection and screening

Generally, colorectal cancer is not viewed as an occupational disease. Social class and lifestyle factors may confound some relationship to any occupational groups. In the 1980ies colorectal cancer was thought to be related to occupational exposure to woods, metals, plastic and solvents, as well as fumes. Direct association is rather poor.

Sporadic colorectal carcinoma might be associated with socio-economic factors, physical activity, nutrition, smoking and hormonal factors. Carcinomas on the basis of chronic infection account for only 1% to 5% of all colorectal carcinomas: 10% are associated with genetically determined syndromes (FAP; HNPCC).

Unsaturated fatty acids and cholesterol are positively associated with colorectal carcinoma, based on a possible activation of mitotic activity of the enterocyte. Degraded acids might be carcinogenic. Meat is

therefore associated with a higher incidence, due to its content of unsaturated fatty acids and also to nitrosamines. Some studies proved the protective effect of vitamins C, E and A, as well as of selen, folic acid and tannins. Red wine contains tannins, but alcohol per se is positively correlated to higher cancer incidence.

Long-term ulcerative colitis is associated with a cumulative risk of plus 40% after 30 years. Patients with a long-term Morbus Crohn show a 20fold increased risk. Genetically determined syndromes are associated with early carcinogenesis.

Most of the colorectal carcinomas develop on the basis of adenomas. By the age of 50 years coloscopy may reveal adenomas in 35% to 50% of the males and about 25 to 40% of the women.

Coloscopy and polypectomy in a screening setting may reduce the incidence of colorectal cancer; mortality therefore may decrease by up to one-third. Hemoccult testing might also be helpful in early detection of colorectal malignancy.

Population-based screening is known in Austria, France, Germany and the UK, however with different strategies. Switzerland, Spain, Italy, Denmark and Finland began screening strategies in the recent past. Ongoing studies to determine the best strategy are reported from the Netherlands and Norway. Differences concern age group, procedures and follow-up periods.

Microsatellite instability testing might be necessary in circumstances of hereditary non-polyposis colorectal carcinoma and also after detection of serrated adenomas which may show a more aggressive vertical growth pattern.

Survival after colorectal cancer is good. Five-year survival for non-symptomatic colorectal cancer is about 70%; whereas patients with symptomatic cancers show 50% five-year survival. In advanced stages (i.e. metastatic cancers) survival is below 10%.

5.4.6 Geographical variation

There are some regions (Sondrio, South Tyrol e.g.) with higher rates of age-standardized annual incidence for colorectal cancer for females and males as well. Mortality in Varese is almost twice as high as in Friuli/Venezia for women, but not for men. Carinthia shows the lowest incidence rates for both females and males. In Switzerland the Ticino shows higher incidence and mortality rates for both sexes, than do the German-speaking Swiss cantons included in this mapping.

Slovenia shows high mortality rates for both sexes in this mapping, as do Varese, Vorarlberg and South Tyrol for women. Also the EUROCARE-4 database shows a poorer outcome in Slovenia with an age-standardized five-year survival of about 45%, whereas in Switzerland it is about 60% and in Austria about 58% (both sexes, period 1995 - 1999). In 2000 - 2002 for Europe the expected five-year survival for colorectal cancer was above 56% (point estimate 56.8%, SE 0.3).

There was no organized screening program for colorectal cancer in Slovenia in the period 2001-2005 and the percentage of patients diagnosed in the localized stage was below 15%. According to the EUROCARE-4 results the five-year relative survival in Slovenia is about 50%.

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Tab. 18: Colon and Rectum – Numbers and Rates - Females

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	782	54.1	20.8 (19.1, 22.6)	0.96 (0.89, 1.02)	329	22.7	6.9 (6.0, 7.8)	0.85 (0.76, 0.95)
Salzburg	655	48.8	24.4 (22.3, 26.5)	1 (0.92, 1.07)	303	22.6	9.2 (8.0, 10.3)	1 (0.89, 1.12)
Tyrol	900	51.4	24.8 (22.9, 26.6)	1.05 (0.98, 1.12)	390	22.3	8.4 (7.4, 9.3)	0.98 (0.89, 1.09)
Vorarlberg	384	42.6	23.1 (20.6, 25.6)	0.93 (0.84, 1.03)	212	23.5	10.5 (8.9, 12.1)	1.13 (0.98, 1.29)
Friuli Venezia Giulia	152	78.0	27.0 (21.5, 32.5)	0.98 (0.83, 1.15)	54	27.7	6.2 (4.0, 8.4)	0.65 (0.49, 0.85)
Varese	175	60.1	25.5 (21.2, 29.8)	1.02 (0.87, 1.18)	81	27.8	9.5 (7.1, 11.9)	0.96 (0.77, 1.2)
Sondrio	295	64.8	27.5 (23.9, 31.2)	1.07 (0.95, 1.2)	113	24.8	7.4 (5.8, 9.1)	0.84 (0.69, 1.01)
South Tyrol	685	58.1	27.3 (24.9, 29.6)	1.1 (1.02, 1.19)	323	27.4	10.2 (8.9, 11.5)	1.09 (0.98, 1.22)
Trentino	730	59.0	23.8 (21.8, 25.8)	0.97 (0.9, 1.04)	392	31.7	10.1 (8.9, 11.4)	1.05 (0.95, 1.16)
Veneto	379	62.8	23.6 (20.7, 26.5)	0.9 (0.81, 0.99)	190	31.5	9.7 (7.5, 11.9)	0.88 (0.76, 1.02)
Slovenia	2,072	53.7	25.3 (24.2, 26.5)	1.05 (1, 1.1)	1,113	28.9	10.7 (10.1, 11.4)	1.31 (1.23, 1.39)
Graubünden/Glarus	272	47.7	21.2 (18.3, 24.0)	0.89 (0.79, 1)	101	17.7	5.9 (4.5, 7.3)	0.67 (0.55, 0.82)
St,Gallen/Appenzell	626	47.6	23.2 (21.1, 25.3)	0.94 (0.87, 1.02)	233	17.7	7.0 (5.9, 8.0)	0.72 (0.63, 0.82)
Ticino	495	59.9	23.8 (21.3, 26.2)	0.98 (0.89, 1.07)	177	21.4	6.8 (5.6, 8.0)	0.7 (0.6, 0.81)
Total	**8,602**	**53.9**	**24.3 (23.7, 24.9)**	**1 (0.98, 1.02)**	**4,011**	**25.1**	**8.8 (8.5, 9.1)**	**1 (0.97, 1.03)**

Tab. 19: Colon and Rectum – Numbers and Rates - Males

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	888	65.7	35.8 (33.3, 38.2)	0.92 (0.86, 0.98)	384	28.4	14.7 (13.2, 16.3)	0.88 (0.8, 0.98)
Salzburg	745	59.2	38.6 (35.7, 41.4)	0.96 (0.89, 1.03)	324	25.8	15.9 (14.1, 17.7)	0.94 (0.84, 1.05)
Tyrol	1,061	63.6	40.6 (38.1, 43.1)	1.02 (0.96, 1.08)	404	24.2	14.8 (13.3, 16.3)	0.89 (0.8, 0.98)
Vorarlberg	468	53.3	37.1 (33.7, 40.5)	0.92 (0.84, 1.01)	188	21.4	14.6 (12.4, 16.7)	0.87 (0.75, 1)
Friuli Venezia Giulia	184	98.4	43.4 (36.7, 50.1)	1.06 (0.92, 1.23)	77	41.2	17.7 (13.5, 21.8)	0.95 (0.75, 1.19)
Varese	226	82.8	45.6 (39.5, 51.7)	1.13 (0.98, 1.28)	82	30.0	16.0 (12.5, 19.6)	0.91 (0.73, 1.13)
Sondrio	299	68.6	37.6 (33.2, 42.0)	0.9 (0.81, 1.01)	131	30.1	15.4 (12.7, 18.1)	0.9 (0.75, 1.06)
South Tyrol	837	73.0	44.1 (41.0, 47.2)	1.09 (1.02, 1.17)	337	29.4	16.8 (15.0, 18.7)	0.98 (0.88, 1.09)
Trentino	875	74.3	39.0 (36.3, 41.7)	0.97 (0.91, 1.04)	444	37.7	18.5 (16.7, 20.3)	1.08 (0.98, 1.18)
Veneto	494	88.7	42.9 (38.9, 46.9)	1.05 (0.96, 1.15)	198	35.5	15.6 (13.3, 17.9)	0.92 (0.79, 1.06)
Slovenia	2,484	67.5	44.2 (42.4, 46.0)	1.1 (1.06, 1.15)	1,302	35.4	25.3 (23.9, 26.7)	1.41 (1.33, 1.48)
Graubünden/Glarus	341	61.3	35.5 (31.6, 39.5)	0.88 (0.79, 0.97)	144	25.9	13.2 (10.9, 15.4)	0.79 (0.66, 0.93)
St.Gallen/Appenzell	730	56.6	36.0 (33.3, 38.7)	0.88 (0.81, 0.94)	304	23.6	14.1 (12.4, 15.8)	0.78 (0.69, 0.87)
Ticino	565	74.9	38.1 (34.8, 41.4)	0.95 (0.87, 1.03)	179	23.7	11.1 (9.4, 12.8)	0.65 (0.56, 0.75)
Total	**10,197**	**67.0**	**40.2 (39.4, 41.0)**	**1 (0.98, 1.02)**	**4,498**	**29.6**	**16.8 (16.3, 17.3)**	**1 (0.97, 1.03)**

Tab. 20: Colon and Rectum – Data quality

	FEMALES			MALES		
Country description	% DCO	% HV	RMI	% DCO	% HV	RMI
Carinthia	5.0%	97.4%	0.42	2.9%	98.7%	0.43
Salzburg	2.0%	94.9%	0.46	0.5%	95.4%	0.43
Tyrol	0.9%	95.9%	0.43	0.8%	98.1%	0.38
Vorarlberg	4.4%	98.4%	0.55	3.0%	98.7%	0.40
Friuli Venezia Giulia	0.7%	94.0%	0.36	0.0%	97.3%	0.42
Varese	0.0%	95.4%	0.46	0.0%	96.5%	0.36
Sondrio	0.7%	94.2%	0.38	0.3%	96.3%	0.44
South Tyrol	1.8%	96.4%	0.47	0.5%	97.6%	0.40
Trentino	1.2%	95.3%	0.54	0.8%	95.9%	0.51
Veneto	1.1%	95.2%	0.50	0.2%	98.8%	0.40
Slovenia	1.5%	98.0%	0.54	0.8%	98.5%	0.52
Graubünden/Glarus	0.4%	95.6%	0.37	0.3%	97.6%	0.42
St.Gallen/Appenzell	0.0%	94.7%	0.37	0.1%	97.3%	0.42
Ticino	1.6%	98.2%	0.36	0.5%	99.3%	0.32
Total	**1.7%**	**96.7%**	**0.47**	**0.9%**	**97.9%**	**0.44**

Fig. 15: Colon and Rectum – Incidence – Smoothed Map - Females

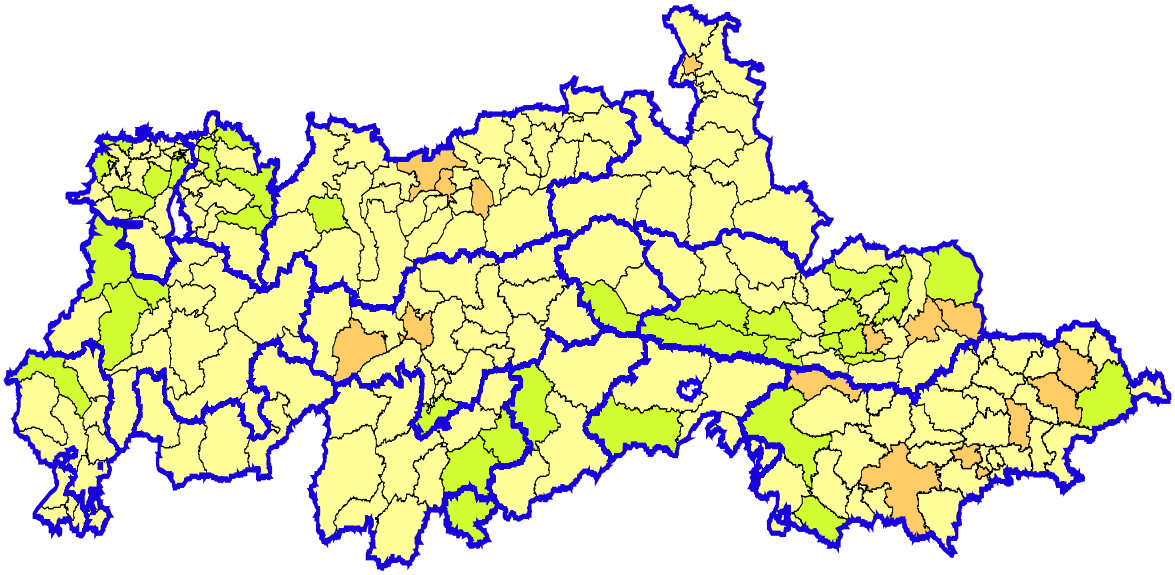


Fig. 16: Colon and Rectum – Mortality – Smoothed Map - Females

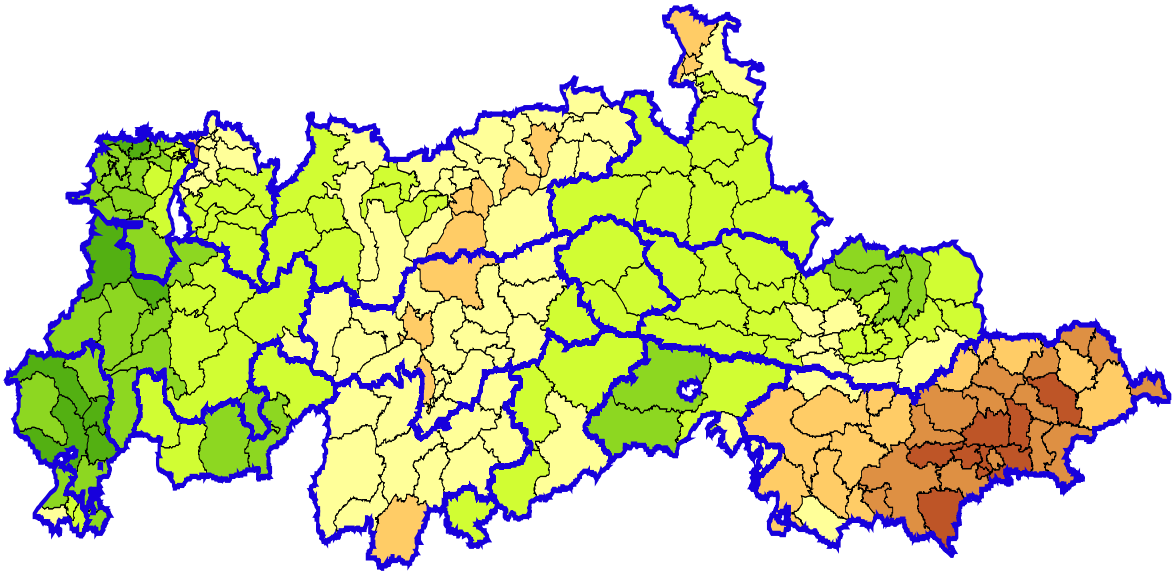


Fig. 17: Colon and Rectum – Incidence – Smoothed Map - Males

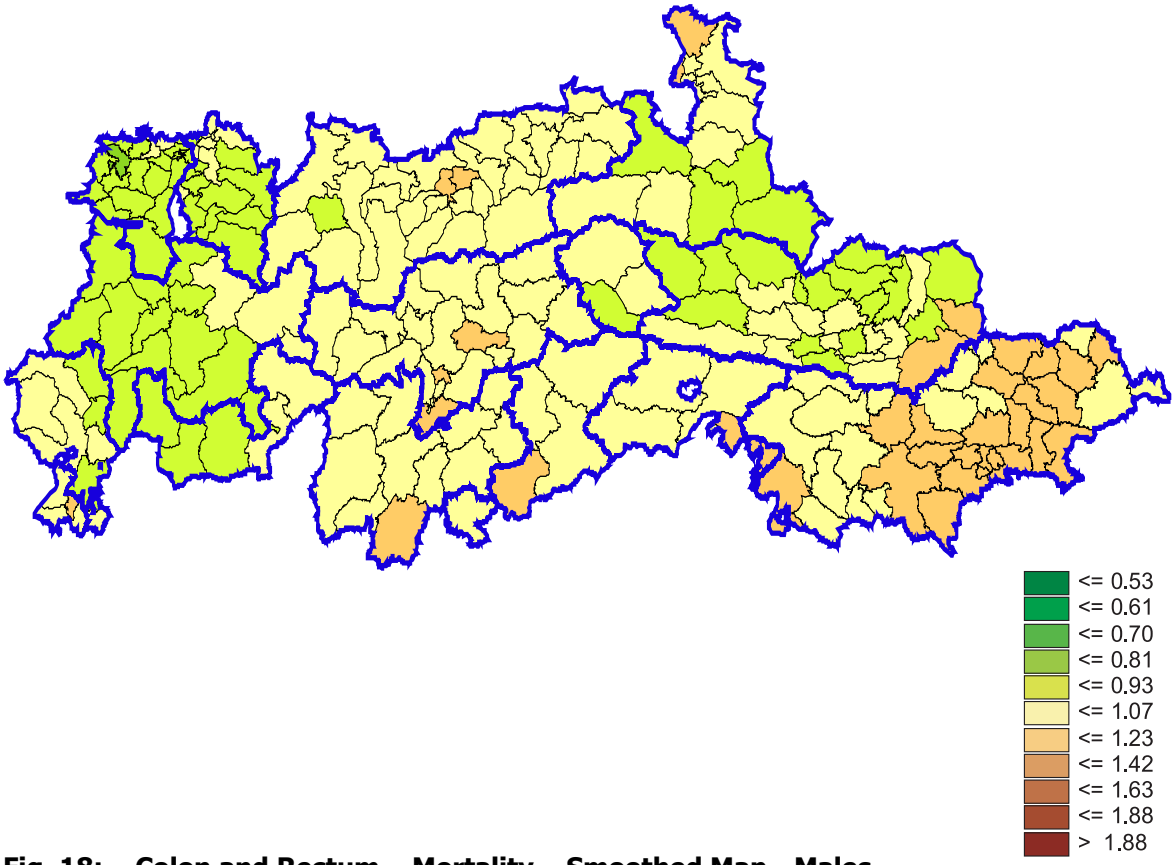
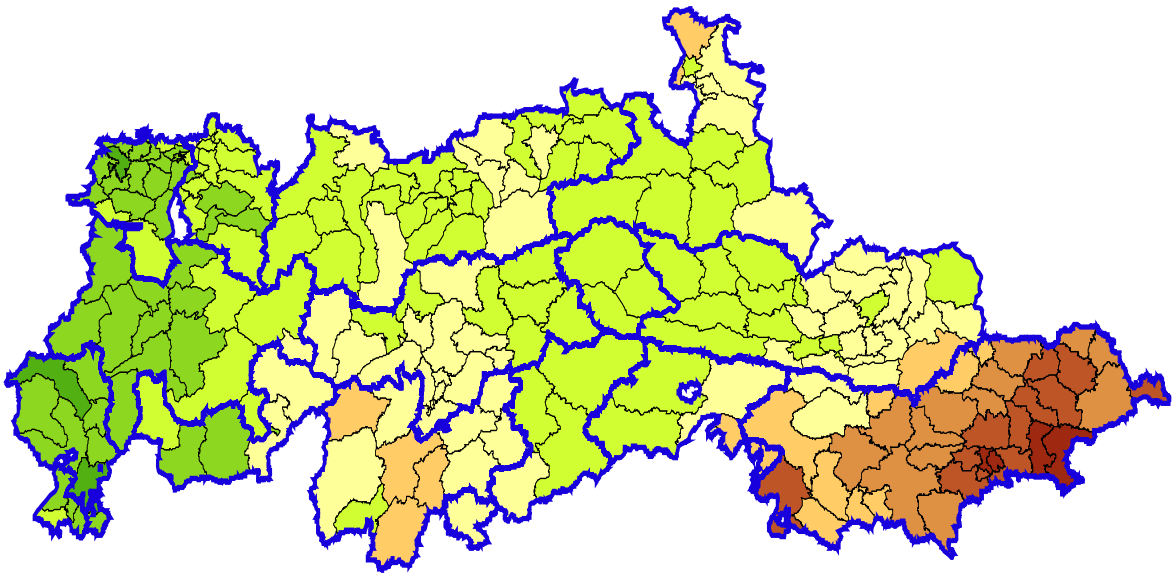


Fig. 18: Colon and Rectum – Mortality – Smoothed Map - Males



5.5 Liver Luigino Dal Maso

Fegato
Leber
Jetra

5.5.1 Summary and Call for Action

Summary and Call for Action

A huge variation in primary liver cancer incidence and mortality rates has emerged in Alpine regions, with consistently higher SIRs and SMRs for Italian areas and Ticino. Reasons for the observation are only partially clear, but probably reflect the prevalence of HCV infection. Half of primary liver cancer in Northern Italy is attributable to HCV. Given the long incubation period of hepatitis viruses, such pattern of liver cancer will probably continue in the next decades, at least in Italy. In addition, the beneficial effect of the vaccine against HBV in children born from 1978 is still to be seen. One-third of liver cancers in Alpine areas are also attributable to alcohol consumption, which, in comparison with other areas, is still very high.

Major steps in the prevention of new HBV and HCV infections have been taken in Italian areas with higher incidence rates, and should be extended to the increasingly numerous immigrants from countries that are highly endemic for the two viruses. The same holds true for the prevention of heavy alcohol drinking. As part of secondary prevention, HCV-infected individuals should be counseled to minimize their risk of transmitting HCV and referred for medical evaluation and treatment.

Sintesi e proposte operative

Le aree alpine mostrano una notevole eterogeneità nei tassi di incidenza e mortalità per tumori primitivi del fegato, con elevati SIR ed SMR nelle aree a sud delle Alpi (Italia e Ticino). Le cause di tale eccesso sono solo parzialmente note e probabilmente riflettono la prevalenza dell'infezione da HCV. Nel nord Italia, metà dei casi di tumore primario del fegato sono attribuibili all'HCV e, dato il lungo periodo di incubazione, elevati tassi di tumore del fegato sono attesi nelle prossime decadi. D'altra parte, le campagne di vaccinazione contro l'HBV, nei nati dal 1978 in poi, devono ancora mostrare completamente il loro effetto. Infine, nelle aree alpine, un terzo dei tumori primitivi del fegato è legato all'eccessivo consumo di bevande alcoliche, ancora molto alto rispetto ad altre aree. Iniziative importanti per la prevenzione delle infezioni da HBV e HCV sono state intraprese nelle aree italiane ad alta incidenza di tumore del fegato e dovrebbero essere estese ai soggetti immigrati da aree endemiche per tali infezioni. Lo stesso vale per la prevenzione dell'abuso di alcol. Per quanto riguarda la prevenzione secondaria, andrebbe minimizzato il rischio di trasmettere l'HCV da parte dei soggetti positivi che dovrebbero essere seguiti e ricevere, se necessario, trattamenti opportuni.

Zusammenfassung und Schlussfolgerungen

Die Daten für Leberkrebs zeigen bezüglich Krebsinzidenz und Mortalität in den Alpenregionen eine große Variationsbreite, wobei durchgehend höhere SIR und SMR in den italienischen Regionen beobachtet werden. Die Gründe dafür sind nur teilweise klar, sie spiegeln jedoch vermutlich die Prävalenz von HCV-Infektionen wieder. Die Hälfte der primären Leberkarzinome in Norditalien ist auf HCV-Infektionen zurückzuführen. Bezieht man die lange Inkubationszeit der Hepatitis mit ein, wird sich dieses Muster vermutlich in den nächsten Jahren fortsetzen, besonders in Italien. Zusätzlich ist der positive Effekt der Impfung gegen HBV von Kindern, die nach 1978 geboren wurden, noch zu beachten. Ein Drittel der Leberkrebsfälle in den alpinen Regionen ist allerdings auch dem Alkoholkonsum zuzuordnen, der im Vergleich mit anderen Gebieten noch immer sehr hoch ist. Entscheidende Schritte in der Prävention von neuen HBV und HCV-Infektion wurden in italienischen Regionen mit hohen Inzidenzraten unternommen und diese Maßnahmen sollten auch ausgeweitet werden auf die wachsende Anzahl der Immigranten aus Ländern mit einer hohen endemischen Verbreitung der zwei Virusarten. Dasselbe gilt auch der Prävention von starkem Alkoholgenuss. Als Teil der Sekundärprävention sollten HCV-infizierte Individuelle Empfehlungen erhalten, ihr Risiko der HCV-Übertragung zu reduzieren.

Povzetek in poziv k ukrepanju

Standardizirani količniki incidence in umrljivosti primarnega jetrnega raka se v alpskih regijah zelo razlikujejo; najvišje vrednosti se pojavljajo v italijanskih območjih ter pokrajini Ticino. Razlogi za to so le delno jasni; verjetno je za takšno stanje najpomembnejša razlika v razširjenosti okužbe z virusom HCV. Polovico vseh primerov primarnega jetrnega raka odkritih v severni Italiji, lahko pripišemo okužbi z virusom HCV. Zaradi dolge inkubacijske dobe virusov hepatitisa, se bo, vsaj v Italiji, jetrni rak še desetletja pojavljal po enakem vzorcu. Poleg tega še vedno ni mogoče opaziti pozitivnega učinka cepljenja proti virusu HBV, ki je bilo opravljeno pri vseh otrocih rojenih po letu 1978. Tretjina jetrnih rakov v alpskih regijah je posledica pretiranega uživanja alkohola, ki je v primerjavi z ostalimi območji tu zelo razširjeno.

V italijanskih pokrajinah z visokimi incidenčnimi stopnjami jetrnega raka so že začeli izvajati najpomembnejše ukrepe za preprečevanje okužb z virusi HBV in HCV; razširiti pa bi jih bilo potrebno tudi na vedno večje število priseljencev iz dežel, v katerih sta oba virusa endemična. Isto velja tudi za omejevanje pretiranega uživanja alkohola. Sekundarno preprečevanje pa med drugim vključuje tudi opozorilo posameznikov, okuženih z virusom HCV, naj skrajno omejijo možnosti prenašanja okužbe z virusom HCV, ter zdravstveno oceno in zdravljenje okuženih.

5.5.2 Introduction

The distribution of primary liver cancer shows huge variations worldwide [1] with rising incidence and mortality rates reported in several European countries [2,3].

5.5.3 Epidemiology

During the period 2001-2005, 2,620 male primary liver cancer cases and 992 female ones were reported in the Alpine regions of the study area. Corresponding numbers for mortality were 2,140 and 1,005, respectively. Annual age-standardized incidence rates were 2.5/100,000 women and 10.6/100,000 men and mortality rates were 2.3 and 8.3/100,000, respectively. They represent 1.4% of all incident cases in women and 3.2% in men; the corresponding figures for mortality were 3.0% and 5.3%, respectively.

In Alpine regions, the male to female ratio for primary liver cancer was 4.2, consistent with data recently reported in Italy [2] and Europe [1]. Only 10% of cases occurred in persons below age 55 years, and the median age at diagnosis was 68 years in men and 75 years in women.

5.5.4 Data quality aspects

The proportion of liver cancer cases identified by death certificates only (DCO) was approximately 5% for all areas combined, although in some it was higher than 10% (i.e., 19% in Carinthia). The misclassification of secondary (metastatic) liver cancer as primary liver cancer poses a major problem in cancer mortality studies, while it should be a less severe drawback in cancer incidence studies.

The proportion of microscopically verified liver cancer cases (58%) was lower than that of all cancers (93%). Proportions below 50% emerged in most Italian areas where imaging techniques (e.g.: ultrasound, multiphasic computed tomography scan, magnetic resonance imaging, or angiography) and measurement of serum tumor α-fetoprotein are reliable and consistently performed [4].

The mortality/incidence ratio was 0.87 for the examined Alpine regions, consistent with international incidence [1] and survival data [5]. Ratios >1 (possible over-reporting of deaths or under-reporting of incidence) emerged for women overall (1.01), in particular in Vorarlberg (1.20) and Slovenia (1.27).

5.5.5 Risk factors

The etiology of primary liver cancer is largely established, with three major risk factors accounting for approximately 90% of cases: infection with hepatitis B (HB) or C viruses (HCV) and alcohol abuse. The relative contribution of these three risk factors, however, varies worldwide [6,7]. In Italy HCV prevalence did not vary greatly by age, and the highest prevalence is found among adults aged 35-40 years, suggesting two periods of intense HCV transmission. The first was attributable to iatrogenic transmission before the introduction of disposable syringes (1975). Intravenous drug use in the 1970s and 1980s was at the heart of the second period of HCV spread [2]. Since the latent period between hepatitis infection and hepatocellular carcinoma has been estimated between 3 and 4 decades [8], variations of HCV (and HBV) carcinogenic consequences are expected to be fully seen many decades after changes in hepatitis virus prevalence.

Alcohol abuse poses a health problem in most Alpine regions, and it is responsible for a relevant fraction (approximately one-third) of liver cancers in these areas [6,9]. The reduction in alcohol consumption that has been taking place in several European countries since the 1970s has already reduced mortality from cirrhosis [3], and it should also have a beneficial effect on primary liver cancer incidence.

5.5.6 Early detection, screening

Survival after primary liver cancer is very poor. In Europe, the proportion of patients still alive (relative survival) one year after diagnosis was 30% with even lower estimates for Slovenia and Austria (25%) [5]. Five-year relative survival after liver cancer diagnosis (in 1995-1999) was only 9% and still lower in Slovenia (3%).

HCV screening and early treatments have the potential to improve average life expectancy and prevent liver cancer; however, to be cost-effective, they should be focused on populations with elevated HCV prevalence [10].

Relatively few studies have examined the impact of early detection on survival [11]; moreover, no systematic (effective) screening program was active during that period.

5.5.7 Geographical variations

A significant geographical heterogeneity emerged for liver cancer incidence and mortality in both genders. In men, significantly elevated SIRs emerged for all Italian areas and Ticino with reported IR>20/100,000 for Friuli Venezia Giulia (30), Veneto (27) and Sondrio (24); significantly lower SIRs (IR between 5 and 9) emerged in all other areas. In women, the pattern was less marked with elevated SIRs also in Carinthia, but not in Ticino. For mortality, the results are consistent with incidence. As a consequence SIR > 2 emerged in both genders in Friuli Venezia Giulia and Veneto. Notably, a significant but less marked geographical heterogeneity emerged for mortality (SMR).

Difference in incidence or mortality by regional units (within the cancer registry areas) can be largely explained by random variation due to small numbers.

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Tab. 21: Liver – Numbers and Rates - Females

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	117	8.1	3.0 (2.4, 3.6)	1.23 (1.02, 1.47)	120	8.3	3.1 (2.4, 3.7)	1.24 (1.02, 1.48)
Salzburg	59	4.4	1.9 (1.3, 2.4)	0.79 (0.6, 1.01)	53	3.9	1.7 (1.2, 2.2)	0.7 (0.52, 0.91)
Tyrol	85	4.9	2.2 (1.7, 2.8)	0.87 (0.7, 1.08)	97	5.5	2.4 (1.9, 2.9)	0.98 (0.79, 1.19)
Vorarlberg	41	4.6	2.3 (1.5, 3.1)	0.87 (0.63, 1.19)	49	5.4	2.8 (1.9, 3.6)	1.04 (0.77, 1.37)
Friuli Venezia Giulia	46	23.6	5.5 (3.5, 7.5)	2.46 (1.8, 3.28)	33	16.9	2.6 (1.4, 3.8)	1.64 (1.13, 2.31)
Varese	28	9.6	3.2 (1.9, 4.5)	1.4 (0.93, 2.03)	27	9.3	3.0 (1.7, 4.3)	1.31 (0.86, 1.91)
Sondrio	51	11.2	3.9 (2.6, 5.2)	1.58 (1.18, 2.08)	56	12.3	3.5 (2.4, 4.6)	1.68 (1.27, 2.18)
South Tyrol	70	5.9	2.5 (1.8, 3.2)	0.97 (0.76, 1.23)	59	5.0	1.9 (1.4, 2.5)	0.8 (0.61, 1.03)
Trentino	112	9.1	2.9 (2.3, 3.6)	1.26 (1.04, 1.52)	114	9.2	2.8 (2.2, 3.4)	1.24 (1.02, 1.49)
Veneto	113	18.7	5.9 (4.6, 7.2)	2.25 (1.85, 2.71)	90	14.9	4.4 (3.0, 5.8)	1.7 (1.37, 2.09)
Slovenia	147	3.8	1.7 (1.4, 2.1)	0.66 (0.55, 0.77)	186	4.8	1.9 (1.6, 2.3)	0.84 (0.73, 0.97)
Graubünden/Glarus	24	4.2	2.0 (1.0, 3.0)	0.68 (0.43, 1.01)	24	4.2	1.5 (0.8, 2.2)	0.65 (0.42, 0.97)
St,Gallen/Appenzell	49	3.7	2.0 (1.4, 2.6)	0.64 (0.47, 0.84)	44	3.3	1.5 (1.0, 2.0)	0.55 (0.4, 0.74)
Ticino	50	6.0	2.2 (1.5, 2.8)	0.85 (0.63, 1.12)	53	6.4	1.9 (1.3, 2.4)	0.86 (0.65, 1.13)
Total	**992**	**6.2**	**2.5 (2.3, 2.7)**	**1 (0.94, 1.06)**	**1,005**	**6.3**	**2.3 (2.1, 2.5)**	**1 (0.94, 1.06)**

Tab. 22: Liver – Numbers and Rates - Males

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	207	15.3	8.6 (7.4, 9.8)	0.84 (0.73, 0.97)	180	13.3	7.3 (6.2, 8.5)	0.88 (0.76, 1.02)
Salzburg	139	11.0	7.1 (5.9, 8.3)	0.69 (0.58, 0.82)	115	9.1	5.7 (4.7, 6.8)	0.7 (0.58, 0.84)
Tyrol	187	11.2	7.6 (6.5, 8.8)	0.7 (0.6, 0.81)	146	8.7	5.7 (4.8, 6.7)	0.67 (0.56, 0.78)
Vorarlberg	75	8.5	6.2 (4.7, 7.6)	0.57 (0.45, 0.71)	73	8.3	5.7 (4.3, 7.0)	0.69 (0.54, 0.86)
Friuli Venezia Giulia	116	62.0	29.6 (24.0, 35.2)	2.64 (2.19, 3.17)	64	34.2	14.2 (10.5, 17.9)	1.72 (1.32, 2.19)
Varese	69	25.3	14.2 (10.8, 17.6)	1.34 (1.04, 1.69)	76	27.8	14.7 (11.3, 18.0)	1.79 (1.41, 2.24)
Sondrio	192	44.1	24.3 (20.7, 28.0)	2.26 (1.95, 2.6)	157	36.0	18.8 (15.8, 21.8)	2.24 (1.9, 2.62)
South Tyrol	263	22.9	14.6 (12.8, 16.4)	1.34 (1.18, 1.51)	178	15.5	9.6 (8.1, 11.0)	1.09 (0.94, 1.27)
Trentino	360	30.6	16.0 (14.2, 17.7)	1.57 (1.41, 1.74)	267	22.7	11.3 (9.9, 12.7)	1.39 (1.22, 1.56)
Veneto	302	54.2	26.9 (23.7, 30.0)	2.53 (2.25, 2.83)	236	42.4	20.1 (17.4, 22.7)	2.35 (2.06, 2.67)
Slovenia	333	9.0	6.0 (5.3, 6.6)	0.57 (0.51, 0.63)	341	9.3	6.6 (5.8, 7.3)	0.73 (0.66, 0.81)
Graubünden/Glarus	54	9.7	5.6 (4.1, 7.2)	0.55 (0.41, 0.72)	38	6.8	3.8 (2.5, 5.1)	0.46 (0.32, 0.62)
St.Gallen/Appenzell	110	8.5	5.6 (4.5, 6.7)	0.52 (0.43, 0.63)	89	6.9	4.4 (3.4, 5.4)	0.5 (0.4, 0.61)
Ticino	213	28.2	15.3 (13.2, 17.4)	1.4 (1.22, 1.6)	180	23.9	12.1 (10.3, 13.9)	1.41 (1.21, 1.63)
Total	**2,620**	**17.2**	**10.6 (10.2, 11.0)**	**1 (0.96, 1.04)**	**2,140**	**14.1**	**8.3 (7.9, 8.7)**	**1 (0.96, 1.04)**

Tab. 23: Liver – Data quality

	FEMALES			MALES		
Country description	% DCO	% HV	RMI	% DCO	% HV	RMI
Carinthia	27.4%	64.7%	1.03	14.5%	75.7%	0.87
Salzburg	6.8%	67.3%	0.90	6.5%	60.8%	0.83
Tyrol	4.7%	53.1%	1.14	0.5%	57.5%	0.78
Vorarlberg	2.4%	87.8%	1.20	4.0%	90.7%	0.97
Friuli Venezia Giulia	0.0%	26.1%	0.72	0.0%	47.4%	0.55
Varese	0.0%	71.4%	0.96	0.0%	58.0%	1.10
Sondrio	0.0%	23.5%	1.10	0.5%	41.4%	0.82
South Tyrol	4.3%	38.8%	0.84	1.9%	45.3%	0.68
Trentino	10.7%	39.0%	1.02	1.4%	50.4%	0.74
Veneto	3.5%	47.7%	0.80	2.3%	55.3%	0.78
Slovenia	9.5%	75.9%	1.27	3.3%	71.1%	1.02
Graubünden/Glarus	8.3%	54.5%	1.00	1.9%	62.3%	0.70
St.Gallen/Appenzell	0.0%	77.6%	0.90	0.9%	73.4%	0.81
Ticino	12.0%	52.3%	1.06	6.1%	43.5%	0.85
Total	**8.3%**	**56.8%**	**1.01**	**3.3%**	**58.8%**	**0.82**

Fig. 19: Liver – Incidence – Smoothed Map - Females

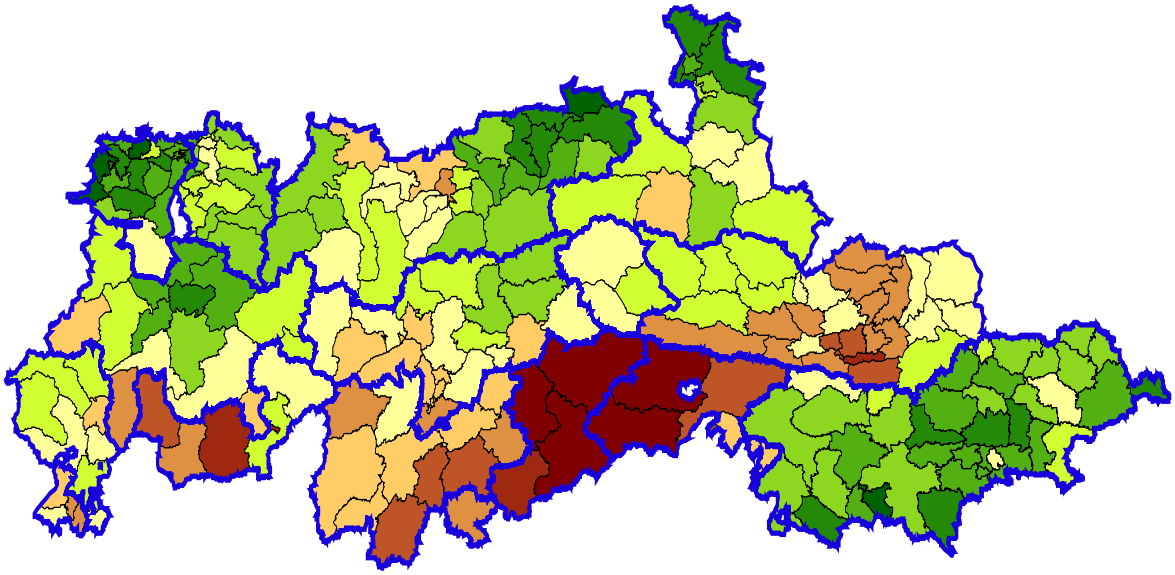


Fig. 20: Liver – Mortality – Smoothed Map - Females

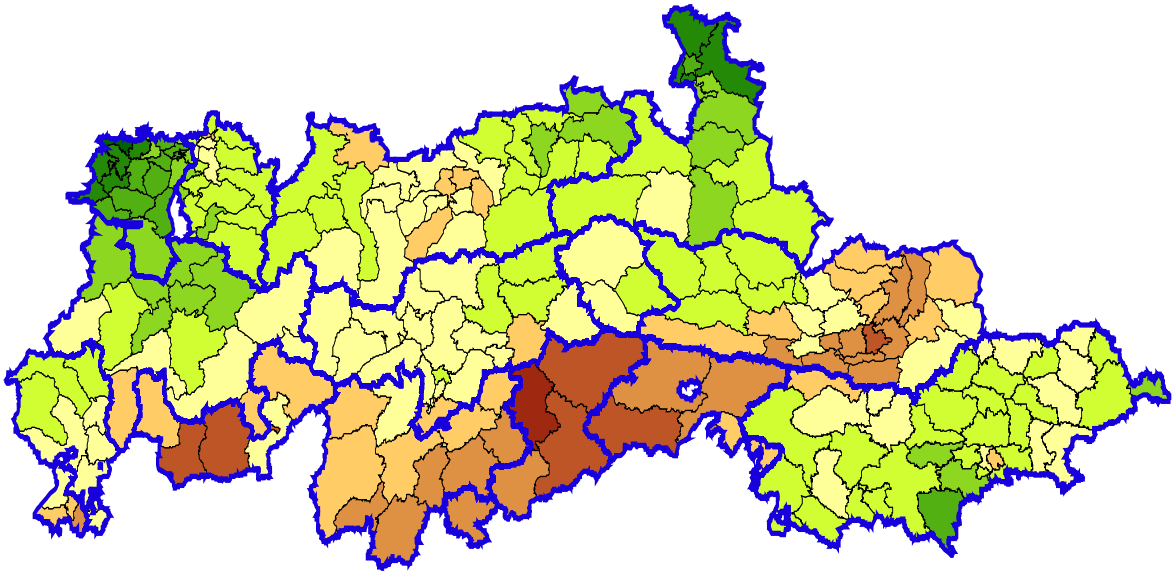


Fig. 21: Liver – Incidence – Smoothed Map - Males

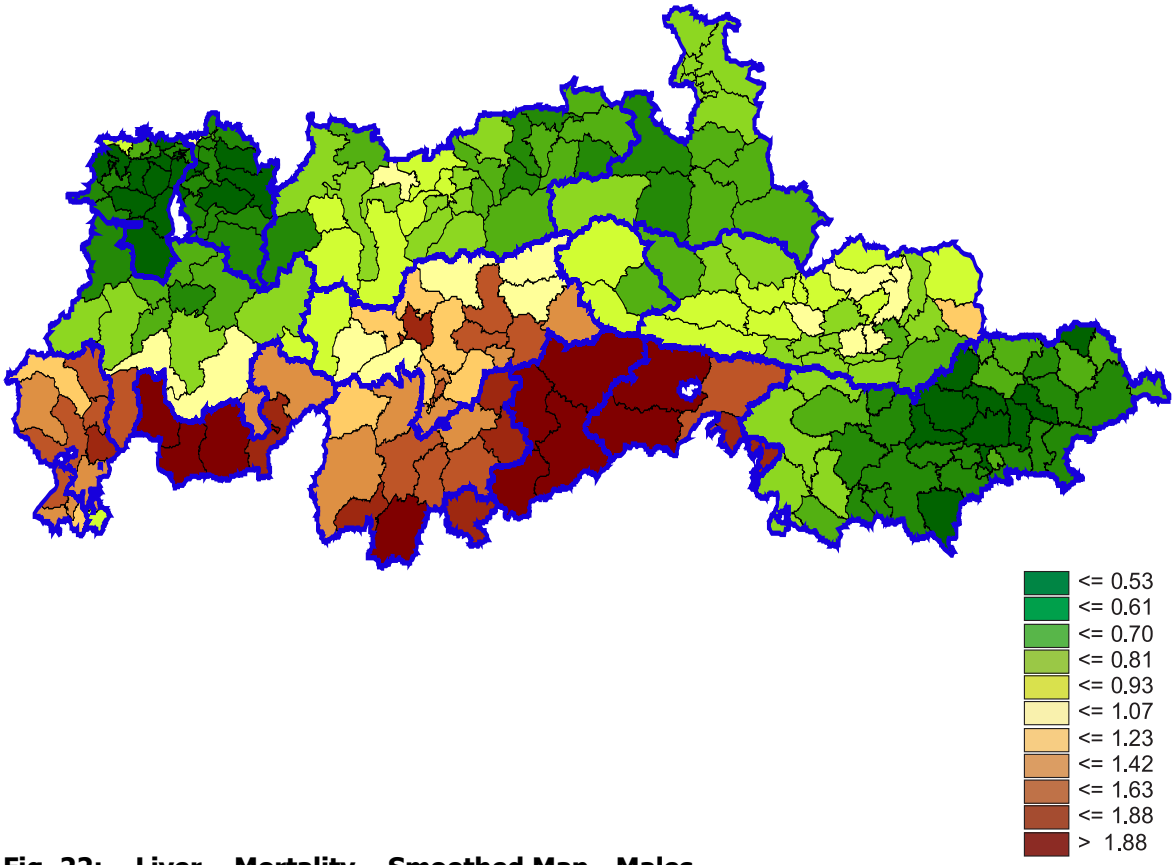
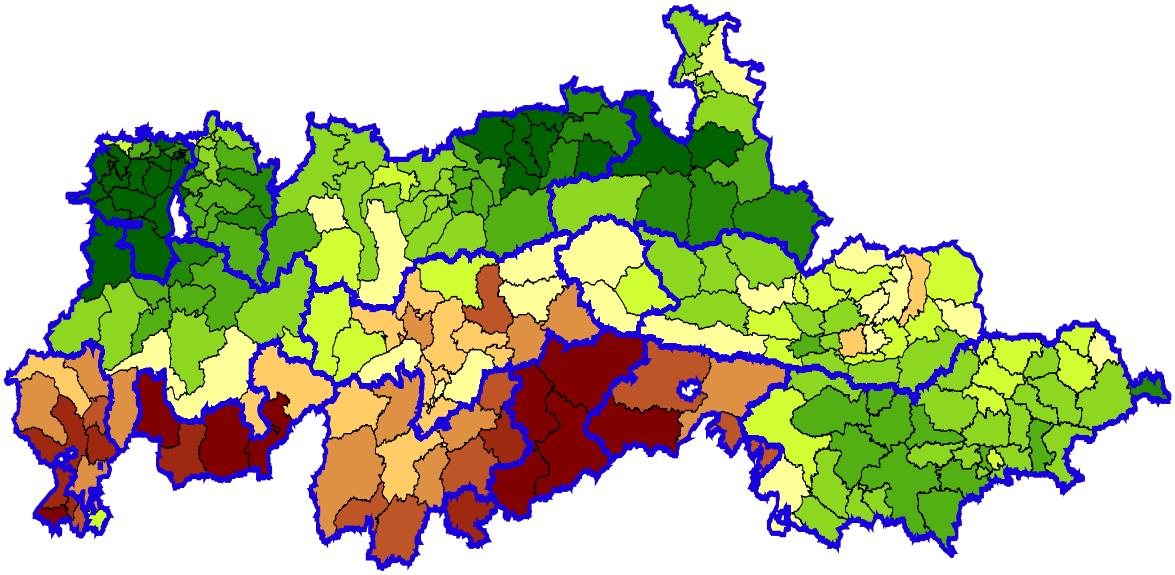


Fig. 22: Liver – Mortality – Smoothed Map - Males



5.6 Bronchus, Lung Silvia Ess

Bronchi e Polmone
Bronchien, Lunge
Sapnici, pljuča

5.6.1 Summary and Call for Action

Summary and Call for Action

Lung cancer, a highly preventable disease, continues to be the most frequent cause of cancer mortality in the study region. The most effective way to reduce the burden of lung cancer (and at the same time reduce the burden of other tobacco-related diseases) is to implement and enforce policies to reduce the use of tobacco products.

Numerous studies provide strong evidence that the smoking burden can be reduced by many interventions. Increased access to smoking cessation therapies, dissemination of information on health risks from smoking, restriction on smoking in public and workplaces, comprehensive bans on advertising and tobacco tax increases are all effective measures. In most countries in the region one or more of these measures are being implemented, but their enforcement is not always satisfactory.

Incidence and mortality rates in men have stabilised or are declining but rates for women continue to increase. Tobacco kills men and women, but gender-specific differences exist. It is therefore important that tobacco control policies recognize and take into account gender norms, differences and responses to tobacco, in order to counteract pressures, reduce tobacco use and improve the health of men and women in the Alpine regions.

Sintesi e proposte operative

Il tumore del polmone, pur essendo una neoplasia largamente prevenibile, rimane la più frequente causa di mortalità per cancro nella regione in studio.

L'adozione ed applicazione di politiche più efficaci per la riduzione dell'uso del tabacco rappresenta lo strumento più efficace per ridurre l'impatto di tale neoplasia (riducendo, allo stesso tempo, l'incidenza e la mortalità di altre malattie legate al fumo). Numerosi studi indicano con forte evidenza la possibilità di ridurre l'incidenza del fumo, attraverso una serie di interventi. Misure di dimostrata efficacia sono l'incremento dell'accessibilità a terapie per smettere di fumare, la disseminazione di informazioni sui connessi rischi per la salute, la restrizione alla possibilità di fumare nei luoghi di lavoro ed ambienti pubblici, i divieti generalizzati sulla pubblicità e l'aumento della tassazione sul tabacco. Nella maggior parte dei Paesi inclusi nella regione sono state adottate alcune di queste misure, ma non sempre la loro applicazione è soddisfacente.

I tassi di mortalità e d'incidenza negli uomini si sono stabilizzati o diminuiscono, ma quelli relativi alle donne continuano ad aumentare. Sebbene il fumo sia letale per entrambi i sessi, esistono comunque

delle differenze di genere. E' quindi importante che le politiche relative al tabacco colgano e tengano conto di "regole" sociali diverse nei due sessi, al fine di contrastare le pressioni sociali, ridurre l'uso del tabacco e migliorare la salute di donne ed uomini nelle regioni Alpine.

Zusammenfassung und Schlussfolgerungen

Lungenkrebs, eine in hohem Ausmaß vermeidbare Erkrankung, bleibt weiterhin die häufigste Ursache für krebsassoziierte Sterblichkeit in der Studienregion. Der effektivste Weg der Reduktion der Belastung durch Lungenkrebs (und gleichzeitig auch der Belastung durch andere tabakassoziierte Erkrankungen), ist es Programme zur Reduktion des Tabakverbrauches zu implementieren bzw. zu verstärken. Eine große Anzahl von Studien zeigt mit hoher Evidenz, dass Rauchen durch viele verschiedene Interventionen reduziert werden kann. Effektive Maßnahmen sind z.B. der Zugang zu Nikotinentwöhnungstherapien, die Verbreitung von Information über Gesundheitsrisiken des Rauchens, die Einschränkung des Rauchens in der Öffentlichkeit und an der Arbeitsstätte, umfassende Verbote von Werbung und Erhöhungen der Tabaksteuer. In den meisten Staaten der Region wurden bereits eine oder mehrere dieser Maßnahmen eingeführt, allerdings ist die Durchsetzbarkeit nicht immer befriedigend. Die Inzidenz- und die Mortalitätsrate der Männer haben sich stabilisiert oder gehen sogar zurück, die Raten bei den Frauen steigen weiterhin, es existieren geschlechtsspezifische Unterschiede. Daher ist es wichtig, dass Tabakkontrollprogramme geschlechtsspezifische Unterschiede erkennen um den Tabakkonsum weiterhin reduzieren und die Gesundheit der Männer und Frauen der Alpenregion steigern zu können.

Povzetek in poziv k ukrepanju

Pljučni rak, bolezen ki jo je možno preprečiti, ostaja v opazovani pokrajini še vedno najpogostejši vzrok smrti za rakom. Najučinkovitejši način, s katerim je mogoče zmanjšati breme pljučnega raka (in obenem tudi vseh ostalih bolezni, ki jih povzroča kajenje tobaka), je uveljavljanje in izvajanje politik, ki spodbujajo k manjši porabi tobačnih izdelkov.

V številnih raziskavah je bilo navedenih že dovolj trdnih dokazov, da zasvojenost s tobakom lahko omilimo s številnimi ukrepi: Poskrbimo za večjo dostopnost do terapij za odvajanje od kajenja, za širšo obveščenost o ogrožanju zdravja s kajenjem, za omejevanja kajenja na javnih in delovnih mestih, za prepoved oglašanja tobačnih izdelkov, za povečanje davkov na tobačne izdelke. Vsi omenjeni ukrepi so zelo učinkoviti. V večini držav v obravnavani pokrajini se eden ali več od omenjenih ukrepov že izvaja, vendar njihova uveljavljenost ni vedno zadovoljiva. Incidenčna in umrljivostna stopnja pljučnega raka sta se pri moških umirili in celo upadata, medtem ko pri ženskah še naprej naraščata. Tobak ubija moške in ženske, vendar med spoloma obstajajo razlike. Zato je pomembno, da vsak nadzor nad uživanjem tobaka upošteva standarde, specifične za moškega ali žensko, ter razlike v odzivu na kajenje tobaka. Le tako bomo lahko nevtralizirali obremenjenost, omejili porabo tobaka ter izboljšali zdravje moških in žensk v alpskih pokrajinah.

5.6.2 Introduction

Lung cancer is the leading cause of cancer mortality in the Alpine region in the study period, killing over 3500 persons per year. It is the first cause of cancer-related mortality among men, while in women it takes third place (after breast and colorectal cancer). Lung cancer shows geographic and temporal variability, which corresponds to the diversity and differences in distribution of its main risk factors, tobacco smoking and radon exposure. In this context disease maps are particularly useful for highlighting geographic regions with high or low morbidity and mortality and for detecting spatial clusters.

5.6.3 Epidemiology

Age-standardized incidence rates for the region were 47.1/100,000 person years (PY) (95% confidence interval (CI) 46.3 – 48.0) for men and 14.1/100,000 PY (95% CI 13.6 – 14.5) for women. The lowest incidence rate for males was reported in Salzburg (35.8/100,000 PY (95% CI 33.0-38.5) and the highest in Varese (68.7/100,000 PY (95% CI: 61.4 -76.3)). Among females the lowest incidence rate was reported in Trentino with 9.6/100,000 PY (95% CI: 8.3 – 11.0) and the highest in Ticino with 16.8/100,000 PY (CI 14.6-19.0). Most Italian regions (Trentino, Friuli Venezia Giulia, South Tyrol, Sondrio, Varese) with the exception of Veneto reported rates below average for women. For males on the contrary no clear-cut differences among nations could be observed.

As expected, annual age-standardized mortality rates reported was lower but close to incidence rates because of the high fatality rate of lung cancer. Incidence and mortality rates followed a similar pattern. Age-standardized mortality rate for the whole region were 39.8/100,000 PY (95% CI 39.0 – 40.6) for men and 10.4/100,000 PY (95% CI 10.0 – 10.8) for women. Among females the lowest mortality rate was reported in Friuli Venezia Giulia with 7.6/100,000 PY (95% CI: 4.9 – 10.3) and the highest in Veneto with 12.4/100,000 PY (CI 10.1-14.6).

5.6.4 Data quality

Within the study region microscopically verified lung cancer cases varied from 68% in Varese to 94% in Slovenia in males and similar values for females.

The RMI ratio for lung cancer is typically high, indicating the high case fatality of lung cancer. Mean RMI ratio for lung cancer in the region was 0.83 for females and 0.88 for males. It varied from 0.73 for St. Gallen-Appenzell to 1.10 for Trentino.

All registries submitting data for this publication reported DCO rates for lung cancer under 10%. DCO rates were highest in Carinthia (8%) and lowest in Varese and Friuli Venezia Giulia (0% of DCO cases). Data quality for lung cancer can therefore be considered satisfactory. However, an RMI ratio over 1 for both females and males in Trentino may indicate less precise information in death certificates or some degree of under-registration [2].

5.6.5 Risk factors, early detection and screening

Tobacco smoking is the most important risk factor for lung cancer. It is estimated that 85%-90% of the cases can be attributed to active or passive smoking. Moreover there is a clear dose-response

relationship between lung-cancer risk and the number of cigarettes smoked per day, degree of inhalation, and age at initiation of smoking [3]. Due to the increasing rate of female smokers lung cancer incidence in women has increased and is expected to rise even more over the next years. Smoking avoidance measures (e.g. measures to reduce starting smoking in those who have never smoked), smoking cessation measures and avoidance of second-hand smoke represent the cornerstone of any program to reduce lung cancer incidence, mortality as well as many other tobacco-related diseases.

Radon exposure is estimated to be the second cause of lung cancer, responsible for 8%-10% of cases. Smokers are more likely to develop lung cancer when exposed to radon than are non-smokers [4]. Some Alpine regions have an increased risk of high indoor radon levels, especially the Ticino, Lombardy and Friuli Venezia Giulia regions, parts of Grison-Glaris and to a lesser degree Carinthia, Tyrol, South Tyrol and Trentino. In general, populations in rural areas have a higher risk of increased indoor radon concentration because of housing types and local geology.

With the advent of a new screening technique the spiral computer tomography (CT) scan, screening for lung cancer has received renewed interest after the negative results with chest X-rays in the 1970s. However it has not yet been shown that screening for lung cancer with any of the available methods (including spiral CT) will lead to a reduction in advanced-stage disease and to a reduction in lung cancer mortality despite the fact that available data show that spiral CT screening can diagnose lung cancer at a significantly earlier stage [5]. At present lung cancer screening is recommended only within a clinical trial and no trial is ongoing in the study region.

5.6.6 Survival

Lung cancer belongs to the group of cancers with the poorest 5-year survival rates. Verdecchia et al. report a mean 5-year European relative survival of 13% in 1997-1999 [6]. Lung cancers are often inaccessible and advanced when diagnosed. Survival decreases with age but even for young patients it remains below 20%.

5.6.7 Geographical variation

Maps show relative differences within the participating regions. For males, the south of the region (Slovenia and the Italian regions of Varese, Sondrio, Veneto and to a lesser extent Friuli Venezia Giulia and Trentino) shows higher standardised incidence and mortality rates (SIR and SMR) than does the north. In women no north-south differences can be observed. Geographic units of high SIR and SMR are seen in all countries in urban areas.

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Tab. 24: Bronchus, Lung – Numbers and Rates - Females

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	448	31.0	14.4 (12.9, 15.9)	1.09 (0.99, 1.19)	351	24.3	10.9 (9.6, 12.2)	1.01 (0.91, 1.13)
Salzburg	295	22.0	12.2 (10.7, 13.7)	0.87 (0.78, 0.98)	229	17.1	8.9 (7.7, 10.2)	0.82 (0.72, 0.94)
Tyrol	490	28.0	15.9 (14.3, 17.4)	1.12 (1.02, 1.22)	411	23.5	12.0 (10.7, 13.3)	1.14 (1.03, 1.25)
Vorarlberg	221	24.5	15.0 (12.9, 17.1)	1.03 (0.9, 1.18)	182	20.2	11.5 (9.7, 13.3)	1.04 (0.89, 1.2)
Friuli Venezia Giulia	56	28.7	10.2 (6.9, 13.4)	0.76 (0.58, 0.99)	53	27.2	7.6 (4.9, 10.3)	0.81 (0.6, 1.06)
Varese	78	26.8	12.1 (9.1, 15.2)	0.9 (0.71, 1.13)	69	23.7	9.1 (6.6, 11.6)	0.95 (0.74, 1.2)
Sondrio	123	27.0	11.5 (9.2, 13.8)	0.89 (0.74, 1.07)	93	20.4	8.0 (6.1, 9.9)	0.79 (0.64, 0.97)
South Tyrol	262	22.2	10.8 (9.3, 12.2)	0.83 (0.73, 0.94)	223	18.9	8.5 (7.2, 9.7)	0.84 (0.74, 0.96)
Trentino	262	21.2	9.6 (8.3, 11.0)	0.7 (0.62, 0.79)	270	21.8	8.6 (7.4, 9.9)	0.84 (0.74, 0.95)
Veneto	258	42.8	16.1 (13.8, 18.4)	1.25 (1.11, 1.42)	213	35.3	12.4 (10.1, 14.6)	1.19 (1.03, 1.36)
Slovenia	1,103	28.6	15.1 (14.2, 16.1)	1.06 (1, 1.12)	940	24.4	11.1 (10.3, 11.9)	1.12 (1.05, 1.2)
Graubünden/Glarus	151	26.5	14.9 (12.3, 17.5)	0.99 (0.83, 1.16)	122	21.4	10.9 (8.8, 13.1)	0.94 (0.78, 1.12)
St,Gallen/Appenzell	342	26.0	15.4 (13.6, 17.2)	1.02 (0.92, 1.14)	249	18.9	10.3 (8.9, 11.8)	0.88 (0.77, 1)
Ticino	285	34.5	16.8 (14.6, 19.0)	1.13 (1, 1.27)	222	26.8	12.0 (10.2, 13.8)	1.03 (0.9, 1.17)
Total	**4,374**	**27.4**	**14.1 (13.6, 14.5)**	**1 (0.97, 1.03)**	**3,627**	**22.7**	**10.4 (10.0, 10.8)**	**1 (0.97, 1.03)**

Tab. 25: Bronchus, Lung – Numbers and Rates - Males

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	1,033	76.4	42.7 **(**40.0**,** 45.5**)**	0.93 (0.88, 0.99)	897	66.3	37.3 (34.8, 39.9)	0.91 (0.85, 0.97)
Salzburg	677	53.8	35.8 (33.0, 38.5)	0.75 (0.7, 0.81)	543	43.2	27.7 (25.3, 30.1)	0.69 (0.63, 0.75)
Tyrol	1,071	64.2	42.1 (39.5, 44.7)	0.89 (0.84, 0.95)	924	55.4	35.2 (32.9, 37.6)	0.88 (0.82, 0.94)
Vorarlberg	534	60.8	42.0 (38.4, 45.6)	0.9 (0.83, 0.98)	475	54.1	36.9 (33.5, 40.3)	0.93 (0.85, 1.02)
Friuli Venezia Giulia	215	114.9	51.1 (43.9, 58.3)	1.09 (0.95, 1.25)	199	106.4	43.6 (37.2, 50.1)	1.11 (0.96, 1.27)
Varese	341	124.9	68.9 (61.4, 76.4)	1.47 (1.32, 1.64)	303	111.0	59.4 (52.5, 66.2)	1.48 (1.32, 1.66)
Sondrio	511	117.3	62.5 (56.9, 68.1)	1.34 (1.23, 1.46)	454	104.2	53.2 (48.2, 58.3)	1.35 (1.23, 1.48)
South Tyrol	722	63.0	37.6 (34.7, 40.4)	0.82 (0.76, 0.88)	630	55.0	32.0 (29.4, 34.6)	0.8 (0.74, 0.87)
Trentino	854	72.5	38.0 (35.3, 40.6)	0.83 (0.77, 0.88)	940	79.8	40.3 (37.5, 43.0)	1.01 (0.95, 1.08)
Veneto	737	132.3	61.6 (56.9, 66.3)	1.37 (1.28, 1.48)	661	118.6	53.4 (48.9, 57.8)	1.36 (1.26, 1.47)
Slovenia	3,191	86.7	57.1 (55.1, 59.1)	1.21 (1.16, 1.25)	2,794	75.9	53.2 (51.1, 55.2)	1.25 (1.2, 1.29)
Graubünden/Glarus	421	75.7	45.1 (40.6, 49.6)	0.95 (0.86, 1.05)	343	61.7	35.8 (31.8, 39.8)	0.85 (0.76, 0.95)
St.Gallen/Appenzell	804	62.3	39.8 (37.0, 42.7)	0.85 (0.79, 0.91)	661	51.2	32.9 (30.3, 35.6)	0.77 (0.71, 0.83)
Ticino	661	87.6	46.6 (42.9, 50.3)	0.97 (0.9, 1.05)	493	65.4	33.3 (30.2, 36.3)	0.8 (0.73, 0.88)
Total	**11,772**	**77.4**	**47.1 (46.3, 48.0)**	**1 (0.98, 1.02)**	**10,317**	**67.8**	**39.8 (39.0, 40.6)**	**1 (0.98, 1.02)**

Tab. 26: Bronchus, Lung – Data quality

	FEMALES			MALES		
Country description	% DCO	% HV	RMI	% DCO	% HV	RMI
Carinthia	8.0%	83.5%	0.78	7.9%	83.3%	0.87
Salzburg	2.4%	91.0%	0.78	2.5%	90.9%	0.80
Tyrol	0.8%	90.3%	0.84	1.0%	92.7%	0.86
Vorarlberg	2.3%	92.8%	0.82	5.6%	94.6%	0.89
Friuli Venezia Giulia	0.0%	69.6%	0.95	0.5%	82.2%	0.93
Varese	0.0%	67.9%	0.88	0.3%	71.8%	0.89
Sondrio	0.8%	76.2%	0.76	1.0%	80.0%	0.89
South Tyrol	3.8%	83.3%	0.85	2.8%	89.7%	0.87
Trentino	3.1%	73.2%	1.03	1.8%	78.1%	1.10
Veneto	4.3%	76.5%	0.83	1.8%	78.9%	0.90
Slovenia	1.5%	94.3%	0.85	1.1%	95.6%	0.88
Graubünden/Glarus	2.0%	84.5%	0.81	0.0%	89.1%	0.81
St.Gallen/Appenzell	0.9%	92.9%	0.73	0.1%	90.5%	0.82
Ticino	2.1%	93.9%	0.78	2.1%	91.8%	0.75
Total	**2.5%**	**87.9%**	**0.83**	**2.1%**	**89.1%**	**0.88**

Fig. 23: Bronchus, Lung – Incidence – Smoothed Map - Females

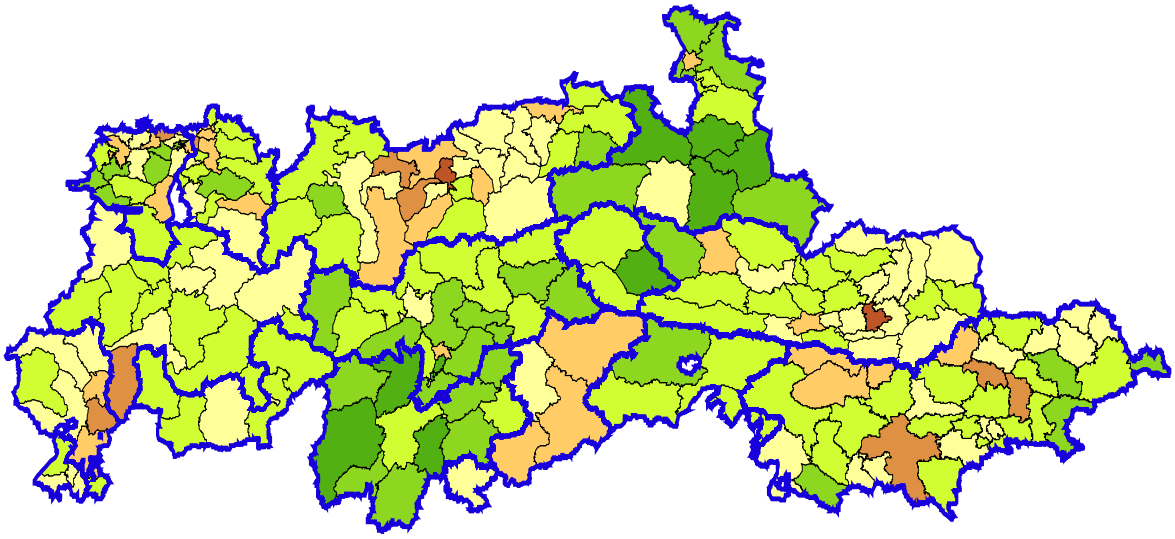


Fig. 24: Bronchus, Lung – Mortality – Smoothed Map - Females

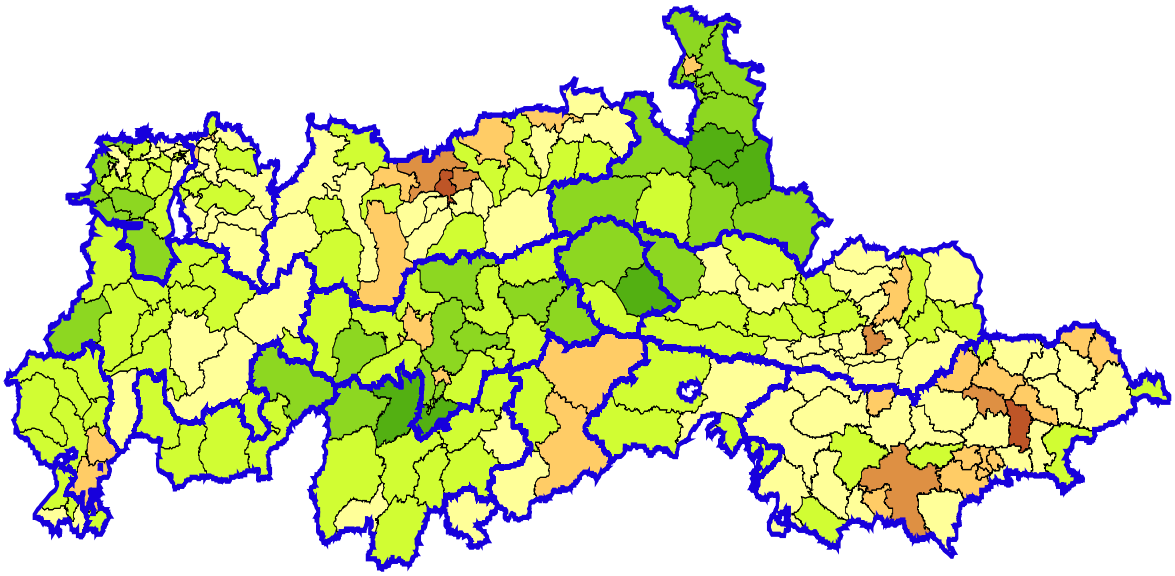


Fig. 25: Bronchus, Lung – Incidence – Smoothed Map - Males

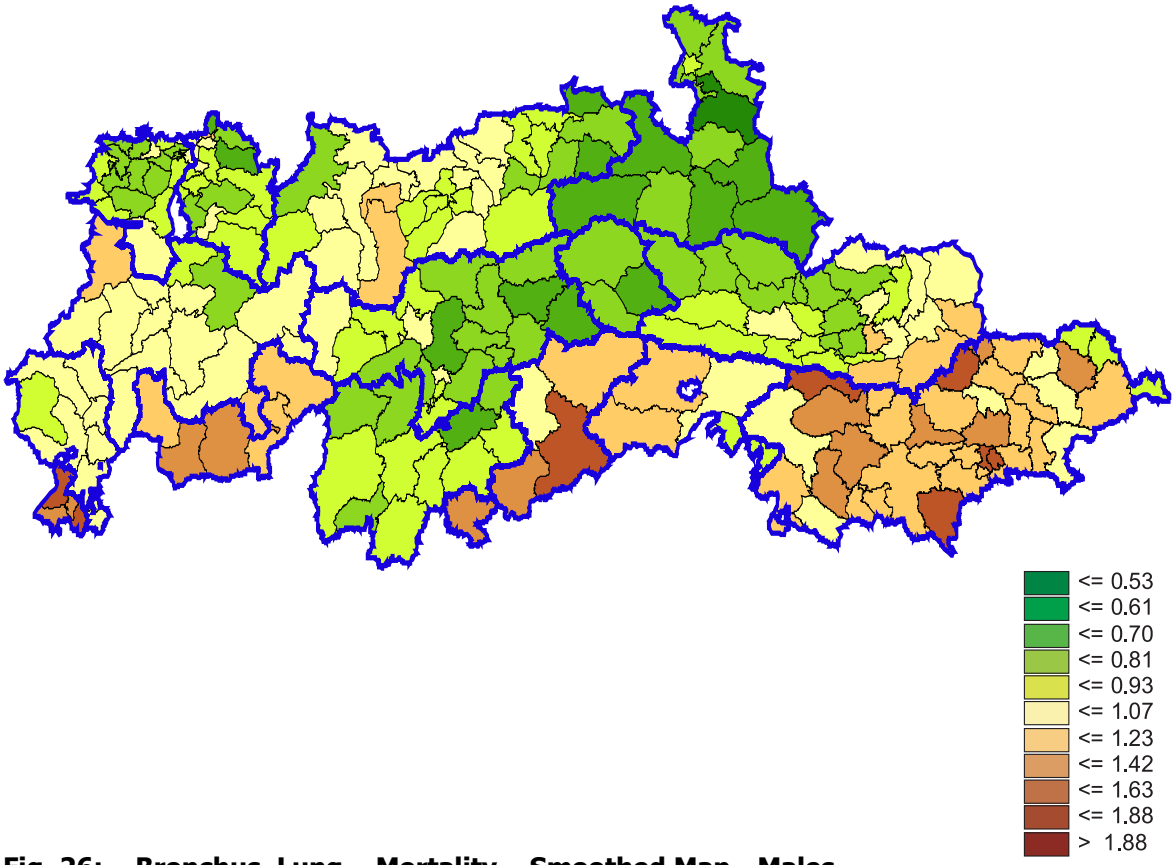
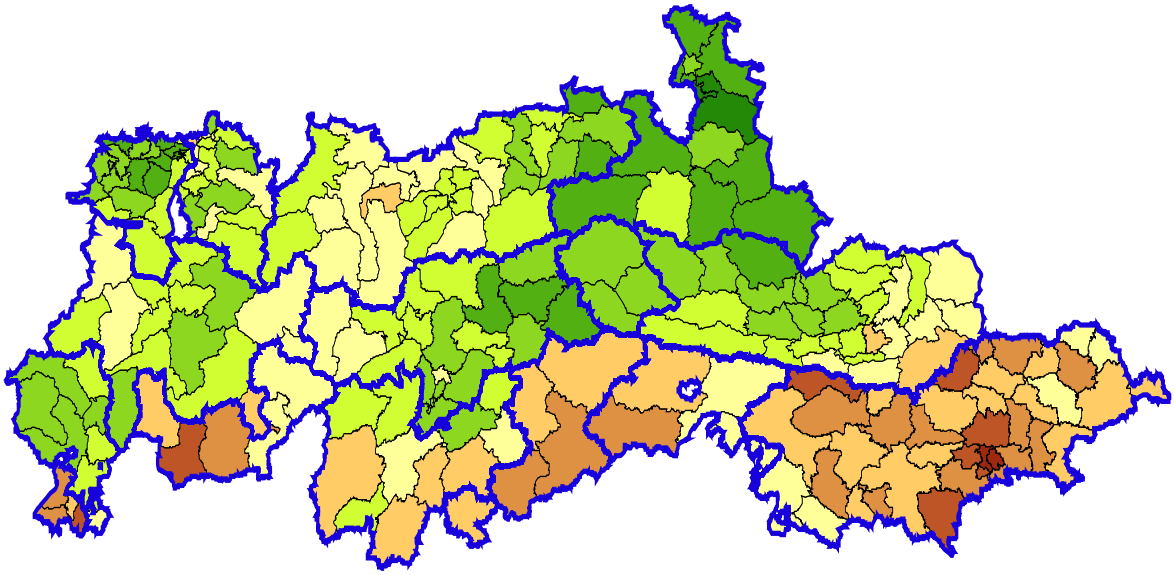


Fig. 26: Bronchus, Lung – Mortality – Smoothed Map - Males



5.7 Breast (Females) Silvano Piffer

Mammella
Brust
Dojka

5.7.1 Summary and Call for Action

Summary and Call for Action

Breast cancer is the most frequent cancer seen in females and accounts for 28.2% of all incident cancer cases, except NMSC. The Incidence rate for the whole area is lower than the average EU estimated value.

The (mountains part of the) Veneto region shows the highest values of all the regions, followed by Varese.

Breast cancer is the most frequent cause of mortality for cancer in females, accounting for 17.6% of all cancer deaths, except NMSC. Mortality is substantially more homogeneously distributed than incidence with the exception of Varese and Slovenia that show the highest mortality with a statistically significant difference as compared to the expected value.

Call for action:

Strengthen and promote breast cancer screening across the whole region, promote proper diet and adequate daily physical activity to lower the risk for the general population.

Sintesi e proposte operative

Il cancro della mammella è il tumore più frequente nelle donne, e rappresenta il 28,2% di tutte le neoplasie, escludendo i tumori cutanei non melanotici; con il 17,6% dei decessi per cancro (sempre escludendo i tumori cutanei), esso appare anche come la più frequente causa di morte per tumore, sempre nelle donne.

Il tasso d'incidenza complessivo della regione è inferiore al valore medio stimato per l'Unione Europea; i valori più elevati si riscontrano nella aree montane del Veneto, seguite da quelle Varesine. La mortalità invece, è distribuita in modo sostanzialmente omogeneo, con l'eccezione delle aree Slovene e Varesine che mostrano valori di mortalità più elevati, con una differenza statisticamente significativa rispetto al valore atteso.

Per ridurre il rischio nella popolazione generale occorre rafforzare e promuovere lo "screening" del tumore al seno nell'intera regione, oltre a promuovere una dieta corretta ed un'adeguata attività fisica giornaliera.

Zusammenfassung und Schlussfolgerungen

Brustkrebs ist die häufigste Krebsform bei Frauen und beträgt 28,2 % aller Krebsarten (außer NMSC) Die Inzidenzrate für die gesamte Region liegt unter dem EU-Durchschnitt.

Die Region Veneto (der gebirgige Anteil) zeigt die höchsten Raten aller Regionen gefolgt von Varese. Brustkrebs ist die häufigste Ursache der Krebsmortalität bei Frauen und verantwortlich für 17,6% aller Krebstoten (ausgenommen NMSC). Die Mortalität ist wesentlich homogener verteilt als die Inzidenz mit Ausnahme von Varese und Slowenien, die die höchsten Mortalitätsraten zeigen, die Unterschiede sind statistisch signifikant verglichen mit dem erwarteten Wert.

Zu Fördern und Auszubauen sind Brustkrebs-Screeningprogramme, Diätprogramme und Programme zur Erhöhung der täglichen Aktivität um das Risiko in der Region zu reduzieren.

Povzetek in poziv k ukrepanju

Rak dojke je najpogostejši ženski rak in predstavlja 28,2 % vseh na novo odkritih rakov, z izjemo nemelanomskega kožnega raka. Incidenčna stopnja raka dojke je na tem področju nižja od povprečne stopnje, ocenjene za države Evropske skupnosti, očitno pa je, da se povečuje od severa proti jugu. Med vsemi pokrajinami je bila najvišja incidenčna stopnja zabeležena v Benečiji (v njenem hribovitem delu), takoj za njo pa v pokrajini Varese. Rak dojke je med bolnicami z rakom tudi najpogostejši vzrok smrti, saj predstavlja kar v 17,6 % vseh smrti zaradi raka, z izjemo nemelanomskega kožnega raka. Umrljivost zaradi raka dojke je v alpski regiji bolj homogeno porazdeljena kot incidenca, presežki se pojavljajo v pokrajini Varese in v Sloveniji, kjer je umrljivost najvišja in se statistično pomembno razlikuje od pričakovanih vrednosti.

V celotni regiji bi bilo potrebno podpirati in pospeševati presejalne programe za odkrivanje raka dojk, širiti znanje o pravilni prehrani in primerni vsakodnevni telesni vadbi in tako med prebivalstvom zmanjšati tveganje nastanka tega raka.

5.7.2 Introduction

Breast cancer is the most common cancer in women worldwide, accounting for about 25 per cent of all malignancies in women; the proportion is higher in women in western countries, developed, countries [1]. Incidence has been rising in many parts of the world, including many European countries. An important part of this increase could be attributed to a spread of organized screening programs [2]. Breast cancer is also the most common cancer in females in Europe. IARC estimates that in the year 2006 there were 430,000 new breast cancer cases in Europe, while the number of deaths from breast cancer was estimated at around 132,000. Breast cancer is responsible for 28.9% of all new cancer cases among women in Europe and 17.6% of all cancer death [3].

5.7.3 Epidemiology

Per year, an average of 3,983 breast cancer cases is diagnosed in the whole area. Breast cancer accounts for 28.2% of all incident cancer cases, except NMSC (from 25.4% for Slovenia to 33.4% for Varese). Incidence rate for the whole area is lower than the average EU estimated value. Area values are coherent with the particular country profiles, as previously reported by Globocan-IARC in 2002 [4]. Breast cancer accounts for 17.6% of all cancer deaths, except NMSC (from 15.7 for Carinthia to 20.4 for Varese).

5.7.4 Data quality aspects

The quality of registered data is good for the whole area, considering that DCO percentage is 0.8% (range 0.0-2.2) and that the percentage of cases microscopically verified is 97.8% (range 96.1-99.8). Mortality/incidence ratio per 100 is 0.3 (range 0.3-0.4), with no differences among regions.

5.7.5 Risk factors, early detection, screening

Most of the known risk factors for breast cancer are related to women's reproductive history: early menarche, late first pregnancy, low parity, and late menopause; endogenous hormones, oestrogens and androgens, probably play an important role, specially linked with dietary factors such as alcohol and fats. In fact avoiding obesity with proper diet and/or regular physical activity may decrease the risk of post-menopausal breast cancer, and switching from a high-fat and low-vegetable diet to a lower-fat, higher-vegetable diet may also contribute to a reduced risk [5,6]. Some kinds of benign breast disease increase the risk of developing malignant breast cancer. None of these risk factors are currently amenable to primary prevention [7]. Oral contraceptive use and hormone replacement therapy have been linked to increased risk [8]. Studies of migrant populations have suggested that differences in incidence between countries are social and environmental, rather than genetic, in origin; only about 5 per cent of breast cancer cases are due to the inheritance of dominant genes, such as BRCA-1 and BRCA-2 [9,10]. Mammography screening is a well proven method for reducing mortality due to breast cancer and there are recommendations for all EU member states to implement programs for women between the ages of 50 and 69.

5.7.6 Geographical variation

Italian regions show the highest incidence rates. In particular, the Veneto region (its mountainous part is included in the study area) shows the highest incidence rate among all regions. The highest (Veneto) to the lowest (St.Gallen/Appenzell) rate ratio is 1.7. Standardized rate confirms the highest value in Veneto and in other Italian regions too.

Moreover, the Italian cancer registry network reports the highest incidence for breast cancer in the northern regions of Italy [11].

The differences between Italian regions and the other regions are remarkable with the exception of South Tyrol, which shows incidence values very close to other German-speaking countries. Some differences in reproductive histories at the population level could partially explain these differences between Italian regions and the other regions, although there are no hard facts to prove this hypothesis. The trend to age-specific rates is similar to those reported for Western countries with a high incidence for breast cancer. On the map, some excess risk areas are evident: Veneto, southeast Trentino, Sondrio and Varese. Scattered excess risk areas are also present in Tyrol, Salzburg and Ticino.

Italian regions show the highest crude mortality rate, just as for incidence. The difference among regions is smaller than for incidence. Varese shows the highest crude mortality rate. The highest (Varese) to the lowest (Tyrol) rate ratio is 1.9. Standardized rates show Varese and Slovenia as the regions with the highest mortality with a statistically significant difference as compared to the expected value, and the difference is large enough (SMR 1.5, 1.2). The map does not show any intra- or interregional differences with the exception of the Varese area and the eastern part of Slovenia. On this basis one could presume that the whole area homogeneously uses standard diagnostic and therapeutic protocols and has some possible problems in Varese and eastern Slovenia.

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Tab. 27: Breast (Females) – Numbers and Rates

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	1,862	128.7	74.2 (70.5, 77.9)	1 (0.96, 1.05)	476	32.9	15.7 (14.1, 17.3)	0.87 (0.79, 0.95)
Salzburg	1,691	126.0	80.2 (76.1, 84.2)	1.07 (1.02, 1.12)	422	31.4	16.3 (14.5, 18.0)	0.95 (0.86, 1.04)
Tyrol	2,043	116.6	73.3 (69.9, 76.6)	1 (0.96, 1.05)	549	31.3	16.3 (14.8, 17.9)	0.95 (0.87, 1.03)
Vorarlberg	967	107.3	71.7 (67.0, 76.5)	0.96 (0.9, 1.02)	288	32.0	16.0 (13.9, 18.0)	1.03 (0.91, 1.15)
Friuli Venezia Giulia	301	154.5	76.0 (66.0, 86.0)	0.98 (0.87, 1.1)	87	44.7	15.6 (11.5, 19.7)	0.82 (0.66, 1.01)
Varese	476	163.4	88.8 (80.0, 97.5)	1.23 (1.12, 1.34)	129	44.3	17.9 (14.3, 21.5)	1.09 (0.91, 1.3)
Sondrio	722	158.7	88.7 (81.7, 95.8)	1.17 (1.09, 1.26)	183	40.2	18.4 (15.3, 21.4)	0.97 (0.84, 1.13)
South Tyrol	1,422	120.7	73.5 (69.3, 77.6)	0.99 (0.94, 1.05)	391	33.2	15.7 (14.0, 17.5)	0.92 (0.83, 1.02)
Trentino	1,774	143.5	80.2 (76.1, 84.3)	1.07 (1.02, 1.12)	507	41.0	17.8 (16.0, 19.6)	0.99 (0.9, 1.08)
Veneto	1,127	186.9	100.9 (94.3, 107.6)	1.27 (1.2, 1.35)	280	46.4	19.6 (16.7, 22.4)	0.97 (0.86, 1.09)
Slovenia	4,111	106.6	63.6 (61.6, 65.7)	0.86 (0.83, 0.88)	1,489	38.6	17.6 (16.6, 18.6)	1.15 (1.09, 1.21)
Graubünden/Glarus	746	130.9	80.3 (74.1, 86.6)	1.07 (1, 1.15)	208	36.5	18.6 (15.7, 21.5)	0.99 (0.86, 1.13)
St,Gallen/Appenzell	1,409	107.2	67.4 (63.6, 71.2)	0.92 (0.87, 0.97)	431	32.8	17.0 (15.2, 18.8)	0.94 (0.85, 1.03)
Ticino	1,266	153.1	83.2 (78.2, 88.2)	1.12 (1.06, 1.18)	324	39.2	16.3 (14.3, 18.4)	0.92 (0.83, 1.03)
Total	**19,917**	**124.7**	**74.2 (73.1, 75.3)**	**1 (0.99, 1.01)**	**5,764**	**36.1**	**16.7 (16.2, 17.2)**	**1 (0.97, 1.03)**

Tab. 28: Breast (Females) – Data quality

Country description	% DCO	% HV	RMI
Carinthia	2.2%	99.0%	0.26
Salzburg	0.7%	97.5%	0.25
Tyrol	0.4%	99.4%	0.27
Vorarlberg	3.3%	99.8%	0.30
Friuli Venezia Giulia	0.3%	98.7%	0.29
Varese	0.2%	96.6%	0.27
Sondrio	0.1%	96.3%	0.25
South Tyrol	0.5%	97.5%	0.27
Trentino	0.6%	97.7%	0.29
Veneto	0.6%	97.5%	0.25
Slovenia	0.9%	99.2%	0.36
Graubünden/Glarus	0.0%	98.3%	0.28
St.Gallen/Appenzell	0.6%	98.1%	0.31
Ticino	0.7%	98.5%	0.26
Total	**0.9%**	**98.5%**	**0.29**

Fig. 27: Breast (Females) – Incidence – Smoothed Map

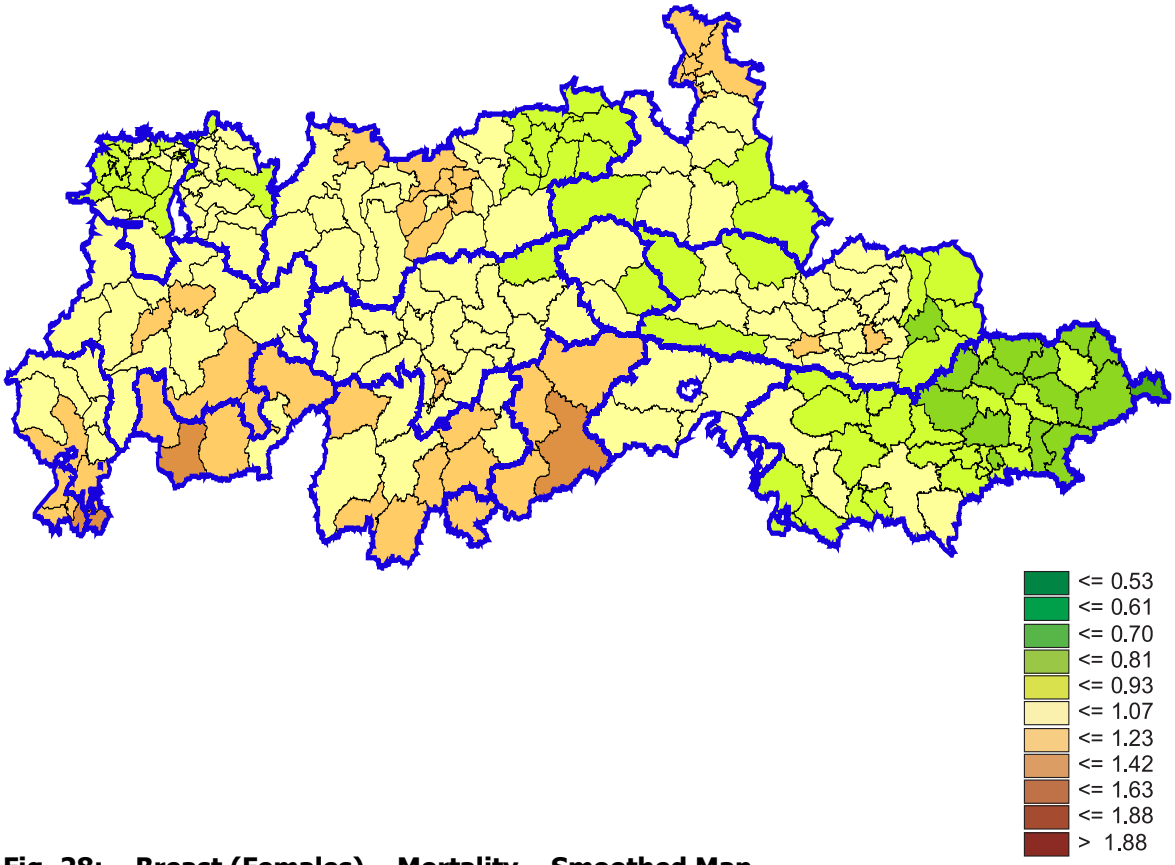
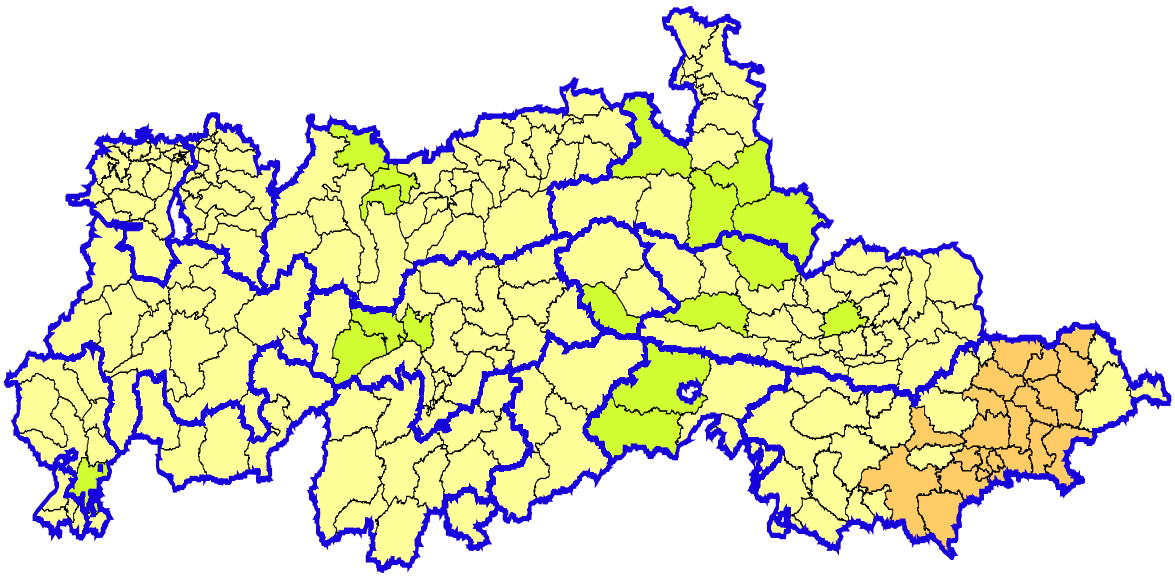


Fig. 28: Breast (Females) – Mortality – Smoothed Map



5.8 Cervix uteri Hans Concin

Collo dell'utero
Gebärmutterhals
Maternični vrat

5.8.1 Summary and Call for Action

Summary and Call for Action

The predominant differences in incidence and mortality in cervical cancer are surprising and difficult to explain. Incidence and mortality are much higher in the northeast than in the southwest. This could be due to problems in coding. Studies have shown that quality-assured Pap screening can abolish regional differences. On 2 December 2003 the Health Ministers of the European Union unanimously adopted a recommendation on breast, cervical and colorectal cancer. For cervical cancer the European Guidelines for quality assurance in screening appeared in their second edition in 2008. Ultimately, these guidelines need to be executed, irrespective of ongoing HPV vaccination.

Sintesi e proposte operative

Le notevoli differenze nell'incidenza e nella mortalità per i tumori cervicali sono sorprendenti e di difficile spiegazione, ed entrambe sono maggiori nel Nord-Est rispetto al Sud-Ovest. Un'eterogeneità geografica nella prevalenza di HPV e problemi di codifica potrebbero avere un ruolo: alcuni studi hanno mostrato come uno "screening" mediante Pap test, con qualità certificata, possa produrre un annullamento delle differenze regionali. Nel 2003, i Ministri della Sanità dell'Unione Europea hanno unanimemente adottato le raccomandazioni per la diagnosi precoce dei tumori mammari, cervicali e colorettali. La seconda edizione delle Linee Guida per la certificazione di qualità nello "screening", per il cancro della cervice, è apparsa nel 2008. Tali linee guida vanno poste in esecuzione, a prescindere dalle vaccinazioni HPV in corso.

Zusammenfassung und Schlussfolgerungen

Die bestehenden Unterschiede in Inzidenz und Mortalität beim Zervixkarzinom sind erstaunlich und schwer zu erklären. Inzidenz und Mortalität sind im Nordosten wesentlich höher als im Südwesten. Dafür verantwortlich könnten auch Codierprobleme sein. Studien haben gezeigt, dass in einem qualitätsgesichertes PAP-Screening regionale Unterschiede verschwinden können.

Povzetek in poziv k ukrepanju

Razlike med incidenčnimi in umrljivosti stopnjami raka maternične vratu v alpski regiji so res presenetljive in težko razumljive. Na severovzhodu sta incidenca in umrljivost višji kot na jugozahodu,

kar je morda tudi posledica problemov s kodiranjem. Kot potrjujejo mnoge študije, pa je razlike med regijami možno odpraviti z zagotovitvijo kakovostnega presejanja s testom Pap.

Ministri za zdravje držav Evropski skupnosti so 2. decembra 2003 soglasno sprejeli priporočilo o presejanju za odkrivanje raka dojk, materničnega vratu ter debelega črevesa in danke. Smernice za zagotavljanje kakovosti presejanja za odkrivanje raka materničnega vratu so bile v 2. izdaji objavljene leta 2008. Smernice je potrebno, ne glede na že uvedeno cepljenje proti virusu HPV, brezpogojno izvajati.

5.8.2 Introduction

During the study period 2,088 cervix carcinomas were diagnosed and 562 deaths recorded. The annual age-standardized incidence rate is 9.21/100,000, the mortality rate is 1.76/100,000.

Cervical cancer is one of the rare malignancies in which pre-stages of the disease (pre-invasive lesions, so called cervical intraepithelial neoplasia (CIN) or squamous intraepithelial lesion (SIL) can be detected many years before the actual invasive cancer develops. Regular Pap screening decreases cervix cancer incidence and mortality by at least 80% [1].

5.8.3 Epidemiology

Epidemiologic studies to evaluate risk factors for the development of SIL and cervical malignancy conclusively demonstrate a sexual mode of transmission of a carcinogen. [2] It is now widely accepted that human papillomavirus (HPV) is the primary etiologic infectious agent [3,4]. Other sexually transmitted factors, including herpes simplex virus 2, may play a co-causative role. The finding of HPV viral DNA integrated in most cellular genomes of invasive cervical carcinomas supports epidemiologic data linking this agent to cervical cancer [5]; however, direct causation has not been demonstrated. More than 100 distinct types of HPV have been identified, approximately 30 of which infect the human genital tract. HPV types 16 and 18 are most often associated with invasive disease. Characterization of carcinogenic risk associated with HPV types is an important step in the process of developing a combination HPV vaccine for the prevention of cervical neoplasia. Persistent infection with oncogenic types of HPV such as HPV-16 and HPV-18 is associated with the development of cervical cancer [8].

Barrier methods of contraception are associated with a reduced incidence of SIL presumptively secondary to protection from sexually transmitted disease [6,7].

Cigarette smoking by women is associated with an increased risk for squamous cell carcinoma [9,10]. This risk increases with longer duration and intensity of smoking and may be present with exposure to environmental tobacco smoke, being as high as four times that of women who are non-smokers and are not exposed to environmental smoking.

High parity has long been recognized as a risk factor for cervical cancer, but the relation of parity to HPV infection was uncertain. A meta-analysis of 25 epidemiologic studies including 16,563 women with cervical cancer and 33,542 women without, showed that the number of full-term pregnancies was associated with increased risk, regardless of age at first pregnancy [11].

Long-term use of oral contraceptives has also been known to be associated with cervical cancer, but its relation to HPV infection was also uncertain. The odds ratio (OR) for women who used oral contraceptives for 5 to 9 years was 2.82 (1.46–5.42), and for 10 or more years the OR was 4.03 (2.09–8.02) [12]. A meta-analysis of 24 epidemiological studies confirmed the increased risk associated with oral contraceptives, which is proportionate to the duration of use. Risk decreases after cessation and returns to normal risk levels in 10 years [13].

Various case-control studies show an association between intake of some micronutrients and lower risk of cervical cancer, but results are conflicting and difficult to control for other risk factors. Two randomized trials of oral folate as a chemo preventive agent have shown no protective effect.

5.8.4 Data quality

During the study period 2,088 cervical cancers were diagnosed. This represents 3% of all cancers (except NMSC). Cervical cancer caused 562 deaths, or 1.7% of all cancer deaths. Within the whole area the quality of registered data is questionable due to large variation in the different regions. Mortality/Incidence ratio shows big differences and lies between 0.10 and 0.42, mean 0.27. The reasons for these variations are primarily unclear. One explanation could be due to incorrect coding, for example to code uterus instead of cervix carcinoma as cause of death, meaning the mortality of cervix carcinoma would be underestimated.

DCO rate lies between 0.0 and 2.47, mean 0.62. Microscopically verified are 86.84% – 100%, mean 98.55%. The 86.84% microscopically verified figure appears unrealistically low as all other regions lie above 95%.

5.8.5 Risk factors (see epidemiology)

5.8.6 Screening with the Papanicolaou test

The Pap test has never been examined in a randomized controlled trial. A large body of consistent observational data, however, supports its effectiveness in reducing mortality from cervical cancer. Both incidence and mortality from cervical cancer have sharply decreased in a number of large populations following the introduction of well-conducted screening programs [14-17]. In Iceland, the mortality rate declined by 80% for more than 20 years, and in Finland and Sweden by 50% and 34%, respectively [18]. Similar reductions have been observed in large populations in the United States and Canada. Reductions in cervical cancer incidence and mortality were proportional to the coverage of screening.

Annual screening has not been found to significantly increase identification of invasive cervical cancer when compared with results from screening every two to three years [19,20].

5.8.7 Geographical variations

Predominant differences in incidence and mortality are seen for cervix cancer. It is surprising and disappointing for a cancer which can be detected and cured easily in a pre-invasive stage. We can see that incidence and above all mortality are much higher in the northeast than in the southwest. The incidence is statistically higher than the mean in Slovenia, Carinthia and Tyrol and lower in Sondrio, Ticino, Varese, St. Gallen, Appenzell, Friulia Venezia Giulia and Trentino. A significantly higher rate than the mean for mortality is seen only in Slovenia, a lower rate in Trentino, Varese and Veneto.

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Tab. 29: Cervix uteri – Numbers and Rates

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	243	16.8	11.5 (10.0, 13.1)	1.27 (1.11, 1.44)	61	4.2	2.0 (1.4, 2.6)	1.16 (0.88, 1.48)
Salzburg	154	11.5	7.8 (6.5, 9.1)	0.89 (0.76, 1.04)	59	4.4	2.6 (1.9, 3.3)	1.35 (1.03, 1.74)
Tyrol	273	15.6	11.3 (9.9, 12.7)	1.22 (1.08, 1.38)	80	4.6	2.7 (2.0, 3.3)	1.41 (1.12, 1.76)
Vorarlberg	89	9.9	7.2 (5.7, 8.8)	0.8 (0.64, 0.98)	26	2.9	1.6 (0.9, 2.3)	0.95 (0.62, 1.38)
Friuli Venezia Giulia	16	8.2	5.2 (2.2, 8.3)	0.57 (0.33, 0.92)	3	1.5	0.5 (0.0, 1.1)	0.31 (0.06, 0.9)
Varese	23	7.9	5.2 (2.9, 7.5)	0.59 (0.37, 0.88)	3	1.0	0.3 (0.0, 0.7)	0.27 (0.05, 0.78)
Sondrio	41	9.0	5.9 (4.0, 7.8)	0.66 (0.47, 0.89)	9	2.0	1.2 (0.3, 2.1)	0.5 (0.23, 0.95)
South Tyrol	119	10.1	7.1 (5.7, 8.4)	0.79 (0.65, 0.94)	27	2.3	1.0 (0.5, 1.4)	0.66 (0.44, 0.96)
Trentino	82	6.6	4.4 (3.4, 5.5)	0.49 (0.39, 0.61)	19	1.5	0.6 (0.3, 0.9)	0.39 (0.23, 0.61)
Veneto	67	11.1	7.5 (5.6, 9.4)	0.79 (0.61, 1)	7	1.2	0.7 (0.1, 1.3)	0.26 (0.1, 0.53)
Slovenia	760	19.7	14.2 (13.2, 15.3)	1.51 (1.41, 1.62)	188	4.9	2.5 (2.1, 2.9)	1.47 (1.27, 1.7)
Graubünden/Glarus	57	10.0	6.4 (4.6, 8.2)	0.78 (0.59, 1)	18	3.2	1.6 (0.8, 2.4)	0.89 (0.53, 1.41)
St.Gallen/Appenzell	95	7.2	5.4 (4.2, 6.5)	0.58 (0.47, 0.71)	40	3.0	1.5 (1.0, 2.1)	0.9 (0.64, 1.23)
Ticino	69	8.3	5.2 (3.8, 6.6)	0.6 (0.47, 0.76)	22	2.7	1.1 (0.6, 1.6)	0.66 (0.41, 1)
Total	**2,088**	**13.1**	**9.2 (8.8, 9.6)**	**1 (0.96, 1.04)**	**562**	**3.5**	**1.8 (1.6, 1.9)**	**1 (0.92, 1.09)**

Tab. 30: Cervix uteri – Data quality

Country description	% DCO	% HV	RMI
Carinthia	2.5%	99.6%	0.25
Salzburg	1.3%	86.8%	0.38
Tyrol	0.7%	100.0%	0.29
Vorarlberg	0.0%	100.0%	0.29
Friuli Venezia Giulia	0.0%	100.0%	0.19
Varese	0.0%	95.7%	0.13
Sondrio	0.0%	97.6%	0.22
South Tyrol	0.0%	99.2%	0.23
Trentino	1.2%	96.3%	0.23
Veneto	0.0%	100.0%	0.10
Slovenia	0.1%	99.6%	0.25
Graubünden/Glarus	0.0%	100.0%	0.32
St.Gallen/Appenzell	0.0%	100.0%	0.42
Ticino	1.4%	100.0%	0.32
Total	**0.6%**	**98.6%**	**0.27**

Fig. 29: Cervix uteri – Incidence – Smoothed Map

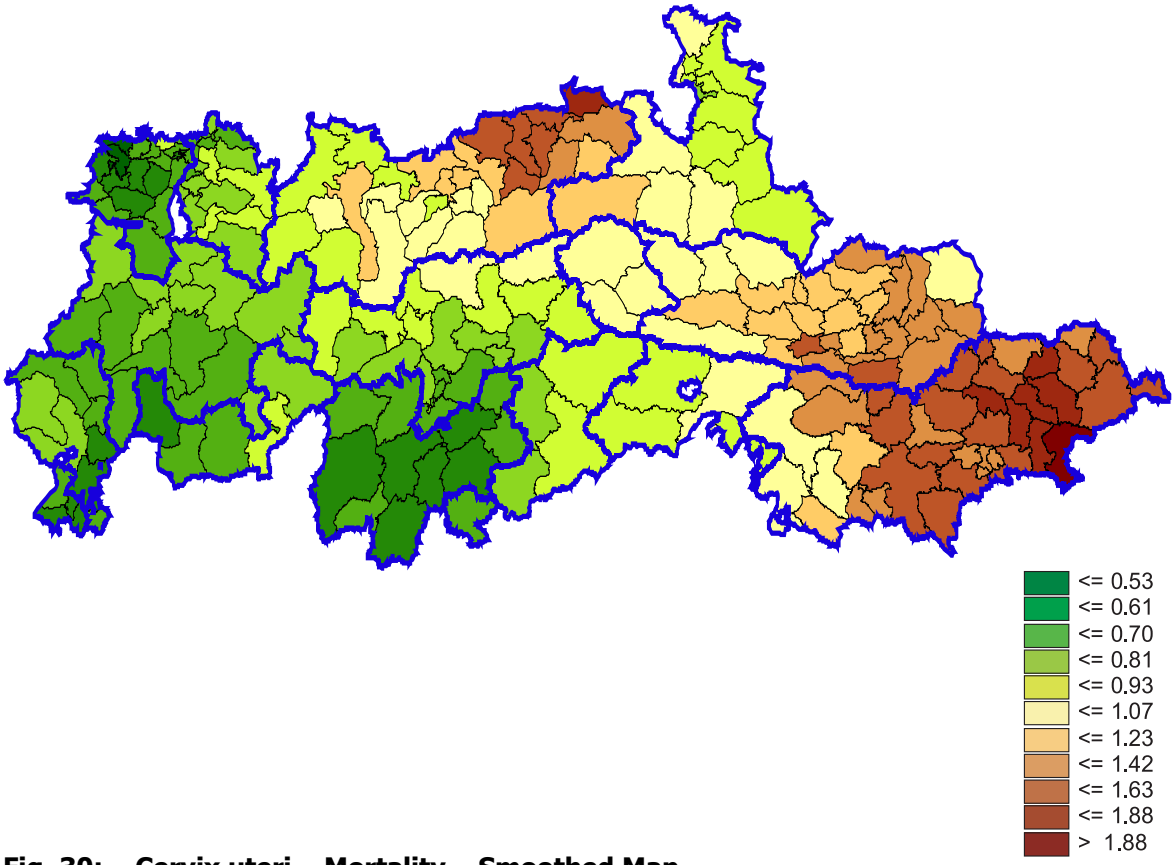
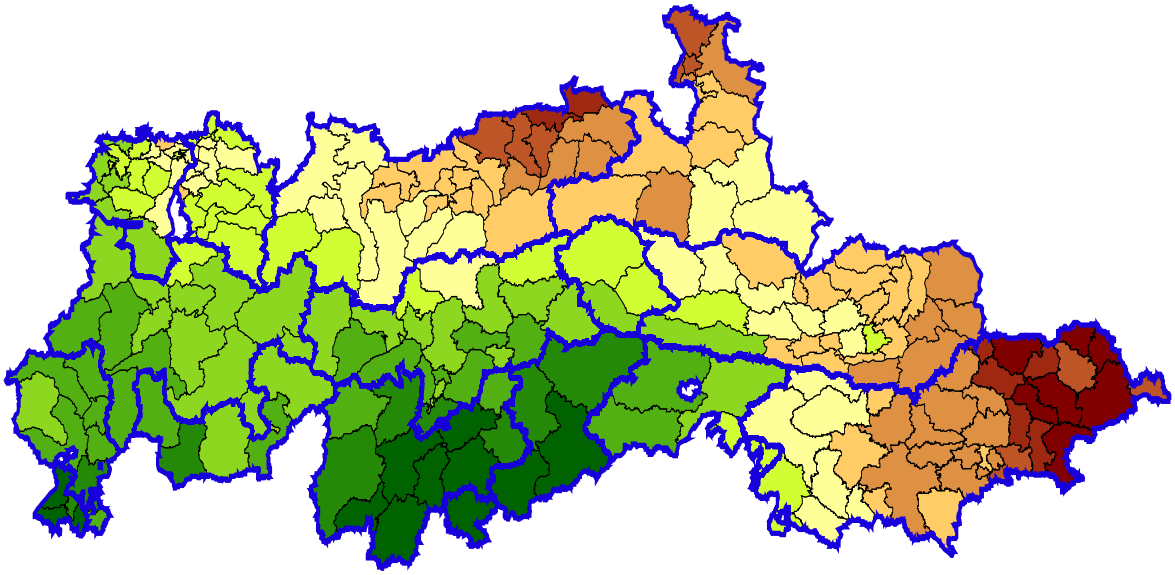


Fig. 30: Cervix uteri – Mortality – Smoothed Map



5.9 Corpus uteri Hans Concin

Corpo dell'utero
Gebärmutterkörper
Maternično telo

5.9.1 Summary and Call for Action

Summary and Call for Action

The cantons of Graubünden, Glarus, St. Gallen, Appenzell and Ticino have lower cancer mortality rates than do other regions for most types of cancer. In contrast, in these regions the mortality rate for cancer of the corpus uteri is the highest among our Alpine regions. This could be due to the relatively high living standard.

In most regions corpus and cervix cancer show opposite incidence and mortality rates.

Screening for early detection of corpus cancer has not yet been established. As bleeding is an obvious early symptom, such women should be immediately referred for investigation for suspected cancer.

Sintesi e proposte operative

Per il cancro del corpo dell'utero (endometrio), i Cantoni svizzeri partecipanti allo studio (Graubünden, Glarus, St. Gallen, Appenzell, Ticino) mostrano il tasso di mortalità più elevato rispetto alle altre aree. Ciò potrebbe essere legato al tenore di vita relativamente elevato.

Nella maggior parte delle aree, i tumori endometriali e quelli cervicali mostrano tassi d'incidenza e mortalità opposti. Non è disponibile uno "screening" efficace per i tumori endometriali e le donne soggette ad emorragia, che è un ovvio sintomo precoce, dovrebbero essere sottoposte ad indagine per sospetto tumore.

Zusammenfassung und Schlussfolgerungen

Die Kantone Graubünden, Glarus, St. Gallen, Appenzell und Ticino haben bei fast allen untersuchten Krebsarten geringere Mortalitätsraten als andere Regionen. Im Gegensatz dazu ist die Rate für das Korpuskarzinom die höchste in der Alpenregion. Verantwortlich dafür könnte der relativ hohe Lebensstandard sein. In den meisten Regionen zeigen Korpus- und Zervixkarzinome entgegengesetzte Inzidenz- und Mortalitätsraten. Screeningprogramme für die Korpuskarzinom-Früherkennung sind noch nicht etabliert. Blutungen sind ein offensichtliches und ernstes Symptom, daher sollten Frauen mit diesen Symptomen unverzüglich untersucht werden.

Povzetek in poziv k ukrepanju

V švicarskih kantonih Graubünden, Glarus, St. Gallen, Appenzell in Ticino je bila pri večini rakov ugotovljena nižja stopnja umrljivosti, umrljivost zaradi raka materničnega telesa pa je na teh območjih alpske regije najvišja. Morda je razlog višje umrljivosti razmeroma visok življenjski standard.

V večini pokrajin smo opazili nasprotne vrednosti incidenčnih in umrljivostnih stopnenj pri raku materničnem vratu in raku endometrija. Presejanje za raka endometrija se ni uveljavilo. Ker je krvavitev zelo očiten zgodnji znak raka endometrija je treba vsako bolnico, ki krvavi, poslati na preiskavo zaradi suma raka.

5.9.2 Introduction

Around three-quarters of women developing endometrial cancer are postmenopausal and 90% of these present with bleeding. As it is an obvious symptom many women seek advice after only one episode and should be immediately referred for investigation for suspected cancer. Consequently approximately 75% of all patients with endometrial cancer present with early stage-disease confined to the body of the uterus.

5.9.3 Epidemiology

Most of the established risk factors for uterine cancer are the result of excess exposure to oestrogen unopposed by progestagens, a process that stimulates proliferation of the cells of the womb, increasing cancer risk [1]. In addition, insulin and insulin-like growth factors may increase the effect of oestrogen on uterine tissue [2]. As all oestrogen exposure is unopposed in postmenopausal women, high circulating levels of oestrogens and androgens in these women are known to increase risk. Being overweight increases oestrogen levels in postmenopausal women [3] and can disrupt ovulation and progesterone production in premenopausal women, resulting in continuous exposure of the womb to unopposed oestrogen [4]. However, women with the highest levels of sex hormone-binding globulin (which governs the bioavailability of oestrogens and androgens) have a significantly reduced risk [5].

Pregnancy and parity reduce the risk of uterine cancer by 30% for a woman's first birth and by 25% for each successive birth, and later maternal age at last birth has also been shown to reduce risk. Pregnancy and childbirth are thought to offer reduced risk through the elimination of pre-malignant cells with the "sloughing-off" of cells during delivery, and/or the break in unopposed oestrogen exposure during pregnancy. Early menarche and late menopause significantly increase risk, because they prolong years of oestrogen exposure.

Other factors associated with increased risk include lack of, infrequent or irregular periods, anovulatory menstrual cycles and more days of menstruation.

Evidence suggests that risk of uterine cancer is 2-3 times higher in overweight and obese women respectively, and it is estimated that around 36% of cases of uterine cancer in the UK are caused by excess bodyweight [8-12]. Prospective studies, mainly among post-menopausal women, report a significant association with BMI at enrollment, but also suggest that women's BMI in younger adulthood is significant and that the increase in risk begins at a relatively modestly raised BMI. Some evidence suggests that waist circumference and waist-to-hip ratio may be more important than BMI, with significant increases in risk reported in women in the two lowest quartiles of BMI but the highest quartile of waist circumference.

Recent results from the UK Million Women Study report an increased risk of 50% among current users of oestrogen-only hormone replacement therapy (HRT) and 80% in those using tibolone preparations. A meta-analysis of published studies reported in the same paper found there was a non-significant reduced risk for ever versus never users of continuous combined therapy, and a small but significant increase in risk for cyclic combined [13].

Users of combined oral contraceptives have a lasting reduction in risk as they have fewer days of unopposed oestrogen exposure each month. The risk reduction is about 10% for each year of use and has been reported in some studies to persist for as long as 20 years after stopping use [14].
Tamoxifen, an oestrogen receptor-modulating hormone used to treat and prevent breast cancer, has been shown to treble the risk of uterine cancer [15].
A recent meta-analysis reported that women with diabetes have double the risk of uterine cancer. Although risks associated with diabetes are difficult to separate from those of excess bodyweight, there is evidence of an independent effect [16] and results of a recent serum study suggest that circulating insulin and free insulin-like growth factor 1 may play a role in uterine cancer [17]. Other studies show a higher risk of uterine cancer in women with higher blood and dietary glucose [18-20].
Some types of ovarian cancers (granulose-cell and theca-cell tumors) can secrete hormones such as oestrogens or androgens. Women with such tumors have a 10-fold higher risk of uterine cancer [21].
In the case of contraception use counselling, a point which might be included is that the Pill acts as an effective chemoprevention for corpus (and ovarian) cancer. Even though these epidemiological data are consistent, so far no recommendation has been made by any scientific society.

5.9.4 Data quality aspects

Within the whole area a total of 3,789 carcinomas of the corpus uteri account for 5.4% of all neoplasms. The 643 deaths account for 1.9% of cancer mortality. The quality of registered data is good. DCO rate lies between 0.0 and 1.14, mean 0.24. Microscopically verified are 93.84% – 100%, mean 98.62%. Mortality/Incidence ratio lies between 0.07 and 0.30, mean 0.17.

5.9.5 Early detection, screening

No screening program for asymptomatic women without special risk factors (see above) has been established. It is important that every incidence of irregular bleeding in women over 40 is reviewed and appropriately investigated. The incidental finding of endometrial cells on a Pap smear in postmenopausal women requires investigation. Families with hereditary non-polyposis colon cancer have a higher risk of corpus cancer and require counseling about this risk.

5.9.6 Geographical variations

The age-adjusted incidence rate shows only minor differences within our investigated Alpine Region (8.73 – 13.94, mean 12.97). More pronounced are the differences in mortality which lie three times lower in Trentino than in Graubünden/Glarus.
With the exception of Slovenia, the eastern regions show a lower incidence and mortality rate, which is reversed in cervical cancer.

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Tab. 31: Corpus uteri – Numbers and Rates

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	351	24.3	12.0 (10.6, 13.4)	0.99 (0.89, 1.1)	31	2.1	0.9 (0.5, 1.2)	0.51 (0.34, 0.72)
Salzburg	227	16.9	9.5 (8.1, 10.8)	0.77 (0.68, 0.88)	44	3.3	1.5 (1.0, 2.1)	0.91 (0.66, 1.22)
Tyrol	393	22.4	12.8 (11.4, 14.2)	1.03 (0.93, 1.14)	55	3.1	1.3 (0.9, 1.6)	0.87 (0.65, 1.13)
Vorarlberg	207	23.0	13.9 (11.9, 16.0)	1.11 (0.96, 1.27)	39	4.3	2.0 (1.3, 2.7)	1.28 (0.91, 1.75)
Friuli Venezia Giulia	49	25.2	10.7 (7.1, 14.3)	0.8 (0.59, 1.05)	7	3.6	1.6 (0.3, 2.9)	0.56 (0.23, 1.16)
Varese	61	20.9	11.0 (8.1, 14.0)	0.81 (0.62, 1.04)	4	1.4	0.7 (0.0, 1.4)	0.3 (0.08, 0.77)
Sondrio	111	24.4	13.5 (10.7, 16.2)	0.94 (0.77, 1.13)	14	3.1	1.0 (0.4, 1.7)	0.66 (0.36, 1.1)
South Tyrol	255	21.6	11.6 (10.0, 13.2)	0.93 (0.82, 1.05)	69	5.9	2.1 (1.5, 2.7)	1.46 (1.14, 1.85)
Trentino	260	21.0	11.7 (10.1, 13.2)	0.81 (0.71, 0.91)	19	1.5	0.6 (0.3, 0.9)	0.33 (0.2, 0.51)
Veneto	145	24.0	12.3 (10.0, 14.5)	0.83 (0.7, 0.97)	13	2.2	0.8 (0.3, 1.3)	0.39 (0.21, 0.67)
Slovenia	1,138	29.5	16.5 (15.5, 17.5)	1.25 (1.18, 1.33)	199	5.2	2.1 (1.8, 2.4)	1.4 (1.21, 1.6)
Graubünden/Glarus	130	22.8	13.2 (10.7, 15.6)	0.99 (0.82, 1.17)	35	6.1	2.8 (1.7, 3.9)	1.5 (1.04, 2.08)
St.Gallen/Appenzell	314	23.9	13.7 (12.1, 15.4)	1.09 (0.97, 1.22)	69	5.2	2.4 (1.8, 3.1)	1.36 (1.06, 1.72)
Ticino	148	17.9	8.7 (7.2, 10.3)	0.68 (0.58, 0.8)	45	5.4	2.2 (1.5, 2.9)	1.14 (0.83, 1.53)
Total	**3,789**	**23.7**	**13.0 (12.5, 13.4)**	**1 (0.97, 1.03)**	**645**	**4.0**	**1.6 (1.5, 1.8)**	**1 (0.92, 1.08)**

Tab. 32: Corpus uteri – Data quality

Country description	% DCO	% HV	RMI
Carinthia	1.1%	99.4%	0.09
Salzburg	0.0%	93.8%	0.19
Tyrol	0.0%	98.7%	0.14
Vorarlberg	1.0%	100.0%	0.19
Friuli Venezia Giulia	0.0%	95.9%	0.14
Varese	0.0%	96.7%	0.07
Sondrio	0.0%	97.3%	0.13
South Tyrol	0.4%	99.2%	0.27
Trentino	0.0%	98.1%	0.07
Veneto	0.0%	99.3%	0.09
Slovenia	0.0%	99.4%	0.17
Graubünden/Glarus	0.8%	98.4%	0.27
St.Gallen/Appenzell	0.3%	97.4%	0.22
Ticino	0.0%	99.3%	0.30
Total	**0.2%**	**98.6%**	**0.17**

Fig. 31: Corpus uteri – Incidence – Smoothed Map

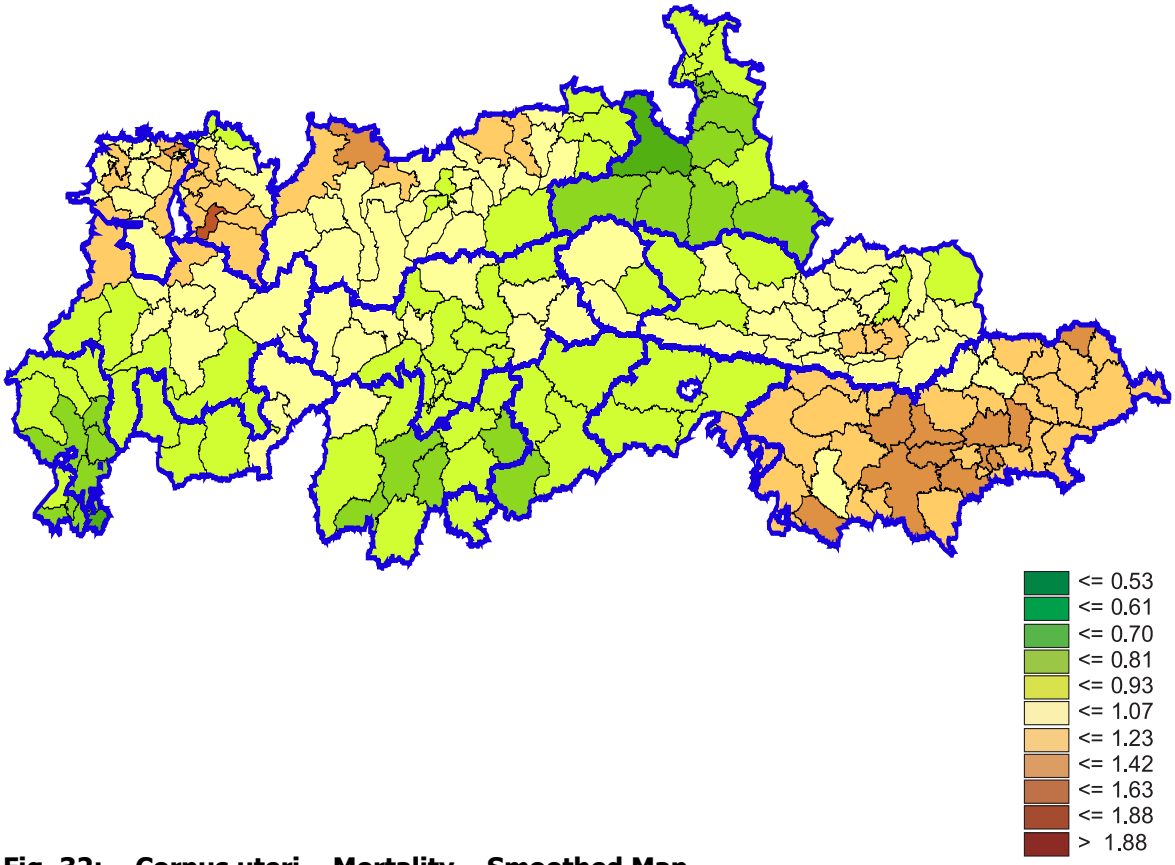
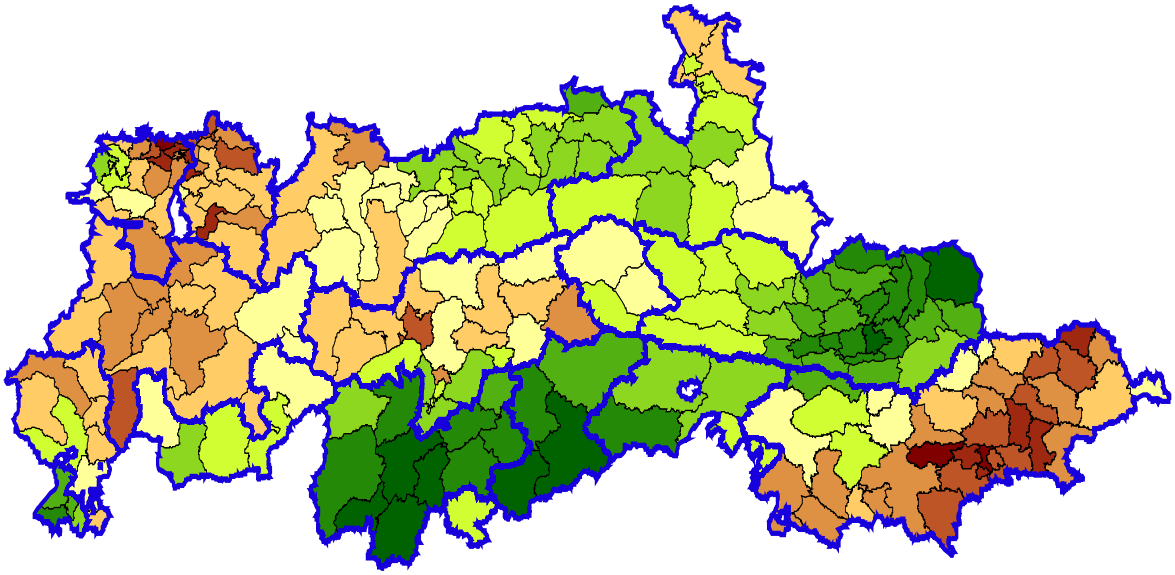


Fig. 32: Corpus uteri – Mortality – Smoothed Map



5.10 Ovary Hans Concin

Ovaio
Eierstock
Jajčnik

5.10.1 Summary and Call for Action

Summary and Call for Action
Little regional variation exists in the incidence and mortality of ovarian cancer in our study. The causes of ovarian cancer are unknown, but several factors are considered to exert an influence on its development. Screening for early detection of ovarian cancer has not yet been established.

Sintesi e proposte operative
Dal presente studio emerge una scarsa variabilità regionale nell'incidenza e mortalità per tale tumore. Le cause del cancro dell'ovaio sono in gran parte sconosciute, ma si ritiene che parecchi fattori influenzino il suo sviluppo.
Non è disponibile uno "screening" efficace per la diagnosi precoce del cancro ovarico.

Zusammenfassung und Schlussfolgerungen
Bei unserer Untersuchung existieren nur geringe regionale Unterschiede in der Inzidenz und Mortalität des Ovarialkarzinoms. Die Ursachen des Ovarialkarzinoms sind unbekannt aber verschiedene Faktoren stehen im Verdacht, einen Einfluss auf die Entwicklung des Karzinoms, auszuüben. Ein Screening für die Früherkennung ist noch nicht etabliert.

Povzetek in poziv k ukrepanju
V študiji smo ugotovili, da so v opazovanih pokrajinah le manjše razlike tako pri incidenci kot pri umrljivosti za rakom jajčnika. Direktnih vzrokov za nastanek raka jajčnika ne poznamo, znanih pa je več dejavnikov, ki lahko k njegovem nastanku vsaj deloma prispevajo. Presejanja za odkrivanje raka jajčnika še ne izvajamo.

5.10.2 Introduction

Of all gynaecological cancers identified in 'Cancer Mapping in the Alpine Regions 2001-2005' ovarian cancer shows the smallest differences in incidence and mortality as compared with the other cancers presented in this evaluation.

The pathogenesis of ovarian carcinoma remains unclear. Several theories have been proposed to explain the epidemiology of ovarian cancer including the theory of "incessant ovulation," gonadotrophin stimulation, excess androgenic stimulation, and inflammation [1-10].

Seventy percent of all ovarian cancers are diagnosed in a progressive state. Despite great efforts, screening for early detection of ovarian cancer is not yet established.

5.10.3 Epidemiology

Ovarian cancer represents the sixth most commonly diagnosed cancer among women in the world, and causes more deaths per year than any other cancer of the female reproductive system. Despite the high incidence and mortality rates, the aetiology of this disease is poorly understood. Established risk factors for ovarian cancer include age and having a family history of the disease, while protective factors include increasing parity, oral contraceptive use, and oophorectomy. Lactation, incomplete pregnancies, and surgeries such as hysterectomy and tubal ligation may confer a weak protective effect against ovarian cancer. Infertility may contribute to ovarian cancer risk among nulliparous women. Other possible risk factors for ovarian cancer include postmenopausal hormone-replacement therapy and lifestyle factors such as cigarette smoking and alcohol consumption. Many of the causes of ovarian cancer are yet to be identified. Additional research is needed to better understand the aetiology of this disease [1].

In the case of contraception use counselling, a point which might be included is that the Pill acts as an effective chemoprevention for ovarian (and corpus) cancer. The epidemiological data are consistent; so far no recommendation has been made by any scientific society.

5.10.4 Data quality aspects

During the study period 2,844 ovarian cancers were diagnosed. This represents 4.1% of all cancers (except NMSC). Ovarian cancer caused 1991 deaths representing 6% of all cancer deaths. The annual standardized incidence rate is 10.03/100,000 (range 6.46 – 11.74). The standardized mortality rate is 5.53/100,000 with a range of 3.68 -7.30.

Statistically, the mortality rate in the evaluated region is only significantly below the mean in Veneto and significantly over the mean in Salzburg. All other regions show no differences in mortality rates.

The quality of registered data varies from good to moderate. The average DCO rate is 2.14% (range 0.0 – 8.59). On average, microscopically verified cases are 92.09% (range 77.13 – 100%). Mortality/incidence ratio lies between 0.57 and 0.90, mean 0.70.

5.10.5 Risk factors

The risk of ovarian cancer is lower in women who have had children as compared to women who have no children. Risk reduces the more children a woman has, and women who have no children have twice the risk of women with three or more children [2].There was an approximately 20% reduced risk of ovarian cancer in parous women who had ever breastfed as compared to those who had never breastfed in one collaborative study [3]. The only prospective study to examine this issue showed a significant reduction in risk for women breastfeeding for 18 months or longer [4].

A recent pooled analysis of eight case-control studies investigating the relationship between infertility and ovarian cancer reported that nulligravid women who had been attempting pregnancy for more than five years had an increased odds ratio of 2.67 (95%CI 1.91 to 3.74) as compared to women who had been trying to conceive for less than a year [2].

The use of oral contraceptives is protective, perhaps due to cessation of ovulation. A recent collaborative analysis showed a 27% reduction in ovarian cancer risk in ever versus never users. This protective effect of the oral contraceptive pill appeared to be prolonged, with no significant differences between women who discontinued use within the last 10 years as compared to those who ceased use over 20 years ago. Risk reduces further with increasing years of use, with women who use the contraceptive pill for 15 or more years having half the risk of never users [5].

Tubal ligation has a protective effect on ovarian cancer with an estimated reduced risk of between 18% and 70% [11]. Hysterectomy may also reduce risk.

Ever use of hormone replacement therapy (HRT) is associated with a 19%-24% increase in risk of ovarian cancer, according to the most recent meta-analysis. The results support a greater risk of oestrogen-only therapy as compared to oestrogen-progestin therapy [12]. Risk is not increased in women using HRT for less than five years and reduces once a woman stops taking it.

The International Agency for Research in Cancer (IARC) was unable to draw a conclusion on a possible association between body mass index (BMI) and ovarian cancer, because the published studies were inconsistent in their analysis [9].

A large study linking records of women with ovarian cysts to cancer registry data showed that women with a hospital discharge diagnosis of ovarian cysts before the age of 29 had a higher risk of ovarian cancer, with an relative risk (RR) of 2.2 (95%CI 1.3 to 3.9), and women who had surgical resection of cysts or a unilateral oophorectomy as treatment had an RR of 8.8 (95%CI 5.2 to 15) [13].

On average, women with a mother or sister diagnosed with ovarian cancer have an RR of 2.6 (95%CI 2.2 to 3.08) for ovarian cancer. BRCA1 and BRCA2 mutations are known to increase the risk of ovarian cancer, with cumulative risks of developing ovarian cancer by the age of 70 among carriers of 40% (95% CI 35% to 46%) and 18% (95%CI 13% to 23%), respectively [14]. Women with previous breast cancer have a doubled risk of ovarian cancer, and the risk is almost four-fold for women diagnosed with breast cancer before the age of 40.

A meta-analysis showed an RR of 2.1 (95%CI 1.7 to 2.7) for mucinous ovarian tumors in current smokers. On the other hand, the same analysis showed a reduction in risk of clear cell cancers in current smokers, with an RR of 0.6 (95%CI 0.3 to 0.9) [15].

5.10.6 Early detection and screening

Screening for early detection of ovarian cancer has not yet been established.

5.10.7 Geographical variation

The data show a higher incidence rate in the eastern parts of Salzburg State, whereas all other regions show no variation in ovarian cancer incidence. Mortality is higher in the eastern part of Salzburg State and lower in some southern regions.

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Tab. 33: Ovary – Numbers and Rates

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	291	20.1	10.8 (9.4, 2.2)	1.1 (0.97, 1.23)	201	13.9	6.1 (5.1, 7.1)	1.06 (0.92, 1.22)
Salzburg	268	20.0	11.7 (10.2, 13.3)	1.2 (1.06, 1.36)	205	15.3	7.3 (6.2, 8.4)	1.35 (1.17, 1.55)
Tyrol	325	18.6	10.6 (9.3, 11.8)	1.13 (1.01, 1.25)	211	12.0	5.5 (4.6, 6.3)	1.07 (0.93, 1.22)
Vorarlberg	126	14.0	8.5 (6.9, 10.1)	0.89 (0.74, 1.06)	92	10.2	5.3 (4.1, 6.5)	0.96 (0.78, 1.18)
Friuli Venezia Giulia	29	14.9	6.5 (3.7, 9.3)	0.63 (0.42, 0.91)	26	13.3	4.2 (2.2, 6.1)	0.71 (0.46, 1.03)
Varese	60	20.6	10.3 (7.4, 13.2)	1.07 (0.82, 1.38)	34	11.7	5.2 (3.3, 7.2)	0.84 (0.58, 1.17)
Sondrio	92	20.2	10.4 (8.0, 12.8)	1.04 (0.84, 1.27)	62	13.6	5.5 (3.9, 7.1)	0.96 (0.74, 1.23)
South Tyrol	207	17.6	10.5 (8.9, 12.1)	1.01 (0.88, 1.16)	136	11.5	4.9 (3.9, 5.8)	0.94 (0.78, 1.11)
Trentino	225	18.2	9.7 (8.2, 11.1)	0.94 (0.82, 1.07)	174	14.1	6.0 (5.0, 7.0)	0.98 (0.84, 1.14)
Veneto	111	18.4	6.7 (5.2, 8.3)	0.85 (0.7, 1.03)	73	12.1	3.9 (2.8, 5.0)	0.73 (0.57, 0.92)
Slovenia	669	17.3	10.6 (9.7, 11.4)	0.99 (0.91, 1.07)	446	11.6	5.4 (4.9, 5.9)	0.99 (0.9, 1.09)
Graubünden/Glarus	93	16.3	9.1 (7.0, 11.2)	0.93 (0.75, 1.14)	67	11.8	5.3 (3.8, 6.7)	0.93 (0.72, 1.19)
St.Gallen/Appenzell	203	15.4	8.9 (7.5, 10.2)	0.93 (0.8, 1.06)	157	11.9	5.9 (4.8, 7.0)	1.01 (0.86, 1.18)
Ticino	145	17.5	9.4 (7.7, 11.1)	0.89 (0.75, 1.05)	107	12.9	5.7 (4.4, 7.0)	0.89 (0.73, 1.08)
Total	**2,844**	**17.8**	**10.0 (9.6, 10.4)**	**1 (0.96, 1.04)**	**1,991**	**12.5**	**5.5 (5.3, 5.8)**	**1 (0.96, 1.04)**

Tab. 34: Ovary – Data quality

Country description	% DCO	% HV	RMI
Carinthia	8.6%	94.4%	0.69
Salzburg	1.9%	81.7%	0.76
Tyrol	1.8%	94.7%	0.65
Vorarlberg	4.0%	100.0%	0.73
Friuli Venezia Giulia	0.0%	89.7%	0.90
Varese	0.0%	91.7%	0.57
Sondrio	0.0%	88.0%	0.67
South Tyrol	1.9%	92.1%	0.66
Trentino	0.9%	77.1%	0.77
Veneto	4.5%	88.7%	0.66
Slovenia	0.9%	97.7%	0.67
Graubünden/Glarus	0.0%	84.9%	0.72
St.Gallen/Appenzell	0.0%	95.6%	0.77
Ticino	2.1%	93.7%	0.74
Total	**2.1%**	**92.1%**	**0.70**

Fig. 33: Ovary – Incidence – Smoothed Map

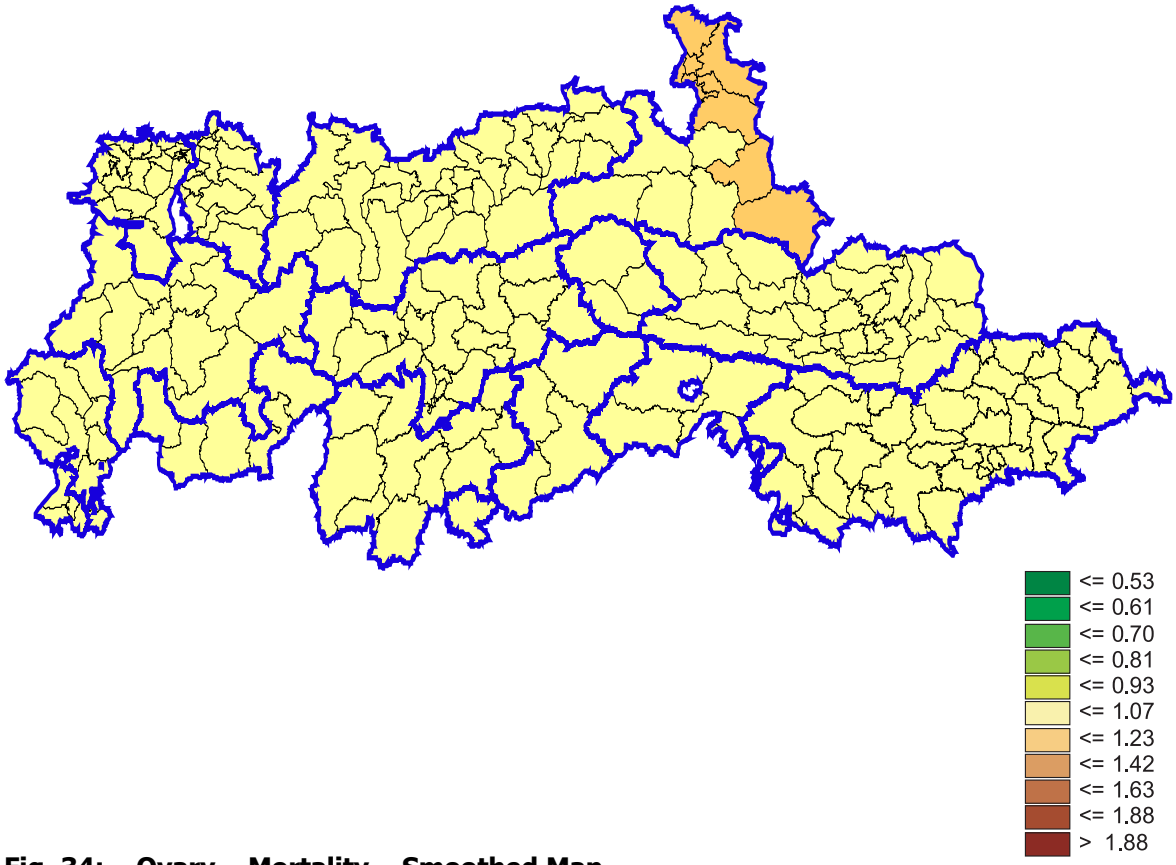
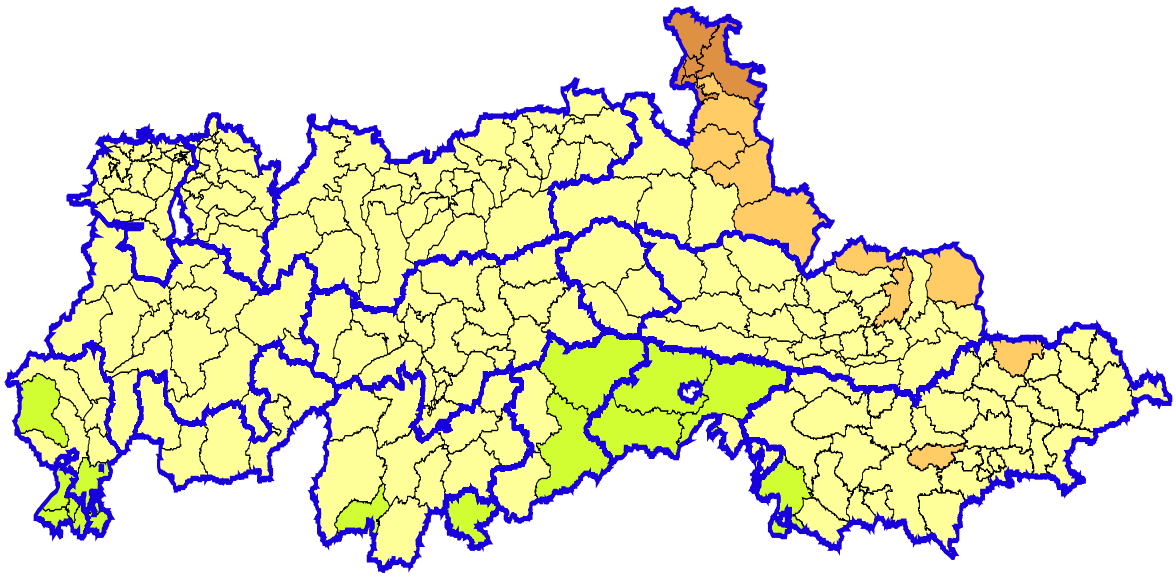


Fig. 34: Ovary – Mortality – Smoothed Map



5.11 Prostate Willi Oberaigner

Prostata
Prostata
Prostata

5.11.1 Summary and Call for Action

Summary and Call for Action
We see a clear geographic pattern in incidence, namely very high risk in the Austrian regions, which is correlated with intensive PSA testing. Concerning mortality, we observe a higher risk in some parts of Carinthia and Slovenia.
PSA screening is still discussed controversially worldwide. Although some studies show benefits, it is too early to make final recommendations. In Slovenia and parts of Carinthia improving outcome of prostate cancer could diminish the risk of prostate cancer mortality.

Sintesi e proposte operative
L'incidenza mostra un'evidente struttura geografica, caratterizzata da un rischio elevatissimo nelle zone Austriache, correlato all'uso intensivo del test PSA. Riguardo alla mortalità, si rileva un rischio maggiore in alcune zone della Carinzia e della Slovenia.
Lo screening mediante test PSA è ancora oggetto di controversie in tutto il mondo. Sebbene alcuni studi mostrino dei benefici, è ancora troppo presto per fornire delle indicazioni definitive. In Slovenia ed in alcune parti della Carinzia, un miglioramento dei trattamenti per il tumore prostatico potrebbe ridurre i tassi di mortalità.

Zusammenfassung und Schlussfolgerungen
Es ist ein klares geographisches Verteilungsmuster der Prostatakarzinominzidenz festzustellen: Besonders in Teilen Österreichs besteht ein sehr hohes Risiko, welches allerdings korreliert ist mit intensiven PSA-Untersuchungen. Was die Mortalität betrifft, so ist ein höheres Risiko in einigen Teilen Kärntens und Sloweniens zu beobachten.
PSA-Screening wird nach wie vor weltweit sehr kontroversiell diskutiert, obwohl einige Studien einen Benefit zeigen, ist es noch zu früh für endgültige Empfehlungen. In Slowenien und in Teilen von Kärnten könnte eine Verbesserung des Outcomes das Mortalitätsrisiko senken.

Povzetek in poziv k ukrepanju
Iz prikazanega geografskega vzorca je razvidno, da je ogroženost z rakom prostate zelo velika v avstrijskem delu alpske regije, kar pojasnjujemo z intenzivnim določanjem PSA v tem delu. V nekaterih predelih Koroške in Slovenije smo opazili povečano umrljivost za rakom prostate.

Po svetu še vedno potekajo nasprotujoče si razprave o presejanju za odkrivanje raka prostate z določanjem PSA. Čeprav so nekatere študije potrdile prednosti takšnega testiranja, je še vedno preuranjeno za objavo končnih priporočil. Z izboljšanjem rezultatov zdravljenja raka prostate bi na Koroškem in v Sloveniji lahko zmanjšali tveganje smrti za tem rakom.

5.11.2 Introduction

The Prostate is now the most frequent incident cancer site for males in all registries of the study region with the exception of Slovenia. In terms of cancer mortality, prostate cancer takes second place in Swiss registries, second to third place in Austrian registries, third place in Slovenia and third to sixth place in Italian registries. Not only in Austrian registries, has PSA testing caused a doubling of prostate cancer incidence rates. However, PSA testing started at different time points. Whereas in Tyrol, the rate has been decreasing in recent years, we now observe the highest ASR in Vorarlberg. In countries with a high degree of PSA testing, prostate cancer counts for about 30% of incident cancer cases (even 40% in Vorarlberg) whereas in the other countries the proportion is about 15%. Also the proportion of prostate cancer mortality varies largely from 6% in Italian registries to 15% in Swiss registries. These figures also reflect the lower baseline incidence in the Italian population.

5.11.3 Epidemiology

As PSA testing is widespread in many countries in Europe and also worldwide, the key fact for understanding the maps of prostate cancer is understanding the effect of PSA testing. PSA testing produces an approximate doubling of prostate cancer incidence. Most of these prostate cancer cases are in an early stage and thus have a favourable prognosis. The ultimate goal of PSA testing and PSA screening is to reduce prostate cancer mortality and in fact some studies have shown a reduction in prostate cancer mortality [2,3].

For prostate cancer incidence, we observe a wide range of SMR from 0.6 in Trentino to 1.9 in Vorarlberg. Age-standardised rates (per 100,000 men, SEGI weights) vary from 46.7 in Trentino to 152.9 in Vorarlberg, the ASR in the whole study region being at 79.3. Concerning mortality, the range in SMR is smaller from 0.6 in Veneto to 1.3 in Slovenia. Age-standardised rates vary from 13.3 in Trentino to 20.0 in Slovenia, the ASR in the whole study region being 14.7 per 100,000 men.
In most central European countries, prostate cancer is the second-leading cancer cause of death and the leading incident cancer site for males. In Europe, prostate cancer mortality has a wide range and we observe higher mortality rates in France and the Scandinavian countries. In northern Europe, the incidence rate is 45.4 and the mortality rate is 20.0. In contrast, prostate cancer rates are considerably lower in southern parts of Europe with an incidence rate of 23.9 and a mortality rate of 13.0 [4].

5.11.4 Data quality

DCO-rates are fairly low, ranging from 0.1 in Sondrio and St. Gallen/Appenzell to 2.2 in Carinthia. We observe a small variation in HV proportion ranging from 92.6% in Ticino to 99.1% in Tyrol. The mortality to incidence ratio (M/I) is expected to show a large variation due to the large variation in prostate cancer incidence rates: in the study area, the RMI ratio varies between 0.13 in Tyrol and Vorarlberg and 0.36 in Slovenia.

5.11.5 Risk factor, early detection, screening

Little is known about risk factors. Some authors conclude that risk factors for prostate cancer remain poorly understood. Only a few facts on family history of prostate cancer [5] and ethnic groups [6,7] are known, but many questions remain unanswered, notably concerning aspects of lifestyle (diet, tobacco etc.).

In many countries, PSA testing is applied very frequently. Several analyses have shown a reduction in prostate cancer mortality in Tyrol after the introduction of PSA screening [2]. A few months ago, both large randomised studies were published, one with reduced mortality and one without [3,8]. However, many methodological questions have been raised and the question whether PSA screening should be recommended remains open [9]. It is well agreed that mortality reduction is only one point, but also the harms of PSA screening, like prostatectomy leading to incontinence and impotence, have to be carefully discussed.

5.11.6 Survival

Prostate cancer survival is rather favourable in the early stages but still poor in the advanced stages: whereas we see five-year relative survival rates between 90 and 100 in the early stages, the respective rates for advanced stages are between 10 and 20 [10]. There is no curative therapy for late stages. Therefore, a shift towards early stages - as appears to be a consequence of screening programs - should substantially improve survival rates. EUROCARE-4 has published relative five-year survival rates without adjusting for staging and has shown a broad variation from 48% in Denmark to 58.2% in Slovenia, 79.1% in Italy and 86.7% in Austria.

5.11.7 Geographical variation

We observe large differences in the regional distribution of both incidence and mortality rates. Incidence rates are high in most parts of Austria and some parts of Switzerland and are low in all parts of Slovenia. In Austria, the highest rates are now observed in Vorarlberg whereas in Tyrol, incidence rate have decreased since the late 1990s (data not shown). Largest SIR are 2 and higher. However, we observe a slightly higher risk for prostate cancer mortality in the northwestern parts (Vorarlberg and some neighbouring Swiss regions) and a distinctly higher risk in the southeastern parts, namely most parts of Slovenia and some part of Carinthia with SMRs in the range of 1.5 to 1.8. The most plausible explanation for the higher risk for prostate cancer mortality in Slovenia is poorer survival, and in Eurocare4 we observed poorer survival in Slovenia (the most recent period analysis results for 2000-02 showed five-year survival rates of 63.3 in Slovenia, 85.0 in Italy, 87.3 in Switzerland and 88.9 in Austria) [11]. However, when interpreting these facts, we must bear in mind that one reason for the lower survival observed in Slovenia is probably less early stages as compared to countries with PSA testing. This fact is not corrected in EUROCARE4 because the analysis is not stratified by stage. In order to understand the fact Slovenia shows only a higher risk for mortality and not for incidence we must consider that during the time period covered by this study, there was a potential problem with under-registration of early stages in Slovenia.

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Tab. 35: Prostate – Numbers and Rates

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	2,311	170.9	94.3 (90.3, 98.3)	1.22 (1.17, 1.27)	468	34.6	15.9 (14.4, 17.4)	1.07 (0.98, 1.18)
Salzburg	1,832	145.6	97.6 (93.0, 102.2)	1.2 (1.14, 1.25)	324	25.8	14.6 (12.9, 16.2)	0.97 (0.87, 1.08)
Tyrol	2,623	157.2	107.3 (103.1, 111.5)	1.28 (1.23, 1.33)	353	21.2	12.0 (10.7, 13.2)	0.8 (0.72, 0.89)
Vorarlberg	1,882	214.3	152.9 (145.9, 159.9)	1.88 (1.79, 1.97)	251	28.6	18.6 (16.2, 20.9)	1.26 (1.1, 1.42)
Friuli Venezia Giulia	408	218.1	93.1 (83.6, 102.6)	1.2 (1.08, 1.32)	71	38.0	12.6 (9.5, 15.7)	0.84 (0.65, 1.06)
Varese	365	133.7	69.7 (62.4, 77.1)	0.91 (0.82, 1.01)	61	22.3	9.9 (7.4, 12.4)	0.69 (0.53, 0.89)
Sondrio	684	157.0	80.4 (74.2, 86.6)	1.04 (0.96, 1.12)	118	27.1	11.9 (9.7, 14.1)	0.83 (0.69, 0.99)
South Tyrol	1,603	139.8	82.7 (78.6, 86.9)	1.05 (1, 1.11)	314	27.4	13.7 (12.2, 15.3)	0.93 (0.83, 1.04)
Trentino	1,091	92.6	46.7 (43.8, 49.6)	0.61 (0.58, 0.65)	358	30.4	12.8 (11.4, 14.1)	0.85 (0.77, 0.94)
Veneto	837	150.2	68.0 (63.2, 72.8)	0.9 (0.84, 0.96)	133	23.9	9.5 (7.6, 11.4)	0.6 (0.51, 0.72)
Slovenia	2,866	77.8	50.6 (48.7, 52.4)	0.64 (0.62, 0.67)	1,040	28.2	20.0 (18.8, 21.3)	1.28 (1.21, 1.37)
Graubünden/Glarus	783	140.8	79.1 (73.3, 84.9)	1.04 (0.96, 1.11)	206	37.0	15.6 (13.4, 17.9)	1.07 (0.93, 1.23)
St.Gallen/Appenzell	1,879	145.6	90.3 (86.0, 94.6)	1.16 (1.11, 1.22)	419	32.5	15.2 (13.7, 16.7)	1.03 (0.93, 1.13)
Ticino	947	125.6	63.7 (59.5, 67.9)	0.8 (0.75, 0.86)	262	34.7	13.4 (11.7, 15.1)	0.93 (0.82, 1.04)
Total	**20,111**	**132.2**	**79.3 (78.2, 80.4)**	**1 (0.99, 1.01)**	**4,378**	**28.8**	**14.7 (14.2, 15.1)**	**1 (0.97, 1.03)**

Tab. 36: Prostate – Data quality

Country description	% DCO	% HV	RMI
Carinthia	2.2%	98.2%	0.20
Salzburg	0.9%	95.8%	0.18
Tyrol	0.7%	99.1%	0.13
Vorarlberg	1.2%	99.6%	0.13
Friuli Venezia Giulia	0.2%	98.0%	0.17
Varese	0.0%	95.6%	0.17
Sondrio	0.1%	95.0%	0.17
South Tyrol	1.1%	94.8%	0.20
Trentino	0.5%	96.6%	0.33
Veneto	0.5%	97.6%	0.16
Slovenia	1.4%	95.9%	0.36
Graubünden/Glarus	0.4%	94.9%	0.26
St.Gallen/Appenzell	0.1%	96.8%	0.22
Ticino	1.6%	92.6%	0.28
Total	**0.8%**	**96.8%**	**0.25**

Fig. 35: Prostate – Incidence – Smoothed Map

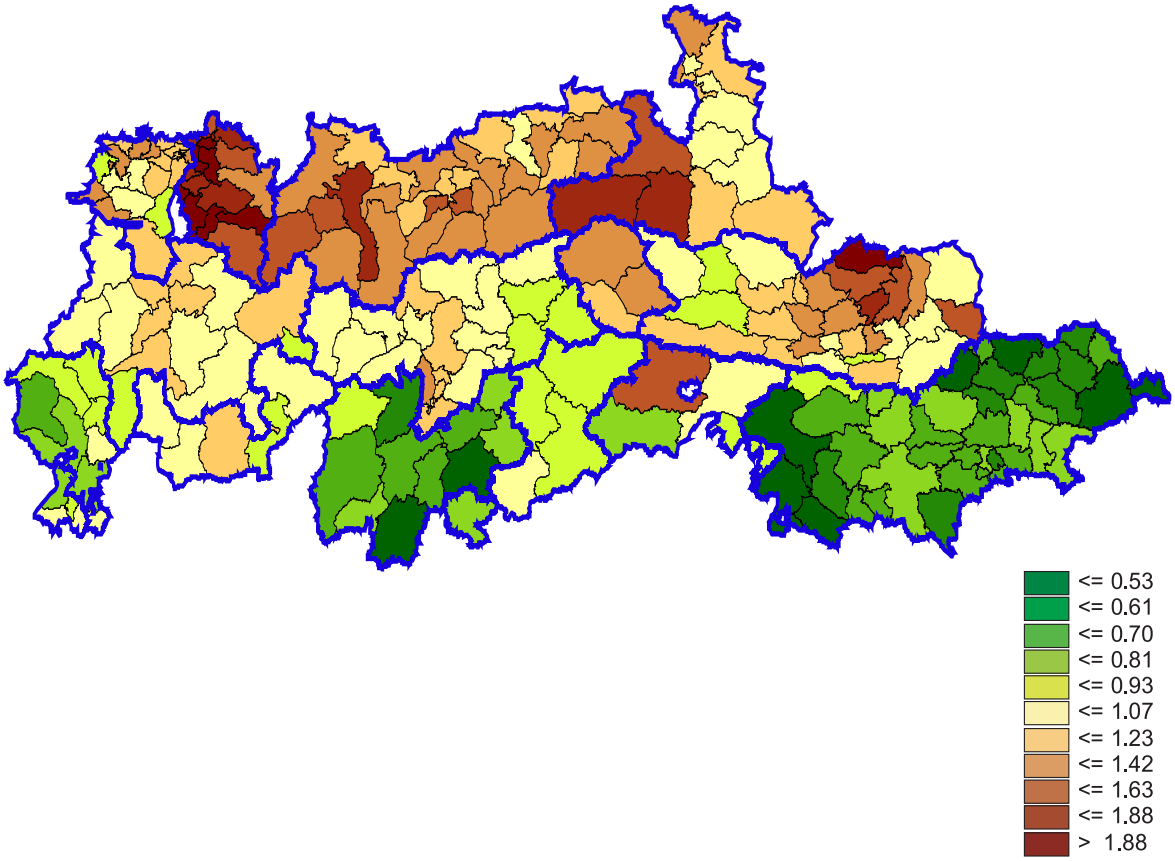
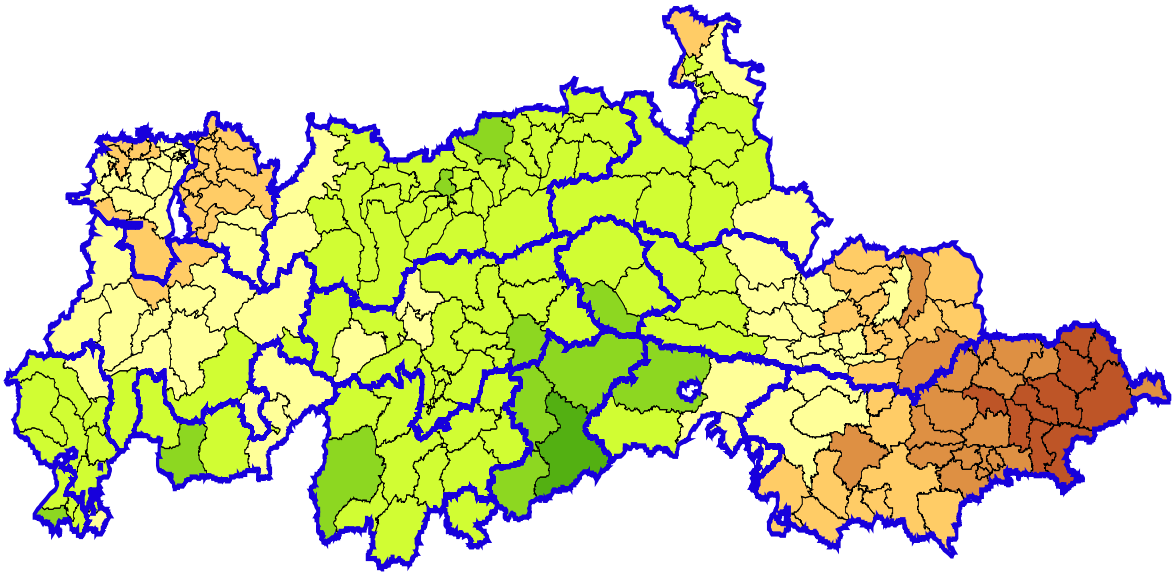


Fig. 36: Prostate – Mortality – Smoothed Map



5.12 Bladder Vesna Zadnik

Vescica
Harnblase
Mehur

5.12.1 Summary and Call for Action

Summary and Call for Action

There is an excess risk for bladder cancer in both sexes in Veneto, Varese and the eastern parts of Trentino and Carinthia. In males there also is an excess of bladder cancers in South Tyrol and Friuli Venezia Giulia. Some of this excess risk (especially in Veneto) is certainly attributable to different practices for pathological invasion assessment in bladder carcinoma. In Slovenia and Sondrio, the mortality rates in males exceed the rates anticipated from their incidence rates.

Different smoking habits (intensity of smoking and type of tobacco used) are the most probable causes for the observed geographical variability in bladder cancer incidence. Well organized smoking prevention and cessation programs are vital for bladder cancer incidence reduction as an immediate decrease in bladder cancer risk (around 40%) is expected after smoking cessation [10]. In regions with high bladder cancer mortality rates but relatively low incidence rates a review of treatment methods would be beneficial.

Sintesi e proposte operative

Un eccesso di rischio nelle aree Venete, Varesine, nelle zone orientali del Trentino ed in Carinzia emerge in entrambi i sessi. Tra i maschi, l'eccesso di tumori vescicali riguarda anche il Alto Adige e il Friuli Venezia Giulia. Parte di tale eccesso di rischio (specie in Veneto) è attribuibile sicuramente a prassi differenti nella valutazione dell'invasione patologica. In Slovenia ed in provincia di Sondrio, i tassi di mortalità maschile eccedono quelli attesi in base ai relativi tassi d'incidenza.

La più probabile ragione della variabilità geografica osservata, nell'incidenza del cancro vescicale, è la diversità nelle abitudini relative al fumo (intensità di consumo e tipo di tabacco usato). Dopo aver cessato di fumare, ci si attende un'immediata diminuzione del rischio per questo tumore (circa -40%). Di conseguenza, per ridurre l'incidenza appaiono essenziali programmi più efficaci per la prevenzione e la cessazione dell'abitudine al fumo.

Nelle regioni con mortalità per cancro vescicale elevata, ma tassi d'incidenza relativamente bassi, sarebbe utile una revisione dei metodi di trattamento.

Zusammenfassung und Schlussfolgerungen

Es besteht ein erhöhtes Risiko für Blasenkrebs in Veneto, Varese und in den östlichen Teilen von Trentino, sowie in Kärnten und zwar für beide Geschlechter. Bei den Männern beobachten wir auch eine Erhöhung in Südtirol und Friaul, sowie in der Region Julisch Venetien. Ein Teil dieses erhöhten Risikos (besonders in Veneto) kann sicherlich auch mit den verschiedenen pathologischen Diagnosemethoden in Zusammenhang gebracht werden. In Slowenien und Sondrio sind die Mortalitätsraten höher als man auf Grund der Inzidenzraten erwarten würde. Rauch (besonders die Intensität des Rauchens und der Tabaktyp) ist die wahrscheinlichste Ursache für die beobachteten geographischen Unterschiede der Blasenkrebsinzidenz. Gut organisierte Antirauchprogramme sind unbedingt zur Senkung der Blasenkrebsinzidenz notwendig. So kommt es unmittelbar nach Beendigung des Rauchens zum Absinken des Blasenkrebskarzinoms um ca. 40%. In Regionen mit hoher Blasenkrebsmortalität bei relativ niedrigen Inzidenzraten würde eine Evaluierung der Behandlungsmethoden sinnvoll sein.

Povzetek in poziv k ukrepanju

Ogroženost z rakom mehurja je pri obeh spolih zelo visoka v Benečiji, v Venetu ter v vzhodnih delih pokrajine Trentino in Koroške. Pri moških smo večjo ogroženost opazili še na Južnem Tirolskem ter v Furlaniji-Julijski krajini. Delno so na povečano tveganje (zlasti v Benečiji) vplivale tudi razlike v patološki oceni invazivnosti raka mehurja. V Sloveniji in pokrajini Sondrio stopnje umrljivosti pri moških presegajo vrednosti, ki so bile pričakovane na osnovi incidenčnih stopenj.

Vzrok za geografsko različno porazdeljeno incidenco raka mehurja so najverjetneje različne kadilske navade (intenzivnost kajenja in vrsta tobaka). K zmanjšanju incidence raka mehurja veliko prispevajo organizirani programi za preprečevanje in prenehanje kajenja, saj se po opustitvi kajenja tveganje raka mehurja zmanjša za 40 % (10). V pokrajinah, kjer so stopnje umrljivosti za rakom mehurja visoke, incidenčne stopnje pa nizke, bi bilo dobro preveriti metode zdravljenja tega raka.

5.12.2 Introduction

Bladder cancer burden indicators are difficult to interpret and even more difficult to compare between countries, as the classification rules change frequently. There is a large variation in coding multiple cancers and there is inconsistent inclusion of non-invasive bladder cancers. In all collaborating cancer registries, data are coded according to protocols that allowed us to exclude non-invasive bladder tumors from our analysis. However, it is known that practices for pathological invasion assessment in bladder carcinoma vary widely [1], which could be recognized as a problem in interpreting geographical variation in incidence statistics. A newly adopted IARC coding rule, which considers histological identical cancers of bladder, ureter and renal pelvis as a single entity, with only one cancer at these sites reported per person [2] and which is supposed to reduce bladder cancer incidence by up to 10% [3], should not affect our results, as the time of its introduction only fairly coincides with the observation period of our study.

5.12.3 Epidemiology

Bladder is the ninth most common cancer site worldwide. More than three-quarters of bladder cancers appear in men: it was estimated that in 2002 there were 274,000 incidence cases in males and 83,000 incidence cases in females [4]. The most common bladder cancer histological type is transitional cell carcinoma, with proportion of over 90% in European countries. The highest incidence rates in the world are observed in North America and Europe, where 59% of all cases occur. The highest rates in Europe (especially in males) were found in Mediterranean countries [1]. In the Alpine region, according to last release of the publication Cancer Incidence in Five Continents, the crude incidence rates per 100,000 inhabitants are the highest in Italy [above 30 in males and above 5 in females] and the lowest in Slovenia (15 and 3 in males in females, respectively). The reported rates for Austria and Switzerland are very similar, being about 20 in males and about 5 in females. In the entire analyzed area, bladder cancer accounts for 5% of all new cancers cases in males and 2% in females.

Worldwide, there were about 145,000 bladder cancer deaths in 2002, making this the 13th most frequent cause of death from cancer [4]. When exploring the variability in rates among Alpine countries in the WHO mortality database, the highest bladder cancer mortality is registered in Italy (about 15/100,000 in males and 3.6/100,000 in females), in Slovenia the rates were 11/100,000 in males and 2.5/100,000 in females but lower in Austria and Switzerland (around 7/100,000 in males and around 4/100,000 in females). In the entire analyzed area, bladder cancer accounts for 4% of all cancers deaths in males and 3% in females.

The average bladder cancer patient's survival in Europe is rather good, reaching 72.5% in patients diagnosed between 1995–1999 (5-year relative survival) [5]. Survival in females is slightly lower then in males. There is a remarkable difference in bladder cancer survival between countries participating in our survey: the 5-year relative survival of Slovenian patients was only 56%, while it was 64% in patients from Switzerland and 77% in patients from Austria and Italy. The survival rates indirectly reflect the quality of treatment and are related to mortality rates but not to incidence rates.

5.12.4 Data quality

The proportion of DCO cases in our data set is small: the area average proportion of DCO is 2.2% in females and 1.0% in males. The highest proportion of DCO cases is noticed in Austrian registries, being 4.0% in females and 1.2% in males. On average, 96% of cases were microscopically verified in females and 97% in males. There is some variation between provinces/states in this indicator: the lowest proportion of microscopically verified cases was noticed in Trentino in females (81.6%) and in Salzburg State in males (87.6%). The variation in the mortality/incidence ratio is considerable. The indicator ranges from 0.2 to 0.7 in females and from 0.2 to 0.6 in males. As there is quite a difference in survival of bladder cancer patients between provinces/states [see above] a variation in mortality/incidence ratio was expected. However, a very low ratio in Veneto and Carinthia could indicate incomplete mortality statistics or a different practice in pathological invasion assessment in bladder carcinoma (some non-invasive cancers are reported as invasive by pathologists in those regions). This should be kept in mind when interpreting the maps. In spite of this, the quality of the data applied seems to be adequate for proper estimation of the bladder cancer burden.

5.12.5 Risk factors, early detection and screening

The most important risk factor for bladder cancer is cigarette smoking, which is thought to account for approximately two-thirds of male and one third of female bladder cancers in Europe [6, 7]. The average relative risk of current smokers is estimated to be 2.8 [8]: still it depends on the intensity and duration of smoking [9]. It was shown that smokers of black tobacco are at greater risk than are smokers of blond tobacco what could explain the higher incidence rates observed in the Mediterranean region, where the smoking of black tobacco was common in the past [10].

Occupational or environmental exposure to aromatic amines is another recognized bladder cancer risk factor. A recent meta-analysis [11] showed a small, but significantly increased risk among miners, bus drivers, rubber workers, motor mechanics, leather workers, blacksmiths, machine setters, hairdressers and mechanics. Exposure to some other chemicals has also been investigated, but the results are typically inconclusive as the relative risks are small and past exposure assessment is difficult [10].

To date, no effective screening approach is available for bladder cancer. However, the vast majority of patients with newly diagnosed bladder tumors have non-muscle invasive bladder cancer with a good prognosis, suggesting that any newly adopted screening test should be applied only to high-risk population groups, particularly bladder cancer patients before disease recurrence [12].

5.12.6 Geographical variation

Females. The smoothed female incidence map shows a statistically significant excess risk in the entire Veneto region and in eastern Carinthia. There is an insignificant excess risk in the eastern part of the Trentino region and the Varese region.

Contrary to the incidence map, the smoothed female mortality bladder cancer map does not show any inter-regional variability. To exclude the possibility of misinterpretation because of over smoothing,

the crude mortality map was also checked [map not printed], but even that map does not show any parts of the analyzed area to have an excess mortality risk.

Males. The regions with excess risk in male bladder cancer are similar to the female regions, only the extremes are even more evident. The highest risk areas are in Varese and Veneto: statistically significant excess risk can also be observed in the eastern parts of Trentino, South Tyrol and Carinthia. There is an insignificant excess risk of male bladder cancer in the Friuli Venezia Giulia region.

The smoothed male bladder cancer mortality map shows a clear north to south gradient with excess risk in southern parts of the Alpine region. When taking into account their low incidence risks, a remarkably high mortality is seen in Slovenia, Sondrio and western Trentino. It looks like the high mortality risk in these regions (especially in Slovenia) reflects limited treatment facilities.

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Tab. 37: Bladder – Numbers and Rates - Females

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	205	14.2	5.7 (4.8, 6.6)	1.52 (1.32, 1.74)	64	4.4	1.2 (0.9, 1.6)	0.98 (0.75, 1.25)
Salzburg	105	7.8	4.0 (3.1, 4.9)	0.98 (0.8, 1.19)	37	2.8	0.9 (0.5, 1.2)	0.73 (0.51, 1.01)
Tyrol	122	7.0	2.8 (2.3, 3.4)	0.87 (0.73, 1.04)	66	3.8	1.2 (0.9, 1.6)	0.99 (0.76, 1.26)
Vorarlberg	48	5.3	2.7 (1.9, 3.6)	0.72 (0.53, 0.95)	35	3.9	1.5 (0.9, 2.0)	1.11 (0.78, 1.55)
Friuli Venezia Giulia	19	9.8	3.6 (1.7, 5.5)	0.71 (0.43, 1.11)	11	5.6	1.3 (0.2, 2.4)	0.75 (0.37, 1.34)
Varese	34	11.7	4.6 (2.8, 6.4)	1.19 (0.82, 1.66)	12	4.1	1.3 (0.4, 2.2)	0.83 (0.43, 1.46)
Sondrio	40	8.8	3.1 (2.0, 4.2)	0.87 (0.62, 1.18)	20	4.4	1.1 (0.5, 1.7)	0.86 (0.52, 1.33)
South Tyrol	110	9.3	3.8 (2.9, 4.6)	1.07 (0.88, 1.29)	57	4.8	1.6 (1.1, 2.1)	1.13 (0.86, 1.47)
Trentino	103	8.3	3.1 (2.4, 3.8)	0.82 (0.67, 0.99)	74	6.0	1.6 (1.2, 2.0)	1.15 (0.9, 1.45)
Veneto	125	20.7	7.7 (6.1, 9.3)	1.75 (1.46, 2.09)	22	3.6	0.8 (0.4, 1.3)	0.58 (0.37, 0.88)
Slovenia	274	7.1	3.0 (2.6, 3.4)	0.86 (0.76, 0.97)	155	4.0	1.4 (1.2, 1.7)	1.11 (0.94, 1.29)
Graubünden/Glarus	33	5.8	2.1 (1.3, 3.0)	0.65 (0.45, 0.91)	23	4.0	1.3 (0.7, 2.0)	0.89 (0.56, 1.33)
St.Gallen/Appenzell	110	8.4	3.8 (3.0, 4.7)	1 (0.82, 1.21)	66	5.0	1.8 (1.3, 2.3)	1.18 (0.91, 1.5)
Ticino	85	10.3	3.3 (2.5, 4.2)	1.01 (0.8, 1.24)	34	4.1	1.2 (0.7, 1.7)	0.78 (0.54, 1.09)
Total	**1,413**	**8.8**	**3.7 (3.4, 3.9)**	**1 (0.95, 1.05)**	**676**	**4.2**	**1.3 (1.2, 1.4)**	**1 (0.93, 1.08)**

Tab. 38: Bladder – Numbers and Rates - Males

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	497	36.8	18.9 (17.2, 20.7)	1.28 (1.17, 1.4)	130	9.6	4.7 (3.8, 5.5)	0.84 (0.7, 0.99)
Salzburg	244	19.4	12.2 (10.6, 13.8)	0.79 (0.69, 0.89)	84	6.7	3.9 (3.1, 4.8)	0.69 (0.55, 0.86)
Tyrol	280	16.8	10.4 (9.1, 11.6)	0.68 (0.6, 0.76)	109	6.5	3.7 (3.0, 4.4)	0.68 (0.56, 0.82)
Vorarlberg	145	16.5	11.2 (9.3, 13.0)	0.73 (0.62, 0.86)	37	4.2	2.9 (2.0, 3.9)	0.5 (0.35, 0.69)
Friuli Venezia Giulia	79	42.2	16.0 (12.2, 19.7)	1.12 (0.89, 1.4)	40	21.4	7.3 (4.9, 9.7)	1.35 (0.96, 1.84)
Varese	184	67.4	37.0 (31.5, 42.6)	2.3 (1.98, 2.65)	45	16.5	7.9 (5.6, 10.3)	1.41 (1.03, 1.89)
Sondrio	134	30.8	16.0 (13.2, 18.7)	1.02 (0.85, 1.2)	74	17.0	7.7 (5.9, 9.5)	1.44 (1.13, 1.81)
South Tyrol	415	36.2	21.1 (19.0, 23.2)	1.35 (1.23, 1.49)	134	11.7	6.2 (5.1, 7.2)	1.1 (0.92, 1.3)
Trentino	333	28.3	14.3 (12.7, 15.9)	0.91 (0.82, 1.02)	202	17.1	7.5 (6.4, 8.6)	1.35 (1.17, 1.55)
Veneto	383	68.7	32.3 (28.9, 35.7)	2.02 (1.82, 2.23)	77	13.8	6.0 (4.6, 7.4)	0.99 (0.78, 1.23)
Slovenia	716	19.4	12.5 (11.6, 13.4)	0.82 (0.76, 0.88)	383	10.4	7.4 (6.6, 8.1)	1.25 (1.13, 1.38)
Graubünden/Glarus	130	23.4	13.7 (11.2, 16.2)	0.82 (0.69, 0.98)	58	10.4	5.2 (3.8, 6.6)	0.86 (0.65, 1.11)
St.Gallen/Appenzell	277	21.5	12.5 (11.0, 14.1)	0.82 (0.73, 0.92)	108	8.4	4.2 (3.3, 5.0)	0.75 (0.62, 0.91)
Ticino	241	32.0	15.4 (13.4, 17.4)	1 (0.88, 1.14)	98	13.0	5.6 (4.4, 6.8)	0.98 (0.79, 1.19)
Total	**4,058**	**26.7**	**15.4 (14.9, 15.9)**	**1 (0.97, 1.03)**	**1,579**	**10.4**	**5.6 (5.3, 5.9)**	**1 (0.95, 1.05)**

Tab. 39: Bladder – Data quality

	FEMALES			MALES		
Country description	% DCO	% HV	RMI	% DCO	% HV	RMI
Carinthia	3.9%	98.5%	0.31	3.4%	99.2%	0.26
Salzburg	1.0%	91.3%	0.35	0.8%	87.6%	0.34
Tyrol	4.9%	99.1%	0.54	0.7%	98.2%	0.39
Vorarlberg	6.3%	100.0%	0.73	0.0%	97.9%	0.26
Friuli Venezia Giulia	0.0%	94.7%	0.58	1.3%	92.3%	0.51
Varese	0.0%	94.1%	0.35	0.0%	95.1%	0.24
Sondrio	2.5%	92.3%	0.50	0.0%	94.8%	0.55
South Tyrol	1.8%	92.6%	0.52	1.4%	97.1%	0.32
Trentino	4.9%	81.6%	0.72	0.9%	93.6%	0.61
Veneto	0.0%	98.4%	0.18	0.3%	98.4%	0.20
Slovenia	1.1%	97.8%	0.57	0.8%	98.5%	0.53
Graubünden/Glarus	0.0%	100.0%	0.70	0.8%	98.4%	0.45
St.Gallen/Appenzell	0.9%	94.5%	0.60	0.4%	98.2%	0.39
Ticino	1.2%	98.8%	0.40	0.4%	98.3%	0.41
Total	**2.2%**	**95.9%**	**0.48**	**1.0%**	**96.9%**	**0.39**

Fig. 37: Bladder – Incidence – Smoothed Map - Females

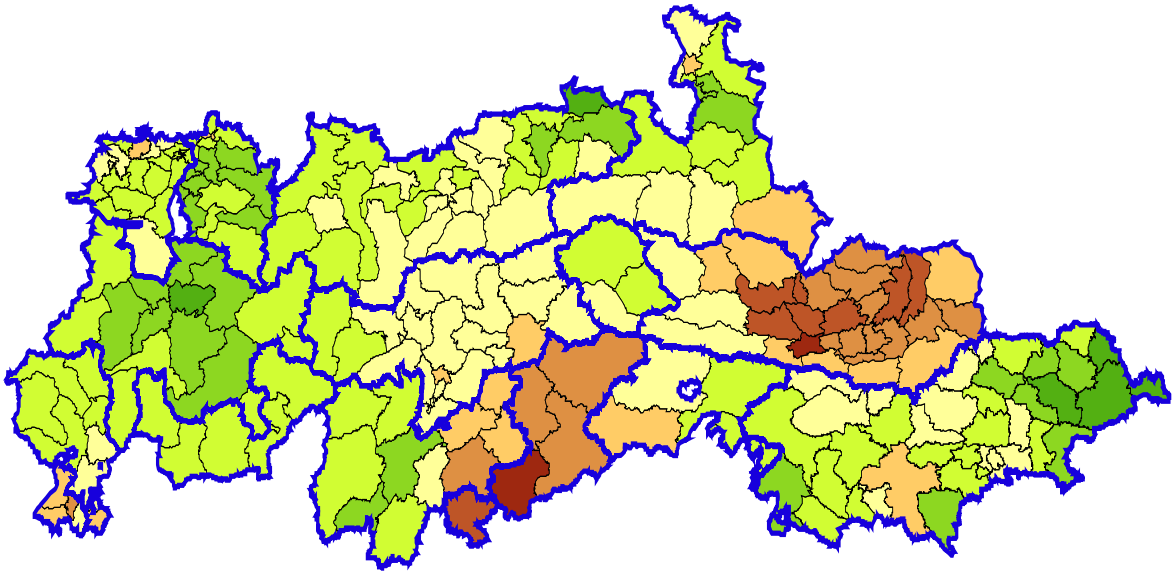


Fig. 38: Bladder – Mortality – Smoothed Map - Females

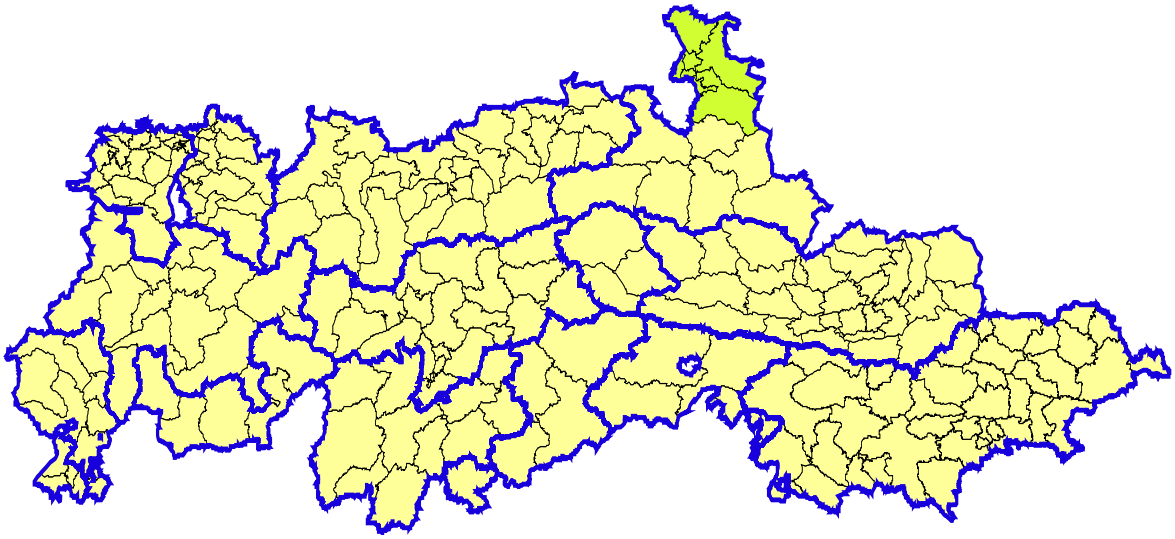


Fig. 39: Bladder – Incidence – Smoothed Map - Males

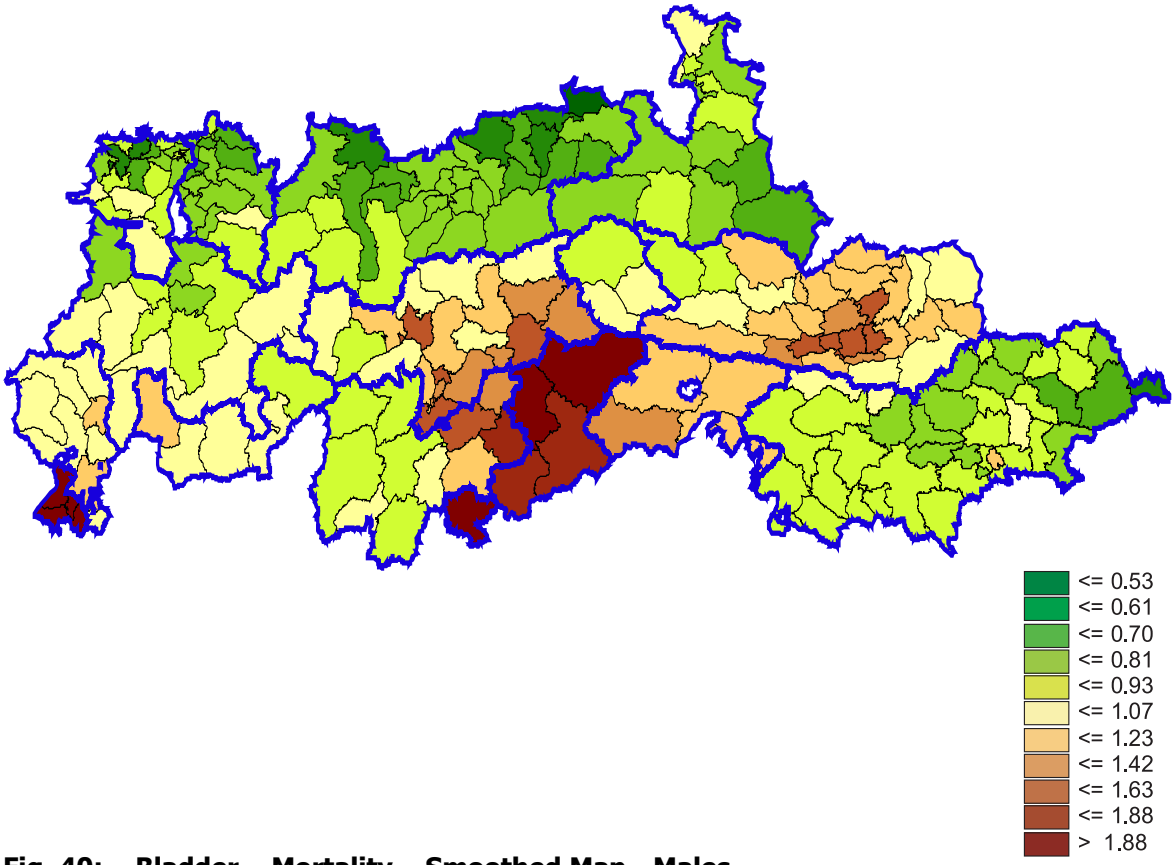
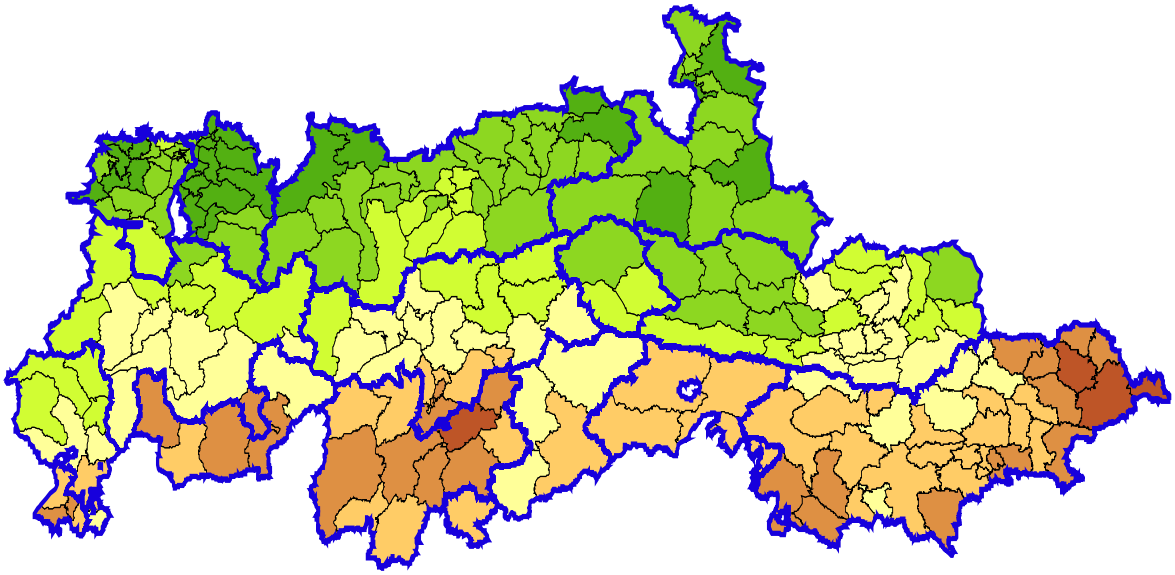


Fig. 40: Bladder – Mortality – Smoothed Map - Males



5.13 Hematologic and Lymphatic Systems

Richard Greil

Sangue e Sistema linfatico
Blut und lymphatisches System
Krvni in limfni obtok

5.13.1 Summary and Call for Action

Summary and Call for Action

Both for females and males we observe higher risk in incidence in most but not all Swiss regions and for females also in the southernmost regions of Italian registries. With regard to mortality, we observe higher risk mainly for males in Slovenia and regions in southern Carinthia. In total, the excess risk is moderate and not consistent between incidence and mortality which could be caused by differences in coding and/or registration procedures.

In the absence of proven screening methods, action should be taken to reduce of exposure to cancerogenetic stimuli, particularly in rural areas, ensure adequate diagnosis and follow-up of preneoplastic clonal conditions like myelodysplastic snydromes and MGUS (monoclonal gammopathy of undetermined significance), long-term follow-up of patients under immunosuppression as a result of organ transplantation or auto immunologic diseases, and of cancer patients previously treated in a curative intention but exposed to certain cytotoxics and irradiation. Finally, apparent discrepancies between incidence and mortality ratios in certain areas should be analyzed for the role of availability and speed of uptake of innovative drugs associated with survival benefits.

Sintesi e proposte operative

Per l'incidenza, in entrambi i sessi si osservano rischi maggiori in gran parte delle aree svizzere e, tra le donne, anche nelle maggior parte delle zone meridionali italiane. Il rischio di mortalità appare maggiore, prevalentemente tra i maschi, in Slovenia ed aree meridionali della Carinzia. Nel complesso, l'eccesso di rischio è moderato e non congruente tra incidenza e mortalità; potrebbe, quindi, essere dovuto a differenze di codifica e/o nelle procedure di registrazione.

In assenza di metodi di "screening" efficaci, le azioni preventive da intraprendere dovrebbero comprendere la riduzione dell'esposizione a stimoli cancerogeni, specialmente nelle aree rurali, un'adeguata diagnosi e "follow-up" delle condizioni clonali pre-neoplastiche (come le sindromi mieolodisplastiche e la gammopatia monoclonale di significato incerto), il "follow-up" a lungo termine dei pazienti sottoposti a immunosoppressione (in seguito a trapianto d'organo o malattie autoimmuni) e dei pazienti neoplastici irradiati o esposti ad alcuni citotossici nel corso della terapia.

Infine, nel valutare le apparenti discrepanze dei rapporti incidenza/mortalità tra alcune zone, bisognerebbe tener conto del ruolo svolto dalla disponibilità e velocità di introduzione dei farmaci innovativi, che hanno consentito miglioramenti nella sopravvivenza.

Zusammenfassung und Schlussfolgerungen

Sowohl für Frauen als auch für Männer kann ein höheres Inzidenzrisiko in den meisten Schweizer Gebieten, und für Frauen auch in den südlichen Regionen Italiens, beobachtet werden. Bezüglich Mortalität beobachten wir ein höheres Risiko besonders für Männer in Slowenien und in den südlichen Regionen Kärntens. Insgesamt ist die Risikoerhöhung gering und zeigt keine Korrelation zwischen Inzidenz und Mortalität, was durch Codierungs- und Registrierungsmaßnahmen verursacht sein könnte.

Bei Fehlen von standardisierten Screening-Methoden sollten Aktionspläne folgendes beinhalten:

Eine Verminderung der Exposition betreffend carcinogenetischer Stimuli, insbesondere in ländlichen Gegenden; adäquate Diagnose und Follow-up von primär aplastischen Syndromen wie z.B. MDS (myelodysplastisches Syndrom) und MGUS (monoklonale Gammopathie of undetermined significance); Langzeitverlauf von Patienten und Immunsuppression als Ergebnis einer Organtransplantation oder autoimmunologische Erkrankungen; Krebspatienten die in kurativer Intention behandelt wurden und dabei zu einer toxischen Substanz und Bestrahlung ausgesetzt waren. Schließlich sollten auch Diskrepanzen, die zwischen Inzidenz- und Mortalitätsratio aufgetreten sind, eingehend analysiert werden, da damit auch die generelle Verfügbarkeit bzw. die raschere Aufnahme in ein innovatives Therapieregime mit Überlebensbenefit verbunden ist.

Povzetek in poziv k ukrepanju

Ker nimamo nobenih uveljavljenih presejalnih metod za odkrivanje rakov krvnega in limfnega obtoka, si je treba prizadevati za čim manjšo izpostavljenost karcenogenim vplivom, še zlasti na podeželju, za natančno diagnozo in ustrezno obravnavo preneoplastičnih klonskih pojavov, kot sta mielodisplastični sindrom in monoklonska gamopatija negotovega ali neznanega značaja, dolgotrajnejše opazovanje bolnikov z imunosupresijo zaradi transplantacije ali avtoimunološke bolezni in bolnikov z rakom, zdravljenih s citostatiki in obsevanjem. Zelo očitne razlike med incidenco in umrljivostjo v nekaterih regijah bi lahko pripisali tudi dostopnosti in hitremu uvajanju novih zdravil, ki dobro vplivajo na preživetje.

5.13.2 Introduction

In the US, non-Hodgkin's lymphomas and leukaemias rank fourth in male tumor incidence (8%) and mortality rates (7%), and fourth in female cancer mortality (7%) [1]. These numbers disregard Hodgkin's disease and myelomas. Lymphoma incidence is continuously rising in both genders. Mortality rates decreased substantially between 1990 and 2005, e.g. in males by 41% for Hodgkin's disease, 12% for non-Hodgkin's lymphoma, 9% for Leukemia, and 7% for myeloma [1]. Similar improvement has been reported for chronic lymphocytic leukemia (CLL) [2] according to the SEER database. At least the improved results for CLL, as well as for follicular [3] and diffuse Large B Cell Lymphomas [4], can be clearly attributed to significant improvements in treatment particularly by means of chemo immunotherapy including CD20 antibodies. This can be observed in randomized trials as well as in retrospective analyses of homogeneous large patient cohorts followed for decades.

5.13.3 Epidemiology

During the period 2001 to 2005 a total of 11,609 cases of myeloid and lymphoid malignancies were detected in the regions studied. The corresponding number of deaths observed was 6,002. The gender ratio was nearly identical with 48% occurring in women and 52% in men. The registry data demonstrate an annual incidence rate (per 100,000) of 35.2 in females and 39,4 in men and the annual mortality rates are 7.4 in females and 11.4 in males. The age-adjusted incidence rates (worldwide) are 19.3 for females and 27.0 for males, and the corresponding mortality figures are 7.4 and 11.7 for females and males, respectively.

The relation between incident cases and number of deaths was 0.52 [0.53 for females, 0.51 for males]. However, when using data with age-adjustments i.e. ASR, the relevant numbers are 0.38 for females and 0.43 for males. These data correspond with the well known effect that age exerts on incidence of most hematological malignancies as well as on mortality, since the frequency of most hematological malignancies increases with advancing age. Moreover, for most diseases like Hodgkin's disease, high-grade malignant non-Hodgkin's lymphoma as well as acute leukaemias advanced age is an important negative prognostic and negative predictive marker for treatment outcome.

Nevertheless, numbers must be interpreted with caution, since the diseases pooled in this analysis comprise malignant entities with highly divergent prognosis, like acute leukaemias and indolent Non-Hodgkin's lymphomas or Hodgkin's disease or myeloma.

5.13.4 Data collection, quality aspects

Major problems in data collection for myeloid and lymphoid malignancies arise from the fact that diagnosis is very frequently obtained by morphological, cytological, immunological or genetical as well as molecular methods from peripheral blood or bone marrow. When these materials are not analyzed by pathology departments, difficulties may occur in adequately tracing incidence data in areas where incidence data collection is mainly dependent on pathology departments. This may be the reason why DCO rates are systematically higher for leukaemias than for lymphoma and myeloma. DCO rates were usually very low in the Italian regions with the exception of Veneto (0.5%-1.8% for lymphomas,

myeloma and 2.4%-4.6% for leukaemias), and the regions analyzed in Switzerland. Austrian data were similarly low with the exception of Carinthia.

5.13.5 Risk factors

Many risk factors have been debated for the occurrence of lymphoid and myeloid malignancies. Among them are occupational factors like pesticides and herbidices for non- Hodgkin´s and Hodgkin´s lymphomas as well as myeloma and probably leukaemia [5-7], exposure to irradiation and alkylating agents as well as other cytotoxics as a part of tumor therapy for the development of myeloid malignancies. In addition, several infectious agents like HIV, hepatitis-C virus-associated mixed cryoglobulinemia, and Epstein-Barr virus infection are associated with an increased risk for non-Hodgkin´s lymphoma, Burkitt lymphoma or in the case of EBV-associated infectious mononucleosis with Hodgkin´s disease [8]. Helicobacter pylori has been identified as causing gastrointestinal mucosa-associated lymphoid tumors. In addition, autoimmune disorders like Lupus [9-10] and Sjögrens syndrome [9] and rheumatoid arthritis [11] are associated with an increased risk for lymphoma. Immunosuppression for autoimmune diseases, organ rejection after transplantation [12] and topical immunosuppressants like pimecrolimus, tacrolimus and medium- to high-potency steroids were reported in association with an increased risk for lymphoid neoplastic disorders [13].

5.13.6 Early detection, screening

Currently there is no recommendation for examinations favoring the early detection of myeloid or lymphoid neoplastic disorders. Even for diseases where molecular markers for clonality and/or malignancy and sensitive techniques for their detection do exist, the role of earlier detection of these diseases has either not been shown to be of value or has not been adequately tested.

5.13.7 Geographical variation

There is a region-specific variation in the incidence and mortality rates in the analyzed regions of Austria, Switzerland, Slovenia and Italy. The highest age-standardized incidence ratios are observed in the Italian regions (world-standardized ASR for females ranges between 18.8 (for South Tyrol) and 26.6 (Friuli Venezia Giulia)) and Switzerland (19.3-23.4) with the lowest ratios in Austria (15.3-19.4) and Slovenia (18.3). The ISR data are closely similar to the lowest numbers in Austria (0.88-0,91) and Slovenia (0.96), and to the highest values in Italy (0.9-1.26) and Switzerland (0.95-1.23). Data are closely similar for males in this regard.

ASR for female mortality ranges between 6.5 and 8.2 for Austrian regions, and 6.1 and 10.3 for Italian regions with the highest numbers occurring in Sondrio (10.3) and Friuli Venezia Giulia (10.3). Data for Slovenia (7.3) and Switzerland (7.0 and 8.6) are within the range distribution for Austria.

Within the regions compared SMR is beyond the average seen in Sondrio (1.23 for females, 1.11 for males) and Trentino (1.15 for females and 1.11 for males). For most areas 95% confidence intervals are largely overlapping. However, 95% CI are different for the St. Gallen region (lowest) and Sondrio, Trentino and Slovenia (highest) for females. For males, the confidence intervals for Slovenia (highest), and Salzburg and Tyrol (lowest) differ substantially.

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Tab. 40: Hematologic and Lymphatic System – Numbers and Rates - Females

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	469	32.4	15.3 (13.7, 17.0)	0.88 (0.81, 0.97)	305	21.1	8.2 (7.1, 9.3)	1.07 (0.96, 1.2)
Salzburg	427	31.8	19.4 (17.2, 21.5)	0.98 (0.89, 1.08)	209	15.6	7.1 (6.0, 8.2)	0.93 (0.81, 1.07)
Tyrol	515	29.4	17.8 (16.0, 19.6)	0.91 (0.83, 0.99)	273	15.6	6.5 (5.6, 7.5)	0.93 (0.82, 1.05)
Vorarlberg	256	28.4	18.5 (15.8, 21.1)	0.92 (0.81, 1.04)	118	13.1	6.5 (5.1, 7.8)	0.84 (0.7, 1.01)
Friuli Venezia Giulia	101	51.8	26.6 (18.3, 34.9)	1.06 (0.86, 1.29)	57	29.3	10.3 (5.7, 14.8)	0.98 (0.74, 1.27)
Varese	100	34.3	20.3 (15.4, 25.2)	0.9 (0.74, 1.1)	47	16.1	6.1 (4.0, 8.1)	0.77 (0.57, 1.02)
Sondrio	222	48.8	25.9 (21.7, 30.1)	1.26 (1.1, 1.43)	120	26.4	10.3 (7.7, 12.8)	1.23 (1.02, 1.47)
South Tyrol	410	34.8	18.8 (16.6, 21.0)	1 (0.91, 1.11)	205	17.4	7.2 (6.0, 8.4)	0.94 (0.82, 1.08)
Trentino	508	41.1	20.9 (18.5, 23.3)	1.05 (0.96, 1.15)	310	25.1	9.1 (7.8, 10.3)	1.15 (1.03, 1.29)
Veneto	309	51.2	23.6 (19.8, 27.4)	1.17 (1.04, 1.31)	143	23.7	7.0 (5.3, 8.7)	0.93 (0.78, 1.09)
Slovenia	1,261	32.7	18.3 (17.1, 19.6)	0.96 (0.91, 1.02)	692	17.9	7.3 (6.7, 8.0)	1.07 (0.99, 1.15)
Graubünden/Glarus	228	40.0	20.8 (17.6, 24.0)	1.14 (1, 1.3)	113	19.8	8.6 (6.6, 10.5)	1.04 (0.86, 1.25)
St.Gallen/Appenzell	417	31.7	19.3 (17.1, 21.4)	0.95 (0.86, 1.05)	201	15.3	7.2 (6.0, 8.4)	0.85 (0.74, 0.98)
Ticino	397	48.0	23.4 (20.4, 26.4)	1.23 (1.11, 1.36)	170	20.6	7.0 (5.7, 8.3)	0.94 (0.8, 1.09)
Total	**5,620**	**35.2**	**19.3 (18.7, 19.9)**	**1 (0.97, 1.03)**	**2,963**	**18.6**	**7.4 (7.0, 7.7)**	**1 (0.96, 1.04)**

Tab. 41: Hematologic and Lymphatic System – Numbers and Rates - Males

	Incidence				Mortality			
Registry	Cases	CR	ASR (world)	SIR	Deaths	CR	ASR (world)	SMR
Carinthia	523	38.7	23.5 (21.4, 25.7)	0.94 (0.86, 1.02)	293	21.7	11.8 (10.3, 13.2)	1 (0.89, 1.12)
Salzburg	466	37.0	27.1 (24.5, 29.7)	1 (0.91, 1.09)	207	16.5	10.3 (8.8, 11.7)	0.89 (0.77, 1.01)
Tyrol	641	38.4	27.1 (24.9, 29.4)	1.03 (0.95, 1.12)	277	16.6	10.4 (9.1, 11.7)	0.89 (0.79, 1.01)
Vorarlberg	282	32.1	25.6 (22.4, 28.8)	0.91 (0.81, 1.03)	151	17.2	12.1 (10.1, 14.0)	1.02 (0.87, 1.2)
Friuli Venezia Giulia	99	52.9	25.6 (20.3, 30.9)	1.04 (0.84, 1.26)	46	24.6	11.0 (7.6, 14.4)	0.85 (0.62, 1.14)
Varese	131	48.0	32.1 (26.0, 38.1)	1.14 (0.95, 1.35)	56	20.5	10.3 (7.8, 13.9)	0.93 (0.7, 1.21)
Sondrio	233	53.5	32.8 (28.0, 37.6)	1.23 (1.08, 1.4)	109	25.0	14.2 (11.2, 17.2)	1.11 (0.91, 1.34)
South Tyrol	451	39.3	27.0 (24.3, 29.8)	1 (0.91, 1.1)	222	19.4	10.9 (9.4, 12.5)	0.95 (0.83, 1.09)
Trentino	487	41.3	27.0 (24.2, 29.7)	0.95 (0.86, 1.03)	262	22.2	11.4 (9.9, 12.9)	0.94 (0.83, 1.06)
Veneto	282	50.6	30.4 (26.2, 34.5)	1.07 (0.95, 1.21)	136	24.4	10.8 (8.9, 12.7)	0.94 (0.79, 1.11)
Slovenia	1,238	33.6	25.0 (23.5, 26.5)	0.92 (0.87, 0.97)	755	20.5	15.2 (14.1, 16.4)	1.2 (1.12, 1.29)
Graubünden/Glarus	210	37.8	26.2 (22.2, 30.2)	0.92 (0.8, 1.06)	108	19.4	10.7 (8.5, 12.9)	0.87 (0.72, 1.05)
St.Gallen/Appenzell	526	40.8	29.0 (26.3, 31.7)	1.06 (0.97, 1.16)	237	18.4	11.1 (9.6, 12.6)	0.9 (0.78, 1.02)
Ticino	420	55.7	33.3 (29.7, 36.9)	1.24 (1.12, 1.36)	180	23.9	12.1 (10.1, 14.1)	0.97 (0.84, 1.13)
Total	**5,989**	**39.4**	**27.0 (26.3, 27.8)**	**1 (0.97, 1.03)**	**3,039**	**20.0**	**11.7 (11.3, 12.1)**	**1 (0.96, 1.04)**

Tab. 42: Hematologic and Lymphatic System – Data quality

	FEMALES			MALES		
Country description	% DCO	% HV	RMI	% DCO	% HV	RMI
Carinthia	9.0%	97.7%	0.65	6.1%	97.6%	0.56
Salzburg	2.3%	96.4%	0.49	0.6%	97.2%	0.44
Tyrol	1.0%	98.6%	0.53	0.6%	99.4%	0.43
Vorarlberg	3.9%	99.6%	0.46	4.3%	99.6%	0.54
Friuli Venezia Giulia	0.0%	99.0%	0.56	0.0%	100.0%	0.46
Varese	0.0%	86.0%	0.47	0.0%	93.9%	0.43
Sondrio	0.9%	95.5%	0.54	0.4%	97.4%	0.47
South Tyrol	0.2%	99.5%	0.50	0.7%	99.6%	0.49
Trentino	0.2%	94.7%	0.61	0.2%	95.9%	0.54
Veneto	2.6%	90.4%	0.46	1.1%	93.9%	0.48
Slovenia	0.5%	99.8%	0.55	0.2%	99.9%	0.61
Graubünden/Glarus	0.4%	99.1%	0.50	0.0%	99.5%	0.51
St.Gallen/Appenzell	0.0%	98.1%	0.48	0.2%	99.4%	0.45
Ticino	2.3%	97.2%	0.43	1.7%	95.9%	0.43
Total	**1.7%**	**97.8%**	**0.53**	**1.2%**	**98.5%**	**0.51**

Fig. 41: Hematologic and Lymphatic Systems – Incidence – Smoothed Map – Females

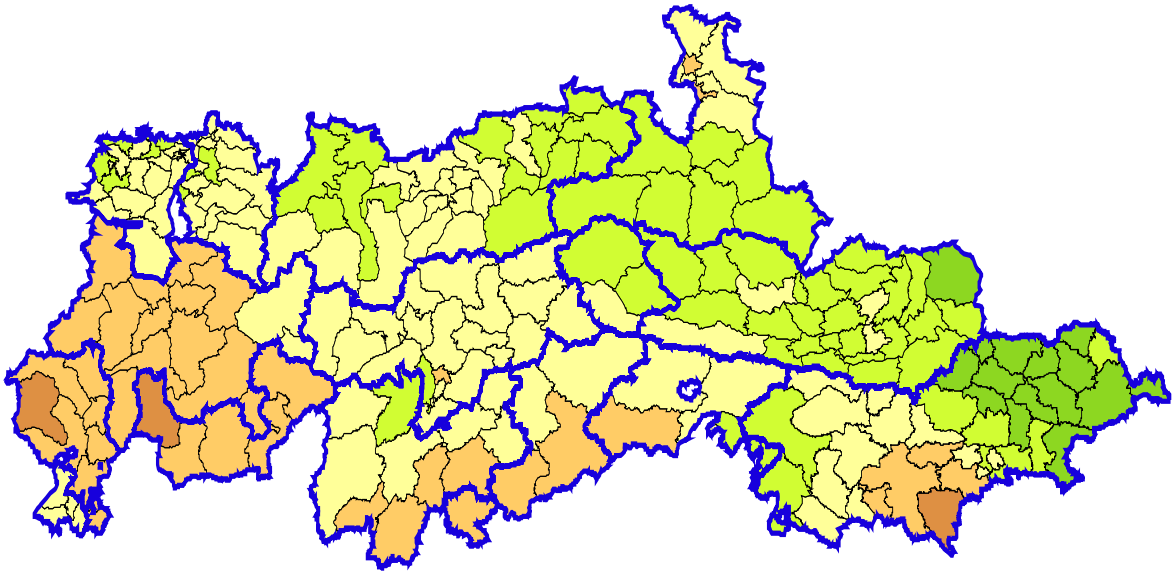


Fig. 42: Hematologic and Lymphatic Systems – Mortality – Smoothed Map - Females

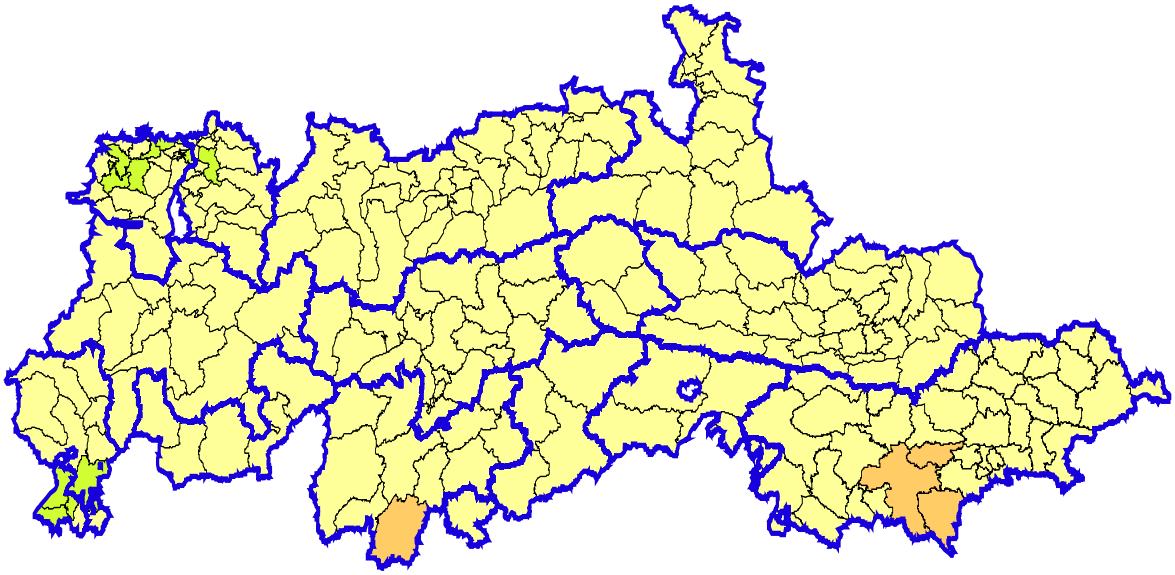


Fig. 43: Hematologic and Lymphatic Systems – Incidence – Smoothed Map - Males

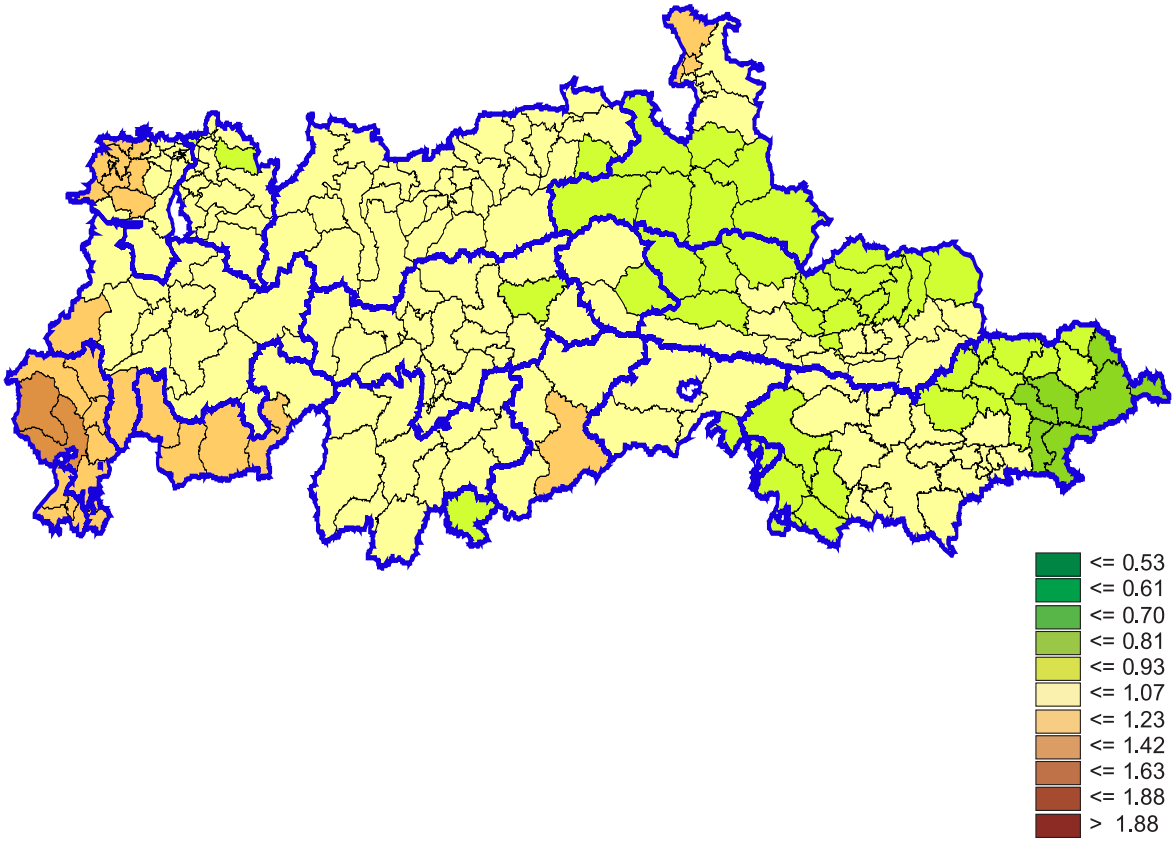
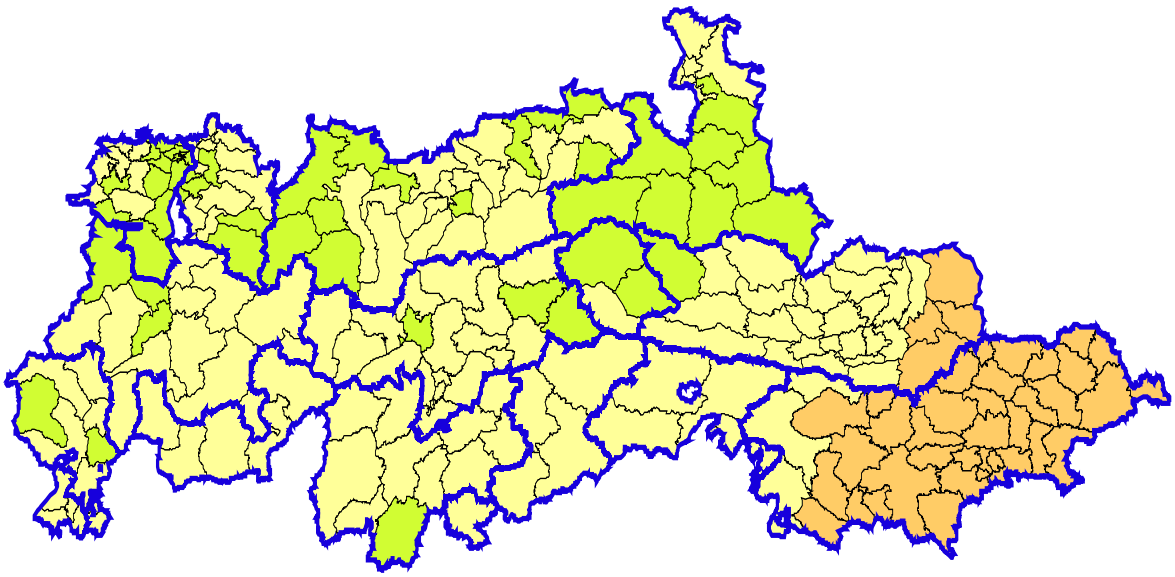


Fig. 44: Hematologic and Lymphatic Systems – Mortality – Smoothed Map – Males



6 ATTACHMENTS

Age-standardised rates using European Population weights: Incidence

	All except for NMSC		Head & Neck and Oesophagus and Larynx	
	Females	Males	Females	Males
Carinthia	339.8 (331.2-348.4)	503.2 (492.0-514.4)	7.1 (5.8-8.3)	35.6 (32.5-38.7)
Salzburg	325.2 (316.1-334.3)	467.8 (455.9-479.8)	6.3 (5.0-7.6)	31.3 (28.2-34.4)
Tyrol	334.8 (326.7-342.8)	492.9 (482.3-503.5)	6.6 (5.5-7.8)	29.6 (27.0-32.2)
Vorarlberg	307.2 (296.2-318.2)	549.9 (534.0-565.8)	7.3 (5.5-9.0)	35.2 (31.2-39.3)
Friuli Venezia Giulia	343.6 (320.4-366.7)	584.8 (555.7-613.9)	9.7 (5.9-13.6)	69.1 (58.8-79.3)
Varese	340.3 (321.3-359.2)	567.2 (541.2-593.1)	6.4 (3.8-9.0)	42.6 (35.5-49.8)
Sondrio	355.2 (339.6-370.8)	569.0 (548.6-589.3)	9.2 (6.7-11.6)	47.4 (41.5-53.3)
South Tyrol	329.7 (320.2-339.3)	508.4 (495.8-521.0)	9.0 (7.3-10.6)	48.1 (44.1-52.0)
Trentino	323.9 (314.9-333)	440.3 (429.4-451.2)	7.1 (5.7-8.4)	46.0 (42.4-49.6)
Veneto	383.8 (369.9-397.6)	589.9 (572.4-607.4)	12.0 (9.5-14.6)	67.1 (61.1-73.2)
Slovenia	323.4 (318.2-328.6)	451.4 (444.5-458.3)	7.3 (6.6-8.1)	40.3 (38.3-42.3)
Graubünden/Glarus	316.0 (302.4-329.6)	451.1 (434.2-467.9)	6.9 (4.9-8.9)	31.1 (26.6-35.5)
St.Gallen/Appenzell	302.1 (293.1-311.0)	452.4 (440.9-463.8)	8.0 (6.5-9.5)	31.9 (28.8-35.0)
Ticino	340.0 (328.8-351.2)	465.8 (452.0-479.7)	7.5 (5.8-9.2)	34.2 (30.4-38.0)
Total	329.1 (326.5-331.7)	486.7 (483.3-490.1)	7.6 (7.2-8.0)	39.6 (38.7-40.6)

	Stomach		Colon and Rectum	
	Females	Males	Females	Males
Carinthia	12.3 (10.8-13.8)	23.5 (21.1-25.8)	31.8 (29.3-34.2)	55.0 (51.3-58.6)
Salzburg	11.4 (9.8-13.0)	20.0 (17.5-22.4)	35.9 (33.0-38.8)	57.5 (53.3-61.6)
Tyrol	12.0 (10.6-13.5)	23.7 (21.4-26.0)	37.2 (34.6-39.8)	61.5 (57.8-65.3)
Vorarlberg	8.7 (7.0-10.5)	18.5 (15.6-21.4)	34.2 (30.6-37.7)	56.3 (51.2-61.5)
Friuli Venezia Giulia	19.0 (14.1-23.9)	26.3 (20.4-32.2)	39.0 (31.6-46.4)	64.8 (55.2-74.3)
Varese	16.1 (12.2-20.0)	32.6 (26.5-38.7)	37.3 (31.4-43.2)	68.7 (59.7-77.7)
Sondrio	14.8 (11.8-17.8)	35.3 (30.3-40.4)	40.3 (35.3-45.3)	56.2 (49.8-62.7)
South Tyrol	17.5 (15.5-19.6)	28.7 (25.7-31.7)	40.3 (37.1-43.6)	66.6 (62.1-71.2)
Trentino	12.1 (10.6-13.7)	25.2 (22.6-27.7)	35.5 (32.6-38.3)	58.9 (54.9-62.8)
Veneto	13.3 (11.1-15.5)	22.6 (19.3-26.0)	34.6 (30.7-38.6)	63.9 (58.1-69.6)
Slovenia	12.4 (11.4-13.3)	28.4 (26.7-30.2)	37.7 (36.0-39.4)	66.2 (63.6-68.9)
Graubünden/Glarus	6.7 (4.9-8.6)	16.1 (13.0-19.3)	32 (27.9-36.1)	53.5 (47.8-59.3)
St.Gallen/Appenzell	4.9 (3.9-6.0)	11.4 (9.6-13.2)	34.6 (31.7-37.5)	53.6 (49.6-57.5)
Ticino	9.5 (7.7-11.2)	17.7 (15.1-20.4)	35.3 (31.9-38.7)	57.1 (52.4-61.9)
Total	11.8 (11.4-12.3)	23.6 (22.9-24.4)	36.2 (35.4-37)	60.5 (59.3-61.7)

	Liver		Bronchus. Lung	
	Females	Males	Females	Males
Carinthia	4.7 (3.8-5.7)	12.9 (11.1-14.7)	21.4 (19.2-23.5)	64.7 (60.7-68.7)
Salzburg	2.9 (2.1-3.7)	10.8 (9.0-12.6)	17.7 (15.6-19.8)	52.8 (48.8-56.8)
Tyrol	3.5 (2.7-4.2)	11.0 (9.4-12.6)	22.9 (20.8-25.0)	62.8 (59.0-66.5)
Vorarlberg	3.4 (2.3-4.5)	8.9 (6.9-10.9)	21.3 (18.4-24.2)	62.9 (57.5-68.3)
Friuli Venezia Giulia	8.8 (5.9-11.8)	43.2 (35.2-51.2)	14.8 (10.3-19.2)	76.0 (65.7-86.4)
Varese	5.1 (3.1-7.1)	20.9 (15.9-25.8)	17.4 (13.2-21.5)	102.8 (91.9-113.8)
Sondrio	6.0 (4.2-7.8)	35.6 (30.5-40.7)	17.0 (13.7-20.3)	93.3 (85.2-101.5)
South Tyrol	3.8 (2.9-4.8)	21.2 (18.6-23.8)	15.8 (13.7-17.8)	56.7 (52.6-60.9)
Trentino	4.7 (3.7-5.7)	23.9 (21.4-26.4)	13.8 (12.0-15.6)	57.1 (53.3-61.0)
Veneto	9.1 (7.2-11.0)	39.6 (35.1-44.1)	23.6 (20.4-26.8)	93.6 (86.8-100.5)
Slovenia	2.6 (2.2-3.1)	8.8 (7.8-9.7)	21.8 (20.4-23.1)	83.5 (80.6-86.5)
Graubünden/Glarus	2.8 (1.6-4.0)	8.4 (6.2-10.7)	21.2 (17.6-24.7)	66.9 (60.4-73.4)
St.Gallen/Appenzell	2.9 (2.0-3.8)	8.1 (6.6-9.7)	21.8 (19.4-24.2)	59.3 (55.2-63.5)
Ticino	3.4 (2.4-4.4)	22.1 (19.1-25.1)	23.7 (20.8-26.6)	68.4 (63.1-73.6)
Total	3.9 (3.6-4.1)	15.6 (15.0-16.2)	20.3 (19.6-20.9)	70.1 (68.8-71.3)

	Breast	Cervix uteri	Corpus uteri	Ovary	Prostate
Carinthia	101.6 (96.7-106.4)	14.6 (12.7-16.5)	17.2 (15.3-19.1)	15.1 (13.2-16.9)	143.8 (137.8-149.7)
Salzburg	109.5 (104.1-114.9)	10.1 (8.4-11.7)	13.6 (11.7-15.4)	16.3 (14.3-18.4)	143.6 (137.0-150.3)
Tyrol	100.6 (96.0-105.1)	14.1 (12.4-15.8)	18.4 (16.5-20.3)	14.9 (13.2-16.6)	154.8 (148.8-160.7)
Vorarlberg	97.6 (91.3-103.9)	9.2 (7.2-11.1)	20.0 (17.2-22.8)	12.2 (10.0-14.4)	222.5 (212.5-232.6)
Friuli Venezia Giulia	104.1 (90.9-117.2)	6.1 (2.8-9.4)	15.0 (10.2-19.7)	9.2 (5.4-13.0)	140.1 (126.3-153.9)
Varese	122.7 (111.1-134.4)	6.9 (3.9-9.8)	15.5 (11.5-19.6)	14.3 (10.5-18.1)	108.0 (96.9-119.1)
Sondrio	121.3 (111.9-130.7)	7.6 (5.2-10.0)	18.5 (14.9-22.2)	14.6 (11.4-17.8)	121.2 (112-130.3)
South Tyrol	100.8 (95.3-106.3)	8.9 (7.3-10.6)	16.6 (14.5-18.8)	14.3 (12.2-16.4)	125.7 (119.5-131.8)
Trentino	109.4 (104.0-114.9)	5.7 (4.4-6.9)	16.4 (14.3-18.5)	13.2 (11.4-15.1)	71.3 (67.0-75.5)
Veneto	136.3 (127.7-145.0)	9.4 (7.0-11.7)	16.7 (13.8-19.7)	9.9 (7.8-12.0)	104.1 (97.0-111.3)
Slovenia	87.2 (84.4-89.9)	17.6 (16.3-18.9)	23.4 (22.0-24.8)	14.2 (13.1-15.4)	77.4 (74.5-80.3)
Graubünden/Glarus	109.9 (101.6-118.2)	8.3 (6.0-10.5)	18.5 (15.1-21.8)	12.7 (10.0-15.5)	121.0 (112.4-129.6)
St.Gallen/Appenzell	92.9 (87.8-98.0)	6.6 (5.2-7.9)	19.7 (17.4-22.0)	12.7 (10.9-14.5)	137.3 (131-143.6)
Ticino	113.9 (107.2-120.5)	6.5 (4.9-8.2)	12.4 (10.2-14.5)	12.8 (10.6-15)	95.9 (89.7-102.0)
Total	101.6 (100.2-103.1)	11.5 (11.0-12.0)	18.4 (17.8-19.0)	13.9 (13.3-14.4)	119.1 (117.5-120.8)

	Bladder		Hematologic and Lymphatic Systems	
	Females	Males	Females	Males
Carinthia	8.7 (7.4-10.0)	30.2 (27.5-32.9)	21.6 (19.5-23.7)	33.6 (30.7-36.5)
Salzburg	5.8 (4.6-7.0)	19.0 (16.6-21.4)	25.9 (23.3-28.5)	36.3 (32.9-39.6)
Tyrol	4.5 (3.6-5.3)	16.3 (14.3-18.2)	23.5 (21.4-25.6)	37.1 (34.2-40)
Vorarlberg	4.0 (2.8-5.2)	17.3 (14.4-20.1)	23.7 (20.7-26.7)	33.3 (29.4-37.2)
Friuli Venezia Giulia	5.3 (2.6-8.0)	25.5 (19.8-31.3)	31.6 (23.8-39.3)	37.0 (29.6-44.4)
Varese	6.9 (4.4-9.4)	55.8 (47.7-63.9)	25.6 (20.2-31.0)	42.1 (34.8-49.4)
Sondrio	4.7 (3.1-6.3)	24.3 (20.2-28.5)	34.0 (29.1-38.9)	44.5 (38.6-50.3)
South Tyrol	5.8 (4.7-7.0)	32.7 (29.5-35.9)	25.2 (22.6-27.9)	36.4 (33.0-39.8)
Trentino	4.8 (3.7-5.8)	22.0 (19.6-24.4)	27.2 (24.6-29.8)	35.0 (31.8-38.2)
Veneto	11.3 (9.1-13.6)	49.0 (44.0-53.9)	30.2 (26.3-34.2)	39.7 (34.9-44.5)
Slovenia	4.6 (4.1-5.2)	19.4 (17.9-20.8)	24.5 (23.1-25.9)	33.9 (32.0-35.9)
Graubünden/Glarus	3.4 (2.1-4.6)	20.4 (16.8-23.9)	28.9 (24.8-32.9)	34.4 (29.7-39.2)
St.Gallen/Appenzell	5.8 (4.6-6.9)	19.6 (17.3-21.9)	25.5 (22.9-28.1)	38.7 (35.4-42.1)
Ticino	5.3 (4.1-6.5)	24.0 (21-27.1)	31.2 (27.8-34.6)	45.2 (40.8-49.6)
Total	5.6 (5.3-5.9)	24.0 (23.2-24.7)	25.7 (25.0-26.4)	36.4 (35.5-37.3)

Age-standardised rates using European Population weights: Mortality

	All except for NMSC		Head & Neck and Oesophagus and Larynx	
	Females	Males	Females	Males
Carinthia	126.5 (121.5-131.4)	222.7 (215.3-230.2)	2.9 (2.1-3.7)	18.7 (16.5-21)
Salzburg	126.5 (121.1-131.8)	196.5 (188.8-204.2)	2.5 (1.7-3.3)	14.5 (12.4-16.7)
Tyrol	130.1 (125.4-134.9)	202.2 (195.4-209.0)	3.1 (2.3-3.9)	15.3 (13.4-17.1)
Vorarlberg	130.9 (124.1-137.7)	216.4 (206.2-226.7)	3.8 (2.6-5.0)	15.0 (12.4-17.7)
Friuli Venezia Giulia	135.4 (122.3-148.5)	289.7 (269.6-309.8)	8.6 (5.0-12.1)	46.4 (38.1-54.6)
Varese	129.8 (119.1-140.6)	285.0 (266.8-303.2)	2.5 (1.0-4.0)	23.2 (17.9-28.5)
Sondrio	134.6 (125.7-143.4)	301.1 (286.4-315.9)	3.6 (2.1-5.2)	26.0 (21.6-30.3)
South Tyrol	129.6 (124-135.1)	231.3 (222.9-239.8)	3.6 (2.6-4.6)	23.0 (20.3-25.7)
Trentino	135 (129.7-140.4)	259.7 (251.5-268)	3.0 (2.2-3.8)	29.0 (26.1-31.8)
Veneto	137.3 (129.7-144.9)	283.4 (271.4-295.4)	5.7 (4.1-7.2)	31.1 (27.1-35.2)
Slovenia	146.4 (143.2-149.7)	332.7 (325.9-339.6)	3.1 (2.6-3.6)	27.1 (25.2-29.0)
Graubünden/Glarus	121.3 (113.3-129.3)	208.7 (197.5-219.9)	3.4 (2.1-4.8)	14.9 (11.8-17.9)
St.Gallen/Appenzell	114.6 (109.4-119.9)	196.3 (188.9-203.8)	2.7 (1.9-3.5)	14.7 (12.6-16.8)
Ticino	122.5 (116.3-128.7)	211.8 (202.6-220.9)	3.9 (2.7-5.1)	18.2 (15.5-20.9)
Total	129.9 (128.4-131.4)	241.9 (239.5-244.3)	3.3 (3.0-3.5)	21.1 (20.4-21.8)

	Stomach		Colon and Rectum	
	Females	Males	Females	Males
Carinthia	7.2 (6.1-8.3)	15.1 (13.2-17)	11.5 (10.1-12.8)	23.3 (21.0-25.7)
Salzburg	7.7 (6.4-8.9)	14.1 (12.0-16.1)	14.4 (12.7-16.2)	25.2 (22.4-28.0)
Tyrol	8.1 (7.0-9.3)	15.9 (14.0-17.8)	13.7 (12.3-15.2)	23.9 (21.5-26.2)
Vorarlberg	7.0 (5.5-8.5)	12.5 (10.0-14.9)	16.8 (14.5-19.2)	23.5 (20.1-26.9)
Friuli Venezia Giulia	8.2 (5.5-10.9)	17.7 (12.9-22.5)	10.0 (6.8-13.3)	27.3 (21.1-33.5)
Varese	11.0 (7.8-14.2)	23.0 (17.8-28.1)	14.9 (11.4-18.4)	24.6 (19.3-30.0)
Sondrio	8.3 (6.2-10.4)	21.8 (17.8-25.8)	12.0 (9.6-14.4)	24.4 (20.2-28.7)
South Tyrol	10.3 (8.8-11.8)	19.4 (17-21.8)	16.2 (14.3-18.2)	26.6 (23.7-29.5)
Trentino	6.8 (5.7-7.9)	17.3 (15.2-19.4)	16.0 (14.2-17.7)	29.2 (26.4-32.0)
Veneto	7.8 (6.1-9.4)	14.4 (11.8-17.1)	14.2 (11.7-16.6)	24.8 (21.3-28.3)
Slovenia	8.8 (8.0-9.6)	26.0 (24.1-27.9)	18.2 (17.1-19.3)	43.3 (40.8-45.8)
Graubünden/Glarus	3.9 (2.6-5.2)	11.3 (8.7-13.9)	9.7 (7.6-11.9)	21.1 (17.6-24.7)
St.Gallen/Appenzell	3.3 (2.4-4.1)	8.5 (6.9-10.0)	11.1 (9.5-12.6)	21.8 (19.4-24.3)
Ticino	5.8 (4.5-7.0)	9.6 (7.6-11.5)	10.7 (9.0-12.5)	17.5 (14.9-20.1)
Total	7.4 (7.1-7.8)	16.5 (15.9-17.2)	14.2 (13.7-14.7)	23.3 (21.0-25.7)

	Liver		Bronchus. Lung	
	Females	Males	Females	Males
Carinthia	4.8 (3.9-5.8)	11.2 (9.6-12.9)	16.2 (14.4-18.1)	56.3 (52.6-60.1)
Salzburg	2.6 (1.9-3.4)	8.9 (7.2-10.5)	13.2 (11.4-15)	42.0 (38.4-45.6)
Tyrol	3.8 (3.0-4.6)	8.5 (7.1-9.9)	18.0 (16.1-19.8)	53.7 (50.2-57.2)
Vorarlberg	4.1 (2.9-5.3)	8.8 (6.8-10.8)	16.9 (14.4-19.5)	56.5 (51.4-61.6)
Friuli Venezia Giulia	4.7 (2.8-6.5)	22.1 (16.5-27.6)	11.5 (7.7-15.2)	67.1 (57.6-76.6)
Varese	4.8 (2.9-6.7)	22.5 (17.4-27.6)	13.7 (10.2-17.2)	90.8 (80.6-101.1)
Sondrio	5.8 (4.2-7.5)	28.5 (24.0-33.0)	12.0 (9.3-14.7)	81.9 (74.3-89.5)
South Tyrol	3.1 (2.2-3.9)	14.2 (12.1-16.3)	12.7 (11-14.5)	49.2 (45.4-53.1)
Trentino	4.5 (3.6-5.4)	17.4 (15.3-19.6)	12.9 (11.2-14.6)	61.9 (57.9-65.9)
Veneto	6.6 (5.0-8.2)	30.4 (26.4-34.3)	18.0 (15.3-20.8)	82.5 (76.1-88.9)
Slovenia	3.1 (2.7-3.6)	10.6 (9.5-11.8)	17.1 (16.0-18.3)	87.6 (84.1-91.0)
Graubünden/Glarus	2.4 (1.4-3.5)	5.8 (3.9-7.7)	16.0 (13.0-19.1)	53.6 (47.8-59.4)
St.Gallen/Appenzell	2.2 (1.5-3.0)	6.5 (5.2-7.9)	15.0 (13.0-17.0)	49.0 (45.2-52.7)
Ticino	3.1 (2.2-4.0)	18.1 (15.4-20.8)	17.4 (15.0-19.9)	50.2 (45.8-54.7)
Total	3.7 (3.4-3.9)	12.7 (12.2-13.3)	15.5 (14.9-16.0)	61.5 (60.3-62.7)

	Breast	Cervix uteri	Corpus uteri	Ovary	Prostate
Carinthia	22.8 (20.6-25)	2.8 (2.1-3.6)	1.3 (0.8-1.8)	9.1 (7.7-10.5)	27.9 (25.3-30.4)
Salzburg	23.8 (21.4-26.2)	3.6 (2.7-4.6)	2.4 (1.6-3.1)	11.1 (9.5-12.7)	25.4 (22.6-28.2)
Tyrol	23.9 (21.8-26.1)	3.7 (2.8-4.5)	2.0 (1.4-2.5)	8.4 (7.2-9.6)	21.3 (19.0-23.5)
Vorarlberg	24.2 (21.3-27.2)	2.4 (1.4-3.3)	3.2 (2.1-4.2)	8.1 (6.3-9.8)	33.0 (28.8-37.1)
Friuli Venezia Giulia	23.1 (17.4-28.9)	0.7 (0.0-1.6)	2.4 (0.5-4.2)	6.2 (3.5-9.0)	22.1 (16.8-27.3)
Varese	26.8 (21.7-31.9)	0.5 (0.0-1.2)	1.0 (0.0-2.0)	7.5 (4.8-10.2)	17.9 (13.4-22.4)
Sondrio	26.4 (22.2-30.6)	1.6 (0.4-2.7)	1.6 (0.7-2.5)	8.3 (6-10.6)	21.7 (17.7-25.7)
South Tyrol	23.2 (20.8-25.7)	1.5 (0.9-2.2)	3.4 (2.5-4.3)	7.5 (6.2-8.9)	24.4 (21.7-27.1)
Trentino	25.6 (23.2-28.1)	0.8 (0.4-1.3)	0.9 (0.5-1.4)	8.8 (7.4-10.3)	22.3 (19.9-24.6)
Veneto	27.7 (24.0-31.4)	0.9 (0.2-1.7)	1.1 (0.5-1.8)	5.8 (4.3-7.3)	16.2 (13.4-19.0)
Slovenia	27.5 (26.0-28.9)	3.6 (3.1-4.2)	3.4 (2.9-3.9)	8.3 (7.5-9.1)	36.9 (34.5-39.3)
Graubünden/Glarus	26.6 (22.7-30.5)	2.4 (1.2-3.6)	4.1 (2.6-5.6)	7.9 (5.9-10.0)	28.0 (24.1-31.9)
St.Gallen/Appenzell	24.8 (22.2-27.3)	2.2 (1.5-3.0)	3.6 (2.7-4.6)	8.7 (7.2-10.2)	27.1 (24.5-29.7)
Ticino	24 (21.1-26.8)	1.6 (0.9-2.3)	3.2 (2.2-4.2)	8.1 (6.4-9.8)	23.9 (20.9-26.8)
Total	24.7 (24.0-25.4)	2.5 (2.3-2.7)	2.5 (2.3-2.7)	8.3 (7.9-8.7)	26.2 (25.4-27)

	Bladder		Hematologic and Lymphatic Systems	
	Females	Males	Females	Males
Carinthia	2.1 (1.6-2.7)	7.9 (6.5-9.3)	12.4 (10.8-13.9)	18.0 (15.9-20.1)
Salzburg	1.5 (1.0-2.0)	6.7 (5.3-8.2)	10.8 (9.2-12.3)	15.9 (13.7-18.0)
Tyrol	2.1 (1.6-2.7)	6.4 (5.2-7.6)	10.2 (8.9-11.5)	16.1 (14.1-18.0)
Vorarlberg	2.4 (1.6-3.3)	5.0 (3.3-6.6)	9.6 (7.8-11.5)	18.4 (15.4-21.4)
Friuli Venezia Giulia	2.2 (0.5-3.8)	12.6 (8.6-16.6)	13.8 (9.2-18.4)	16.2 (11.5-21.0)
Varese	2.2 (0.8-3.6)	13.3 (9.4-17.2)	9.1 (6.3-12.0)	16.9 (12.4-21.3)
Sondrio	1.8 (1.0-2.7)	13.3 (10.2-16.3)	14.5 (11.6-17.5)	21.4 (17.3-25.5)
South Tyrol	2.6 (1.9-3.3)	10.6 (8.8-12.4)	10.8 (9.2-12.4)	17.4 (15.1-19.7)
Trentino	2.7 (2.0-3.4)	12.8 (11.0-14.6)	13.6 (11.9-15.3)	17.4 (15.2-19.5)
Veneto	1.4 (0.7-2.1)	9.6 (7.4-11.8)	10.5 (8.5-12.5)	17.0 (14.1-19.9)
Slovenia	2.5 (2.1-2.9)	13.0 (11.7-14.4)	11.7 (10.8-12.6)	25.7 (23.8-27.7)
Graubünden/Glarus	2.1 (1.2-3.1)	8.4 (6.2-10.5)	12.6 (10.1-15.1)	16.2 (13.1-19.3)
St.Gallen/Appenzell	2.9 (2.1-3.6)	7.2 (5.8-8.6)	10.5 (8.9-12.0)	16.6 (14.5-18.8)
Ticino	2.0 (1.2-2.7)	9.3 (7.5-11.2)	10.8 (9.0-12.6)	18.0 (15.3-20.7)
Total	2.2 (2-2.4)	9.5 (9.0-10.0)	11.2 (10.7-11.6)	18.2 (17.6-18.9)

Carinthia

1	Bad Kleinkirchheim
2	Ebene Reichenau – Oberes Gurktal
3	Feldkirchen – Glantal
4	Gailtal – Lesachtal
5	Gegendtal
6	Glantal – Wimitz
7	Gurktal
8	Görtschitztal
9	Jauntal
10	Klagenfurt Land-Ost
11	Klagenfurt Stadt
12	St. Veit an der Glan – Krappfeld – Zollfeld
13	Lieser- und Maltatal
14	Metnitztal
15	Oberes Drautal
16	Wolfsberg – Oberes Lavanttal
17	Oberes Mölltal
18	Rosental Ost
19	Rosental West
20	Sattnitz West
21	Spittal – Millstättersee
22	Unteres Drautal
23	Unteres Gailtal
24	Unteres Lavanttal
25	Unteres Mölltal
26	Villach Stadt
27	Völkermarkt – Unteres Drautal
28	Wörthersee Ost
29	Wörthersee West

Salzburg

30	Bischofshofen und Pongau Nord
31	Flachgau Nord/West
32	Flachgau Süd/Ost
33	Hallein Umgebung
34	Lungau
35	Oberpinzgau
36	Saalfelden Umgebung
37	Schwarzach und Pongau Süd
38	St.Johann und Pongau Ost
39	Stadt Salzburg
40	Tennengau ohne Hallein Umgebung
41	Zell am See und Pinzgau Süd/Ost

Tyrol

42	Brixental
43	Brixlegg und Umgebung
44	Hall und Umgebung
45	Hinteres Zillertal
46	Imst Umgebung und Pitztal
47	Jenbach und Umgebung
48	Kematen und Sellrain
49	Kitzbühel und Umgebung
50	Kufstein und Umgebung
51	Landeck und Umgebung
52	Landeshauptstadt Innsbruck
53	Lechtal, Tannheimertal
54	Lienz und Umgebung
55	Matrei i.O., Kals, Defereggen
56	Oberes/Oberstes Gericht, Sonnenterrasse
57	Reutte und Umgebung
58	Rietz bis Roppen
59	Salzstraße und Seefeld
60	Schwaz und Umgebung
61	Sillian und Umgebung
62	St. Johann, Pillersee, Söll
63	Stanzertal, Paznaun
64	Stubaital
65	Südöstliches Mittelgebirge
66	Telfs und Mieminger Plateau
67	Untere Schranne und Kössen
68	Vorderes Zillertal
69	Wattens und Umgebung
70	Westliches Mittelgebirge
71	Wipptal
72	Wörgl und Wildschönau
73	Ötztal

Vorarlberg

74	Bregenz
75	Dornbirn
76	Feldkirch
77	Grosses Walsertal Umgebung
78	Hinterer Bregenzerwald /Kleines Walsertal
79	Hofsteig
80	Hohenems
81	Klostertal/Bludenz
82	Leiblachtal
83	Lustenems
84	Mittlerer Bregenzerwald
85	Montafon
86	Rheindelta
87	Rheintal Oberland
88	Rheintal Unterland
89	Vorderer Bregenzer Wald
90	Walgau SüdOst
91	Walgau West

St. Gallen – Appenzell

92	Appenzell I.Rh.
93	Bezirk Alttoggenburg
94	Bezirk Gaster
95	Bezirk Gossau
96	Bezirk Hinterland
97	Bezirk Mittelland
98	Bezirk Neutoggenburg
99	Bezirk Oberrheintal
100	Bezirk Obertoggenburg
101	Bezirk Rorschach
102	Bezirk Sargans
103	Bezirk See
104	Bezirk St. Gallen
105	Bezirk Unterrheintal
106	Bezirk Untertoggenburg
107	Bezirk Vorderland
108	Bezirk Werdenberg
109	Bezirk Wil

Graubunden – Glarus

110	Bernina
111	Bezirk Albula
112	Bezirk Glenner
113	Bezirk Heinzenberg
114	Bezirk Hinterrhein
115	Bezirk Imboden
116	Bezirk Inn
117	Bezirk Maloja
118	Bezirk Oberlandquart
119	Bezirk Plessur
120	Bezirk Unterlandquart
121	Bezirk Val Müstair
122	Bezirk Vorderrhein
123	Glarus
124	Moësa

Ticino

125	Bellinzona
126	Blenio
127	Leventina
128	Locarno
129	Lugano
130	Mendrisio
131	Riviera
132	Vallemaggia

Varese

133	Comunità Montana Valceresio
134	Comunità Montana Valli del Luinese
135	Comunità Montana della Valcuvia
136	Comunità Montana della Valganna e Valmarchirolo

Sondrio

137	Bormio
138	Chiavenna
139	Morbegno
140	Sondrio
141	Tirano

South Tyrol

142	Alta Val Pusteria/Hochpustertal
143	Alta Val Venosta/Oberer Vinschgau
144	Alta Valle Isarco/Oberes Eisacktal
145	Bassa Atesina/Unterland
146	Bolzano/Bozen
147	Bressanone-circondario/Brixen-Umgebung
148	Brunico-circondario/Bruneck-Umgebung
149	Chiusa-circondario/Klausen-Umgebung
150	Laives-Bronzolo-Vadena/Leifers-Branzoll-Pfatten
151	Lana-circondario/Lana-Umgebung
152	Media Val Venosta/Mittlerer Vinschgau
153	Merano-circondario/Meran-Umgebung
154	Naturno-circondario/Naturns-Umgebung
155	Oltradige/Überetsch
156	Salto-Val Sarentino-Renon/Salten-Sarntal-Ritten
157	Tures-Aurina/Tauferer Ahrntal
158	Val Badia/Gadertal
159	Val Gardena/Grödental
160	Val Passiria/Passeiertal
161	Val d'Ega-Sciliar/Eggental-Schlern

Trentino

162	Alta Valsugana
163	Alto Garda e Ledro
164	Bassa Valsugana e Tesino
165	Fiemme
166	Giudicarie e Rendena
167	Ladino di Fassa
168	Primiero
169	Vallagarina
170	Valle dell'Adige
171	Valle di Non
172	Valle di Sole

Veneto

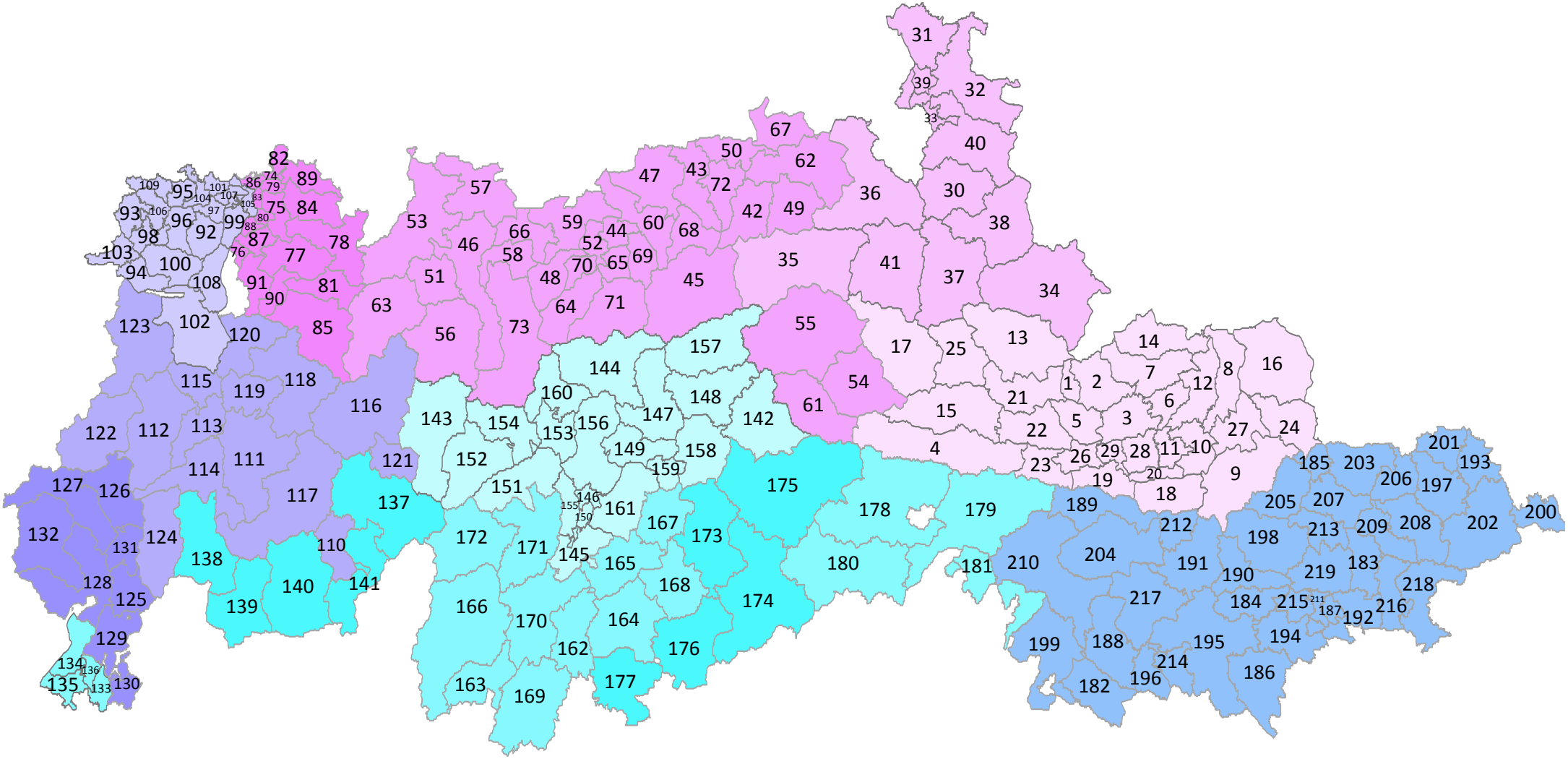
173	Agordo
174	Belluno
175	Cadore
176	Feltre
177	Sette Comuni

Friuli Venezia Giulia

178	District Carnia
179	District Gemonese & Sandanielese
180	District Pordenone Nord
181	District Tarcentino & Cividalese

Slovenia

182	Ajdovščina
183	Celje
184	Domžale
185	Dravograd
186	Grosuplje
187	Hrastnik
188	Idrija
189	Jesenice
190	Kamnik
191	Kranj
192	Laško
193	Lenart
194	Litija
195	Ljubljana
196	Logatec
197	Maribor
198	Mozirje
199	Nova Gorica
200	Ormož
201	Pesnica
202	Ptuj
203	Radlje ob Dravi
204	Radovljica
205	Ravne na Koroškem
206	Ruše
207	Slovenj Gradec
208	Slovenska Bistrica
209	Slovenske Konjice
210	Tolmin
211	Trbovlje
212	Tržic
213	Velenje
214	Vrhnika
215	Zagorje ob Savi
216	Šentjur pri Celju
217	Škofja Loka
218	Šmarje pri Jelšah
219	Žalec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